BIOL 130: HUMAN BIOLOGY



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BIOL 130 - Human Biology

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Licensing

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PREFACE AND ACKNOWLEDGMENTS

DEDICATION

This book is dedicated to the students of Butte College and worldwide. The Biology Department faculty at Butte College have created this book as part of our effort to help make education more affordable. Our goal was to create a book that helps students understand how human systems function and how humans fit into the world around us.

In a few chapters, we have incorporated more inclusive gender-neutral pronouns, such as singular they/their/them. Around 1795, the language authorities Lindley Murray, Joseph Priestly, and Hugh Blair, amongst others, campaigned against pronoun irregularities in pronoun use, such as lack of agreement in gender and number. Without coining words, this can only be done in the third-person singular by use of compound terms like “his or her”. Grammarians in 1879, 1922, 1931, 1957, and the 1970s have accepted “they” as a singular term that could be used in place of “he” or “he or she,” though sometimes limiting it to informal constructions. Others in 1795, 1825, 1863, 1898, 1926, and 1982 argued against it for various reasons. And whatever the grammarians might argue, people have been using the singular “they” for about the last 600 years, though (as mentioned earlier) it can only be applied in certain cases. If new gender-neutral pronouns are not adopted, we are sure that singular “they” will still be a point of contention for centuries to come. For further information on the use of singular “they/them/their” throughout the centuries, see the large body of information that Henry Churchyard has compiled on this subject (LGBTQ+ Resource center; July 2020).

We wish the very best for all our students as they move forward in their goals!

Reference: Gender Pronouns; Lesbian, Gay, Bisexual, Transgender, Queer Plus (LGBTQ+) Resource Center; University of Wisconsin-Milwaukee; accessed on July 8, 2020, CC BY-NC

VOCABULARY

Biology is a field that has many new vocabulary terms. These are bolded throughout the text. Students are encouraged to create flashcards or use other strategies to learn these terms. Knowing the vocabulary terms in a chapter will help make the content easier to understand.

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Suzanne Wakim has designed and developed over a dozen biology courses including five online courses. She has helped write numerous textbooks and learning ancillaries, including content for Nature, Discovery Education, Carnegie Mellon's Open Learning Initiative and OpenStax. She has presented on topics such as: Universal Design for Learning; Open Pedagogy for Equity-Minded Course Development; and Learning Apps for Increased Student Engagement. Her current roles include Open Educational Resources Coordinator, Distance Education Coordinator, Student Learning Outcomes Coordinator, Biology and Honors Faculty at Butte College.



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Mandeep has been teaching since 2008. She started teaching at California State University, Chico, where she co-authored the principles of animal and plant physiology laboratory manuals. When she taught at Yuba College, she co-authored a human anatomy lab manual that contains lab instructions, worksheets, study guides, and competencies. Currently, she is working full time at Butte College. In her human biology course, she teaches with open pedagogy using Wikipedia editing assignments. She is a recipient of the Academic Senate of California Community College Open Educational Resources Initiative (ASCCC OERI) grant. As part of this grant, she has co-curated and published this human biology textbook. This textbook is also available as a Canvas shell which incorporates chapter-specific homework, answers to the review questions, worksheets, assignments, activities, and a quiz bank for each section.



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CHAPTER OVERVIEW

1: INTRODUCTION TO HUMAN BIOLOGY

This chapter introduces the human species. It identifies traits we share with all other living things and basic principles of biology that apply to us as well as to all other life. The chapter also describes the diversity of species on Earth, similarities we share with our closest relatives in the animal kingdom, and traits that make us unique.

1.1: Case Study- Why Should You Study Human Biology?

1.2: Shared Traits of All Living Things

1.3: Diversity of Life

1.4: The Human Animal

1.5: Scientific Investigations

1.6: Case Study Conclusion- Inhabitants and Chapter Summary

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1.1: CASE STUDY- WHY SHOULD YOU STUDY HUMAN BIOLOGY?

CASE STUDY: OUR INVISIBLE INHABITANTS

Wajiha is suffering from a fever, body aches, and a painful sore throat that gets worse when she swallow. She visits her doctor who examines her and performs a throat culture. When the results come back, the doctor tells Wajiha she has strep throat, which is caused by the bacteria *Streptococcus pyogenes*. The doctor prescribes an antibiotic to kill the bacteria and advises Wajiha to take the full course of the treatment even if she is feeling better earlier because stopping early can cause an increase in bacteria that are resistant to antibiotics.



Figure **1.1.1**: being examined for a soar throat

Wajiha takes the antibiotic as prescribed. Towards the end of the course, her throat is feeling much better but she can't say the same for other parts of her body! She has developed diarrhea and an itchy vaginal yeast infection. Wajiha calls her doctor, who suspects that the antibiotic treatment has caused both her digestive distress and her yeast infection. The doctor explains that our bodies are home to many different kinds of microorganisms, some of which are actually beneficial to our bodies by helping us digest our food or keeping the population of harmful microorganisms down. When we take an antibiotic, many of these "good" bacteria are killed along with the "bad" disease-causing bacteria, which can result in diarrhea and yeast infections.

The doctor prescribes an antifungal medication for Wajiha's yeast infection. The doctor also recommends that Wajiha eat yogurt with "live cultures" to try to help replace the beneficial bacteria in her gut. Clearly, our bodies contain a delicate balance of inhabitants that are invisible without a microscope, and changes in that balance can cause unpleasant health effects.

WHAT IS HUMAN BIOLOGY?

As you read the rest of this book, you'll learn more amazing facts about the human organism and how biology relates to your health. **Human biology** is the scientific study of the human species that includes the fascinating story of human evolution and a detailed accounting of our genetics, anatomy, physiology, and ecology. In short, human biology focuses on how we got here, how we function, and the role we play in the natural world. Importantly, this helps us to better understand human health – how to stay healthy and how diseases and injuries can be treated. This is probably of personal interest to you in terms of your own health and the health of your friends and family, and also has broader implications for society and the human species as a whole.

As you read this book, think about what you want to learn about your own human body. What questions or concerns do you have? Make a list of them and use the list to guide your study of human biology. You can revisit the list throughout the course to see if your questions have been answered. If not, you'll have the tools to find the answers. You will have learned how to find sources of information about human biology and how to judge which sources are most reliable.

CHAPTER OVERVIEW: INTRODUCTION TO HUMAN BIOLOGY

In the rest of this chapter, you'll learn about the traits shared by all living things, the basic principles that underlie all of biology, the vast diversity of living organisms, what it means to be human, and our place in the animal kingdom. Specifically, you'll learn:

- The seven traits shared by all living things including the maintenance of a more-or-less constant internal environment, called homeostasis; multiple levels of organization consisting of one or more cells; using energy and exhibiting metabolism; the ability to grow and develop; the ability to evolve adaptations to the environment; the ability to detect and respond to environmental stimuli; and the ability to reproduce.
- The diversity of life, including the different kinds of biodiversity, the definition of a species, the classification and naming systems for living organisms, and how evolutionary relationships can be represented through diagrams such as phylogenetic trees.
- How the human species is classified, our close relatives and ancestors, and some ways in which we evolved.
- The traits humans share with other primates including physical characteristics and social behaviors.

As you read this chapter, think about the following questions about Wajiha's situation:

1. What do single-celled organisms, such as the bacteria and yeast living in and on Wajiha, have in common with humans?
2. How are bacteria, yeast (a fungus), and humans classified?
3. How do the concepts of homeostasis and biodiversity apply to Wajiha's situation?
4. Why can stopping antibiotics early cause the development of antibiotic-resistant bacteria?

ATTRIBUTIONS

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1.2: SHARED TRAITS OF ALL LIVING THINGS

THE THINKER

You've probably seen this famous statue created by the French sculptor Auguste Rodin. Rodin's skill as a sculptor is evident because the statue looks so lifelike. In fact, the statue is made of rock so its only resemblance to life is how it appears. How does a statue made of rock differ from a living, breathing human being or other living organisms? What is life? What does it mean to be alive? Science has answers to these questions.

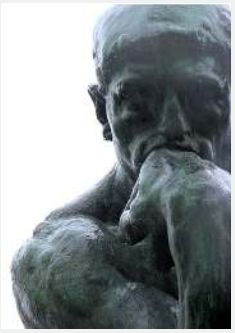


Figure **1.2.1**: The Thinker at Musée Rodin, Paris

CHARACTERISTICS OF LIVING THINGS

To be classified as a living thing, most scientists agree that an object must have all seven of the following traits. These are traits that human beings share with other living things.

1. homeostasis
2. organization
3. metabolism
4. growth
5. adaptation
6. response to stimuli
7. reproduction

HOMEOSTASIS

All living things are able to maintain a more-or-less constant internal environment. They keep things relatively stable on the inside regardless of the conditions around them. The condition in which a system is maintained in a more-or-less steady state is called **homeostasis.** Human beings, for example, maintain stable internal body temperature. If you go outside when the air temperature is below freezing, your body doesn't freeze. Instead, by shivering and other means, it maintains a stable internal temperature.

ORGANIZATION

Living things have multiple levels of organization. Their molecules are organized into one or more cells. A **cell** is the basic unit of the structure and function of living things. Cells are the building blocks of living organisms. An average adult human being, for example, consists of trillions of cells. Living things may appear very different from one another on the outside, but their cells are very similar. Compare the human cells and onion cells in the figure below. What similarities do you see?

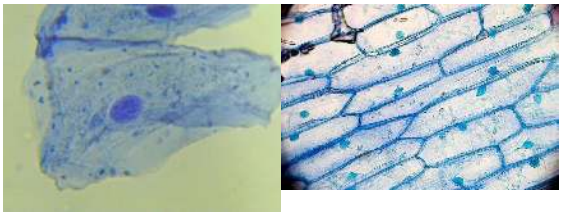


Figure **1.2.2**: A human cell (right) is flake-shaped; the nucleus is visible as a blue sphere in the center of the cell. Onion cells (left) are organized like bricks in a wall. The nucleus of each onion cell is visible as a blue sphere on the edge of the cell.

METABOLISM

All living things can use energy. Their cells have the "machinery" of **metabolism,** which is the building up and breaking down of chemical compounds. Living things can transform energy by converting chemicals and energy into cellular components. This form of metabolism is called **anabolism**. They can also break down, or decompose, organic matter, which is called **catabolism**. Living things require energy to maintain internal conditions (homeostasis), for growth, and other life processes.

GROWTH

All living things have the capacity for growth. Growth is an increase in size that occurs when there is a higher rate of anabolism than catabolism. For example, a human infant has changed dramatically in size by the time it reaches adulthood, as is apparent from the image below. In what other ways do we change as we grow from infancy to adulthood?



Figure **1.2.3**: A human infant has a lot of growing to do before adulthood.

ADAPTATIONS AND EVOLUTION

An **adaptation** is a characteristic of populations. Individuals of a population carry a variety of genes. When the environment changes, some individuals of the population can withstand the changed conditions and reproduce more than the individuals who cannot live in the given environment. A change in the allele frequencies and makeup of the populations over time is called **evolution.** It comes about through the process of natural selection.

RESPONSE TO STIMULI

All living things detect changes in their environment and respond to them. A response can take many forms, from the movement of a unicellular organism in response to external chemicals (called chemotaxis), to complex reactions involving all the senses of a multicellular organism. A response is often expressed by motion; for example, the leaves of a plant turning toward the sun (called phototropism).

REPRODUCTION

All living things are capable of reproduction. **Reproduction** is the process by which living things give rise to offspring. Reproduction may be as simple as a single cell dividing into two cells. This is how bacteria reproduce. Reproduction in human beings and many other organisms is much more complicated. Nonetheless, whether a living thing is a human being or a bacterium, it is normally capable of reproduction.

FEATURE: MYTH VS. REALITY

Myth: Viruses are living things.

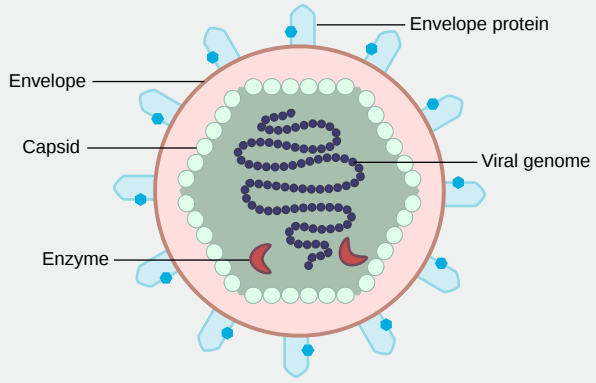


Figure **1.2.4**: Diagram of a general virus. The capsid encloses the genetic material of the virus. The envelope which surrounds the capsid is typically made from portions of the host cell membranes (phospholipids and proteins). Not all viruses have a viral envelope. Some viruses contain other proteins and enzymes

Reality: The traditional scientific view of viruses is that they originated from bits of DNA or RNA that were shed from the cells of living things but that they are not living things themselves. Scientists have long argued that viruses are not living things because they do not have most of the defining traits of living organisms. A single virus called a virion, consists of a set of genes (DNA or RNA) inside a protective protein coat, called a capsid. Viruses have an organization, but they are not cells and do not possess the cellular "machinery" that living things use to carry out life processes. As a result, viruses cannot undertake metabolism, maintain homeostasis, or grow. They do not seem to respond to their environment, and they can reproduce only by invading and using "tools" inside host cells to produce more virions. The only traits viruses seem to share with living things is the ability to evolve adaptations to their environment. In fact, some viruses evolve so quickly that it is difficult to design drugs and vaccines against them. That's why maintaining protection from the viral disease influenza, for example, requires a new flu vaccine each year.

Within the last decade, new discoveries in virology, the study of viruses, suggest that this traditional view about viruses may be incorrect and the "myth" that viruses are living things may be the reality. Researchers have discovered giant viruses that contain more genes than cellular life forms such as bacteria. Some of the genes code for proteins needed to build new viruses, suggesting that these giant viruses may be able — or were once able — to reproduce without a host cell. Some of the strongest evidence that viruses are living things comes from studies of their proteins, which show that viruses and cellular life share a common ancestor in the distant past. Viruses may have once existed as primitive cells but at some point lost their cellular nature to become modern viruses that require host cells to reproduce. This idea is not so far-fetched when you consider that many other species require a host to complete their life cycle.

REVIEW

1. Identify seven traits that most scientists agree are shared by all living things.
2. What is homeostasis? What is one way humans fulfill this criterion of living things?
3. Define reproduction, and describe an example.
4. Assume that you found an object that looks like a dead twig. You wonder if it might be a stick insect. How could you determine if it is a living thing?
5. Describe viruses and what traits they do and do not share with living things. Do you think viruses should be considered living things? Why or why not?
6. People who are biologically unable to reproduce are certainly still considered to be alive! Discuss why this situation does not invalidate the criteria that living things must be capable of reproduction.
7. What are the two types of metabolism described here and what are their differences?
8. What are some similarities between cells of different organisms? If you are not familiar with the specifics of cells, simply describe the similarities you see in the pictures above.
9. What are two processes that use energy in a living thing?
10. Give an example of a response to stimuli in humans.
11. Do unicellular organisms, such as bacteria, have an internal environment that they maintain through homeostasis?
12. Evolution occurs through _____ _____ .
13. If alien life is found on other planets, do you think they will necessarily have cells? Discuss your answer.
14. Movement in response to an external chemical is called _____, while movement towards light is called _____ .

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1.3: DIVERSITY OF LIFE

SO MANY SPECIES!

The collage below shows six kingdoms into which all of Earth's living things are commonly classified. How many species are there in each kingdom? In a word, millions. A total of almost 2 million living species have already been identified, and new species are being discovered all the time. Scientists estimate that there may be as many as 30 million different species alive on Earth today! Clearly, there is a tremendous variety of life on Earth.

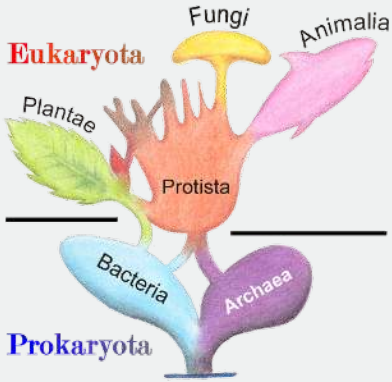


Figure **1.3.1**: Six kingdoms of life: Archaea, Bacteria, Protista, Fungi, Animalia, and Plantae

WHAT IS BIODIVERSITY?

Biological diversity, or **biodiversity**, refers to all of the variety of life that exists on Earth. Biodiversity can be described and measured at three different levels: species, genetic, and ecosystem diversity.

- Species diversity refers to the number of different species in an ecosystem or on Earth as a whole. This is the commonest way to measure biodiversity. Current estimates for Earth's total number of living species range from 5 to 30 million species.
- Genetic diversity refers to the variation in genes within all these species.
- Ecosystem diversity refers to the variety of ecosystems on Earth. An ecosystem is a system formed by populations of many different species interacting with each other and their environment.

DEFINING A SPECIES

Biodiversity is most often measured by counting species, but what is a species? The answer to that question is not as straightforward as you might think. The formal biological definition of **species** is a group of actually or potentially interbreeding organisms. This means that members of the same species are similar enough to each other to produce fertile offspring together. By this definition of species, all human beings alive today belong to one species, *Homo sapiens*. All humans can potentially interbreed with each other but not with members of any other species.

In the real world, it isn't always possible to make the observations needed to determine whether different organisms can interbreed. For one thing, many species reproduce asexually, so individuals never interbreed even with members of their own species. When studying extinct species represented by fossils, it is usually impossible to know whether different organisms could interbreed. Therefore, in practice, many biologists and virtually all paleontologists generally define species on the basis of morphology, rather than breeding behavior. **Morphology** refers to the form and structure of organisms. For classification purposes, it generally refers to relatively obvious physical traits. Typically, the more similar to one another different organisms appear, the greater the chance that they will be classified in the same species.

CLASSIFYING LIVING THINGS

People have been trying to classify the tremendous diversity of life on Earth for more than two thousand years. The science of classifying organisms is called **taxonomy.** Classification is an important step in understanding the present diversity and past evolutionary history of life on Earth. It helps make sense of the overwhelming diversity of living things.

LINNAEAN CLASSIFICATION

All modern classification systems have their roots in the Linnaean classification system. It was developed by Swedish botanist Carolus Linnaeus in the 1700s. He tried to classify all living things that were known at his time. He grouped together organisms that shared obvious morphological traits, such as the number of legs or shape of leaves.

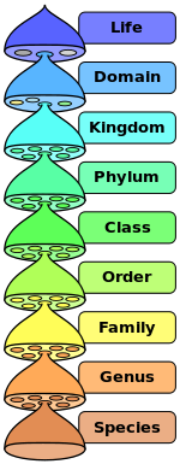


Figure **1.3.2**: Classification of life into smaller subcategories: Domain, Kingdom, phylum, class, order, family, genus, species.

The Linnaean system of classification consists of a hierarchy of groupings, called taxa (singular, taxon). Figure **1.3.2** shows an expanded version of Linnaeus's original classification system. In the original system, taxa range from the kingdom to the species. The kingdom is the largest and most inclusive grouping. It consists of organisms that share just a few basic similarities. Examples are the

plant and animal kingdoms. The species is the smallest and most exclusive grouping. Ideally, it consists of organisms that are similar enough to interbreed, as discussed above. Similar species are classified together in the same genus (plural, genera), similar genera are classified together in the same family, and so on all the way up to the kingdom.

BINOMIAL NOMENCLATURE

Perhaps the single greatest contribution Linnaeus made to science was his method of naming species. This method, called **binomial nomenclature,** gives each species a unique, two-word Latin name consisting of the genus name followed by a specific species identifier. An example is *Homo sapiens*, the two-word Latin name for humans. It literally means "wise human." This is a reference to our big brains.

Why is having two names so important? It is similar to people having a first and a last name. You may know several people with the first name Michael, but adding Michael's last name usually pins down exactly who you mean. In the same way, having two names uniquely identifies a species.

REVISIONS IN THE LINNAEAN CLASSIFICATION

Linnaeus published his classification system in the 1700s. Since then, many new species have been discovered. Scientists can also now classify organisms on the basis of their biochemical and genetic similarities and differences rather than just their outward morphology. These changes have led to revisions in the original Linnaean system of classification.

A major change to the Linnaean system is the addition of a new taxon called the domain. The **domain** is a taxon that is larger and more inclusive than the kingdom, as shown in Figure **1.3.2**. Most biologists agree that there are three domains of life on Earth: Bacteria, Archaea, and Eukarya (Figure **1.3.3**). Both the Bacteria and the Archaea domains consist of single-celled organisms that lack a nucleus. This means that their genetic material is not enclosed within a membrane inside the cell. The Eukarya domain, in contrast, consists of all organisms whose cells have a nucleus. In other words, their genetic material is enclosed within a membrane inside the cell. The Eukarya domain is made up of both single-celled and multicellular organisms. This domain includes several kingdoms, including the animal, plant, fungus, and protist kingdoms.

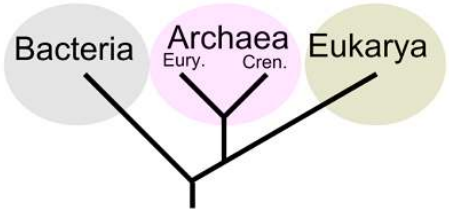


Figure **1.3.3**: Three domains of life: Bacteria, Archaea, and Eukarya

PHYLOGENETIC CLASSIFICATION

Linnaeus classified organisms based on morphology. Basically, organisms were grouped together if they looked alike. After Darwin published his theory of evolution in the 1800s, scientists looked for a way to classify organisms that took into account phylogeny. **Phylogeny** is the evolutionary history of a group of related organisms. It is represented by a phylogenetic tree, or some other tree-like diagram, like the one in Figure **1.3.3** for the three domains. A **phylogenetic tree** shows how closely related different groups of organisms are to one another. Each branching point represents a common ancestor of the branching groups. Figure **1.3.3**, for example, shows that the Eukarya shared a more recent common ancestor with the Archaea than they did with the Bacteria. This is based on comparisons of important similarities and differences between the three domains.

REVIEW

1. What is biodiversity? Identify three ways that biodiversity may be measured.
2. Define biological species. Why is this definition often difficult to apply?
3. Explain why it is important to classify living things and outline the Linnaean system of classification.
4. What is binomial nomenclature? Give an example.
5. Contrast Linnaean and phylogenetic systems of classification.
6. Describe the taxon called the domain, and compare the three widely recognized domains of living things.
7. *True or False.* Humans have identified all of the species on Earth.
8. *True or False.* In the binomial nomenclature for humans, *Homo* is the genus and *sapiens* refers to the specific species.
9. A kingdom is a:
   A. domain
   B. taxon
   C. genera
   D. phylogeny
10. In Linnaean classification, similar classes together make up a _____ .
11. Based on the phylogenetic tree for the three domains of life above, explain whether you think Bacteria are more closely related to Archaea or Eukarya.
12. A scientist discovers a new single-celled organism. Answer the following questions about this discovery.
    A. If this is all you know, can you place the organism into a particular domain? If so, what is the domain and if not, why not?
    B. What is one type of information that could help the scientist classify the organism?
13. Define morphology. Give an example of a morphological trait in humans.
14. Which type of biodiversity is represented by the differences between humans?
15. Why do you think it is important for the definition of a species that members of a species can produce *fertile* offspring?

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1.4: THE HUMAN ANIMAL

"COUSINS"

Relative to all animals, this child and monkey are practically "cousins." From genes to morphology to behavior, they are similar in many ways. That's because both of them are primates, and they share an evolutionary past.



Figure **1.4.1**: Child and monkey

HOW HUMANS ARE CLASSIFIED

You probably know that modern humans belong to the species *Homo sapiens*. But what is our place in nature? How are our species classified? A simple classification is represented in Figure **1.4.2**. Humans can move on their own and are placed in the animal kingdom. Further, humans belong to the animal phylum known as chordates because we have a backbone. The human animal has hair and milk glands, so we are placed in the class of mammals. Within the mammal class, humans are placed in the primate order.

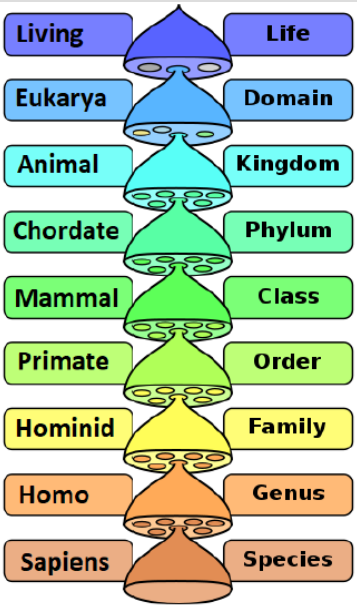


Figure **1.4.2**: This taxonomic diagram shows how our species, *Homo sapiens*, is classified. Our scientific name indicates that we are in the genus and species homo and sapiens. Our family is the hominid, within the order primate, within the class mammal, within the phylum chordate, within the kingdom animalia, within the domain Eukarya.

HUMANS AS PRIMATES

Living members of the primate order include monkeys, apes, and humans; and any member of this order of mammals is called a **primate.** At some point in the distant past, we shared ape-like ancestors with all these modern groups of primates. We share between 93 percent and almost 99 percent of our DNA sequences with them, providing hard evidence that we have relatively recent common ancestors. Besides genes, what traits do we share with other primates? Primates are considered generalists among mammals. A **generalist** is an organism that can thrive in a wide variety of environmental conditions and make use of a variety of different resources, such as consuming many different types of food. Although primates exhibit a wide range of characteristics, there are several traits that are shared by most primates.

PRIMATE TRAITS

Primates have five digits (fingers or toes) on each extremity (hand or foot). The fingers and toes have nails instead of claws and are covered with sensitive tactile pads. The thumbs (and in many species the big toes as well) are opposable, meaning they can be brought into opposition with the other digits, allowing both a power grasp and a precision grip. You can see these features of the primate extremities in the capuchin monkey pictured below.



Figure **1.4.3**: The five fingers, opposable thumb, and other primate features of the hand give this capuchin monkey great manual dexterity. This is the primary reason these primates are trained to assist quadriplegic human beings with daily tasks.

The primate body is generally semi-erect or erect, and primates have one of several modes of locomotion, including walking on all four legs (quadrupedalism), vertical clinging and leaping, swinging from branch to branch in trees (brachiation), or walking on two legs (bipedalism), the last of which applies only to our own species today. The primate shoulder girdle has a collar bone (clavicle), which is associated with a wide range of motion of the upper limbs.

Relative to other mammals, primates rely less on their sense of smell. They have a reduced snout and relatively small area in the brain for processing olfactory (odor) information. Primates rely more on their sense of vision, which shows several improvements over that of other mammals. Most primates can see in color. Primates also tend to have large eyes with forward-facing placement in a relatively flat face. This results in an overlap of the visual fields of the two eyes, allowing stereoscopic vision, or three-dimensional, vision. Other indications of the importance of vision to primates are the protection given to the eyes by a complete bony eye socket and the large size of the occipital lobe of the brain where visual information is processed.

Primates are noted for their relatively large brains, high degree of intelligence, and complex behaviors. The part of the brain that is especially enlarged in primates is the cerebrum, which analyzes and synthesizes sensory information and transforms it into motor behaviors appropriate to the environment. Primates tend to have longer lifespans than most other mammals. In particular, there is a lengthening of the prenatal period and the postnatal period of dependency of infants on adults, providing an extended opportunity for learning in juveniles. Most primates live in social groups. In fact, primates are among the most social of animals. Depending on the species, adult nonhuman primates may live in mated pairs or in groups of up to hundreds of members.

LIFE IN THE TREES

Scientists think that many primate traits are adaptations to an arboreal, or tree-dwelling, lifestyle. Primates are thought to have evolved in trees, and the majority of primates still live in trees. For life in the trees, the sense of vision trumps the sense of smell, and three-dimensional vision is especially important for grasping the next branch or limb. Having mobile limbs, a good grip, and manual dexterity are matters of life and death when one lives high above the ground. While some modern primates are mainly terrestrial (ground-dwelling) rather than arboreal, all primates possess adaptations for life in the trees.

Figure **1.4.4** shows the present distribution of nonhuman primates around the world. Tropical forests in Central and South America are home to many species of monkeys, including the capuchin monkey pictured above. Old World tropical forests in Africa and Asia are home to many other species of monkeys, including the crab-eating macaque pictured above, as well as all modern apes.



Figure **1.4.4**: This map shows the present worldwide distribution of nonhuman primates.

HUMANS AS HOMINIDS

Who are our closest relatives in the primate order? We are placed in the family called *Hominidae*. Any member of this family is called a **hominid.** Hominids include four living genera: chimpanzees, gorillas, orangutans, and humans. Among these four genera are just seven living species: two in each genera except humans, with our sole living species, *Homo sapiens.* The Orangutan mother pictured in figure **1.4.5** cradling her child shows how similar these hominids are to us.



Figure **1.4.5**: Orangutan mother and child

Hominids are relatively large, tailless primates, ranging in size from the bonobo, or pygmy chimpanzee, which may weigh as little as 30 kg (66 lb), to the eastern gorilla, which may weigh over 200 kg (440

lb). Most modern humans fall somewhere in between that range. In all species of hominids, males are somewhat larger and stronger, on average, than females, but the differences may not be great. Except for humans, hominids are mainly quadrupedal, although they can get around bipedally if need be to gather food or nesting materials. Humans are the only habitually bipedal species of living hominids.

THE HUMAN GENUS

Within the hominid family, our species is placed in the genus ***Homo.*** Our species, *Homo sapiens*, is the only living species in this genus. Several earlier species of *Homo* existed but have since gone extinct, including the species *Homo erectus.* An artist's reconstruction of a *Homo erectus* individual is shown in figure **1.4.6**.



Figure **1.4.6**: A *Homo erectus* individual, reconstructed here, shows both similarities and differences with modern *Homo sapiens*.

By about 2.8 million years ago, early *Homo* species such as *Homo erectus* were probably nearly as efficient at bipedal locomotion as modern humans. Relative to quadrupedal primates, they had a broader pelvis, longer legs, and arched feet. However, from the neck up, they were still quite different from us. They typically had bigger jaws and teeth, a sloping forehead, and a relatively small brain.

HOMO SAPIENS

During the roughly 2.8 million years of the evolution of the *Homo* genus, the remaining features of *Homo sapiens* evolved. These features include:

- small front teeth (incisors and canines) with relatively large molars, at least compared to other primates.
- a decrease in the size of the jaws and face, and an increase in the size of the cranium, forming a nearly vertical forehead.
- a tremendous enlargement of the brain, especially in the cerebrum, which is the site of higher intellectual functions.

The increase in brain size occurred very rapidly as far as evolutionary change goes, between about 800,000 and 100,000 years ago. During this period, the size of the brain increased from about 600 cm^3 to about 1400 cm^3 and the earliest *Homo sapiens* appeared. This was also a period of rapid climate change, and many scientists think that climate change was a major impetus for the evolution of a larger, more complex brain. In this view, as the environment became more unpredictable, bigger, "smarter" brains helped our ancestors survive. Paralleling the biological evolution of the brain was the development of culture and technology as behavioral adaptations for exploiting the environment. These developments, made possible by a big brain, allowed modern humans and their recent ancestors to occupy virtually the entire world and become the dominant land animals.

Our species *Homo sapiens* is the most recent iteration of the basic primate body plan. Because of our big, complex brain, we clearly have a much greater capacity for abstract thought and technological advances than any other primate, even chimpanzees who are our closest living relatives. However, it is important to recognize that in other ways, we are not as adept as other living hominids around the world. We are physically weaker than gorillas, far less agile orangutans, and arguably less well-mannered than bonobos.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Imagine squeezing through a seven-inch slit in rock to enter a completely dark cave full of lots and lots of old bones. It might sound like a nightmare to most people, but it was a necessary part of a recent exploration of human origins in South Africa as reported in the *New York Times* in September 2015. The cave and its bones were actually first discovered by spelunkers in 2013, who reported it to paleontologists. An international research project was soon launched to explore the cave. The researchers would eventually conclude that the cave was a hiding place for the dead of a previously unknown early species of *Homo*, whom they gave the name *Homo naledi*. Members of this species lived in South Africa around 2.5 to 2.8 million years ago.

Homo naledi individuals were about 5 feet tall and weighed around 100 pounds, so they probably had no trouble squeezing into the cave. Modern humans are considerably larger on average. In order to retrieve the fossilized bones from the cave, six very slender female researchers had to be found on social media. They were the only ones who could fit through the crack to access the cave. The work was difficult and dangerous but also incredibly exciting. The site constitutes one of the largest samples for any extinct early *Homo* species anywhere in the world, and the fossils represent a completely new species of that genus. The site also suggests that early members of our genus were intentionally depositing their dead in a remote place. This behavior was previously thought to be limited to later humans.

Like other early *Homo* species, *Homo naledi* exhibits a mosaic of old and modern traits. From the neck down, these early hominins were well adapted for upright walking. Their feet were virtually indistinguishable from modern human feet (see image below), and their legs were also long like ours. *Homo naledi* had relatively small front teeth but also a small brain, no larger than an average orange. Clearly, the spurt in brain growth in *Homo* did not occur in this species.



Figure **1.4.7**. The reconstructed foot bones of *H. naledi* are virtually the same as our own

Watch the news for more exciting updates about this early species of our genus. Paleotontolgists researching the cave site estimate that there are hundreds if not thousands of fossilized bones still remaining in the cave. There are sure to be many more discoveries reported in the news media about this extinct *Homo* species.

REVIEW

1. Outline how humans are classified. Name their taxa, starting with the kingdom and ending with the species.
2. List several primate traits. Explain how they are related to life in the trees.
3. What are hominids? Describe how living hominids are classified.
4. Discuss species in the genus *Homo*.
5. Relate climatic changes to the evolution of the genus *Homo* within the last million years.
6. What is the significance of the fact that we share 93 to 99 percent of our DNA sequence with other primates?
7. Which species do you think we are more likely to share a greater amount of DNA sequence with — nonprimate mammals or nonmammalian chordates? Explain your answer.
8. What is the relationship between shared DNA and shared traits?
9. Compared to other mammals, primates have a relatively small area of their brain dedicated to olfactory processing. What does this tell you about the sense of smell in primates compared to other mammals? Why?
10. The part of the brain in primates that is specially enlarged is the:
    A. cerebrum
    B. cerebellum
    C. clavicle
    D. brainstem
11. Why do you think it is interesting that nonhuman primates can use tools?
12. *True or False*. All primates are primarily quadrupedal.
13. *True or False*. *Homo erectus* was in the same family as modern humans.
14. *True or False*. Humans are superior in all ways to other primates.
15. Explain why the discovery of *Homo naledi* was exciting.

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1.5: SCIENTIFIC INVESTIGATIONS

WHAT TURNED THE WATER ORANGE?

If you were walking in the woods and saw this stream, you probably would wonder what made the water turn orange. Is the water orange because of something growing in it? Is it polluted with some kind of chemicals? To answer these questions, you might do a little research. For example, you might ask local people if they know why the water is orange, or you might try to learn more about it online. If you still haven't found answers, you could undertake a scientific investigation. In short, you could "do" science.



Figure **1.5.1**:Rio Tinto river

"DOING" SCIENCE

Science is more about doing than knowing. Scientists are always trying to learn more and gain a better understanding of the natural world. There are basic methods of gaining knowledge that is common to all of science. At the heart of science is the scientific investigation. A **scientific investigation** is a plan for asking questions and testing possible answers in order to advance scientific knowledge.

Figure **1.5.2** outlines the steps of the **scientific method.** Science textbooks often present this simple, linear "recipe" for a scientific investigation. This is an oversimplification of how science is actually done, but it does highlight the basic plan and purpose of any scientific investigation: testing ideas with evidence. We will use this flowchart to help explain the overall format for scientific inquiry.

Science is actually a complex endeavor that cannot be reduced to a single, linear sequence of steps, like the instructions on a package of cake mix. Real science is nonlinear, iterative (repetitive), creative, unpredictable, and exciting. Scientists often undertake the steps of an investigation in a different sequence, or they repeat the same steps many times as they gain more information and develop new ideas. Scientific investigations often raise new questions as old ones are answered. Successive investigations may address the same questions but at ever-deeper levels. Alternatively, an investigation might lead to an unexpected observation that sparks a new question and takes the research in a completely different direction.

Knowing how scientists "do" science can help you in your everyday life, even if you aren't a scientist. Some steps of the scientific process — such as asking questions and evaluating evidence — can be applied to answering real-life questions and solving practical problems.

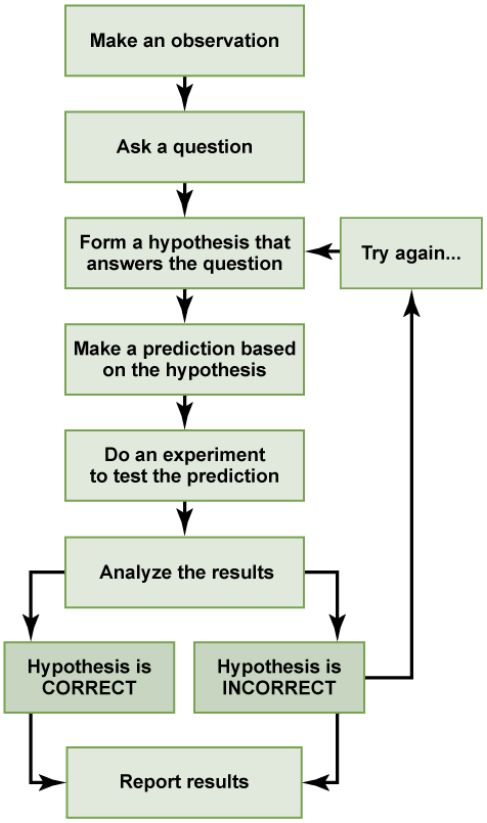


Figure **1.5.2**: The Scientific Method: The scientific method is a process for gathering data and processing information. It provides well-defined steps to standardize how scientific knowledge is gathered through a logical, rational problem-solving method. This diagram shows the steps of the scientific method, which are listed below.

MAKING OBSERVATIONS

A scientific investigation typically begins with observations. An **observation** is anything that is detected through human senses or with instruments and measuring devices that enhance human senses. We usually think of observations as things we see with our eyes, but we can also make observations with our sense of touch, smell, taste, or hearing. In addition, we can extend and improve our own senses with instruments such as thermometers and microscopes. Other instruments can be used to sense things that human senses cannot detect at all, such as ultraviolet light or radio waves.

Sometimes chance observations lead to important scientific discoveries. One such observation was made by the Scottish biologist Alexander Fleming (Figure **1.5.3**) in the 1920s. Fleming's name may sound familiar to you because he is famous for the discovery in question. Fleming had been growing a certain type of bacteria on glass plates in his lab when he noticed that one of the plates had been contaminated with mold. On closer examination, Fleming observed that the area around the mold was free of bacteria.

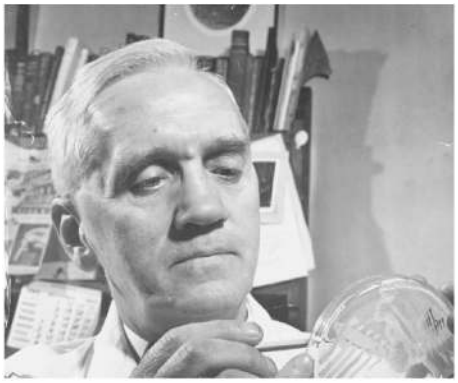


Figure **1.5.3**: Alexander Fleming experimenting with penicillin and bacteria in his lab in the 1940s.

ASKING QUESTIONS

Observations often lead to interesting questions. This is especially true if the observer is thinking like a scientist. Having scientific training and knowledge is also useful. Relevant background knowledge and logical thinking help make sense of observations so the observer can form particularly salient questions. Fleming, for example, wondered whether the mold — or some substance it produced — had killed bacteria on the plate. Fortunately for us, Fleming didn't just throw out the mold-contaminated plate. Instead, he investigated his question and in so doing, discovered the antibiotic penicillin.

HYPOTHESIS FORMATION

To find the answer to a question, the next step in a scientific investigation typically is to form a hypothesis. A **hypothesis** is a possible answer to a scientific question. But it isn't just any answer. A hypothesis must be based on scientific knowledge. In other words, it shouldn't be at odds with what is already known about the natural world. A hypothesis also must be logical, and it is beneficial if the hypothesis is relatively simple. In addition, to be useful in science, a hypothesis must be testable and falsifiable. In other words, it must be possible to subject the hypothesis to a test that generates evidence for or against it, and it must be possible to make observations that would disprove the hypothesis if it really is false.

A hypothesis is often expressed in the form of prediction: If the hypothesis is true, then B will happen to the **dependent variable**. Fleming's hypothesis might have been: "If a certain type of mold is introduced to a particular kind of bacteria growing on a plate, the bacteria will die." Is this a good and useful hypothesis? The hypothesis is logical and based directly on observations. The hypothesis is also simple, involving just one type each of mold and bacteria growing on a glass plate. This makes it easy to test. In addition, the hypothesis is falsifiable. If bacteria were to grow in the presence of the mold, it would disprove the hypothesis if it really is false.

HYPOTHESIS TESTING

Hypothesis testing is at the heart of a scientific investigation. How would Fleming test his hypothesis? He would gather relevant data as evidence. **Evidence** is any type of data that may be used to test a hypothesis. **Data** (singular, datum) are essentially just observations. The observations may be measurements in an experiment or just something the researcher notices. Testing a hypothesis then involves using the data to answer two basic questions:

1. If my hypothesis is true, what would I expect to observe?
2. Does what I actually observe match what predicted?

A hypothesis is supported if the actual observations (data) match the expected observations. A hypothesis is refuted if the actual observations differ from the expected observations.

TESTING FLEMING'S HYPOTHESIS

To test his hypothesis that the mold kills bacteria, Fleming grew colonies of bacteria on several glass plates and introduced mold to just some of the plates. He subjected all of the plates to the same conditions except for the introduction of mold. Any differences in the growth of bacteria on the two groups of plates could then be reasonably attributed to the presence/absence of mold. Fleming's data might have included actual measurements of bacterial colony size, like the data shown in the data table below, or they might have been just an indication of the presence or absence of bacteria growing near the mold. Data like the former, which can be expressed numerically, are called **quantitative data.** Data like the latter, which can only be expressed in words, such as present or absent, are called **qualitative data.**

Table **1.5.1**: Hypothetical data of bacterial growth on plates with and without mold introduction.

Bacterial Plate Identification Number	Introduction of Mold to Plate?	Total Area of Bacterial Growth on Plate after 1 Week (mm^2)
1	yes	48
2	yes	57
3	yes	54
4	yes	59
5	yes	62
6	no	66
7	no	75
8	no	71
9	no	69
10	no	68

ANALYZING AND INTERPRETING DATA

The data scientists gather in their investigations are raw data. These are the actual measurements or other observations that are made in an investigation, like the measurements of bacterial growth shown in the data table above. Raw data usually must be analyzed and interpreted before they become evidence to test a hypothesis. To make sense of raw data and decide whether they support a hypothesis, scientists generally use statistics.

There are two basic types of statistics: descriptive statistics and inferential statistics. Both types are important in scientific investigations.

- **Descriptive statistics** describe and summarize the data. They include values such as the mean, or average, value in the data. Another basic descriptive statistic is the standard deviation, which gives an idea of the spread of data values around the mean value. Descriptive statistics make it easier to use and discuss the data and also to spot trends or patterns in the data.
- **Inferential statistics** help interpret data to test hypotheses. They determine how likely it is that the actual results obtained in an investigation occurred just by chance rather than for the reason posited by the hypothesis. For example, if inferential statistics show that the results of an investigation would happen by chance only 5 percent of the time, then the hypothesis has a 95 percent chance of being correctly supported by the results. An example of a statistical hypothesis test is a t-test. It can be used to compare the mean value of the actual data with the expected value predicted by the hypothesis. Alternatively, a t-test can be used to compare the mean value of one group of data with the mean value of another group to determine whether the mean values are significantly different or just different by chance.

Assume that Fleming obtained the raw data shown in the data table above. We could use a descriptive statistic such as the mean area of bacterial growth to describe the raw data. Based on these data, the mean area of bacterial growth for plates with mold is 56 mm^2, and the mean area for plates without mold is 69 mm^2. Is this difference in bacterial growth significant? In other words, does it provide convincing evidence that bacteria are killed by the mold or something produced by the mold? Or could the difference in mean values between the two groups of plates be due to chance alone? What is the likelihood that this outcome could have occurred even if mold or one of its products does not kill bacteria? A t-test could be done to answer this question. The p-value for the t-test analysis of the data above is less than 0.05. This means that one can say with 95% confidence that the means of the above data are statistically different.

DRAWING CONCLUSIONS

A statistical analysis of Fleming's evidence showed that it did indeed support his hypothesis. Does this mean that the hypothesis is true? No, not necessarily. That's because a hypothesis can never be proven conclusively to be true. Scientists can never examine all of the possible evidence, and someday evidence might be found that disproves the hypothesis. In addition, other hypotheses, as yet unformed, may be supported by the same evidence. For example, in Fleming's investigation, something else introduced onto the plates with the mold might have been responsible for the death of the bacteria. Although a hypothesis cannot be proven true without a shadow of a doubt, the more evidence that supports a hypothesis, the more likely the hypothesis is to be correct. Similarly, the better the match between actual observations and expected observations, the more likely a hypothesis is to be true.

Many times, competing hypotheses are supported by evidence. When that occurs, how do scientists conclude which hypothesis is better? There are several criteria that may be used to judge competing hypotheses. For example, scientists are more likely to accept a hypothesis that:

- explains a wider variety of observations.
- explains observations that were previously unexplained.
- generates more expectations and is thus more testable.
- is more consistent with well-established theories.
- is more parsimonious, that is, is a simpler and less convoluted explanation.

CORRELATION-CAUSATION FALLACY

Many statistical tests used in scientific research calculate correlations between variables. Correlation refers to how closely related two data sets are, which may be a useful starting point for further investigation. However, correlation is also one of the most misused types of evidence, primarily because of the logical fallacy that correlation implies causation. In reality, just because two variables are correlated does not necessarily mean that either variable causes the other.

A simple example can be used to demonstrate the correlation-causation fallacy. Assume a study found that both ice cream sales and burglaries are correlated; that is, rates of both events increase together. If correlation really did imply causation, then you could conclude that ice cream sales cause burglaries or vice versa. It is more likely, however, that a third variable, such as the weather, influences rates of both ice cream sales and burglaries. Both might increase when the weather is sunny.

An actual example of the correlation-causation fallacy occurred during the latter half of the 20th century. Numerous studies showed that women taking hormone replacement therapy (HRT) to treat menopausal symptoms also had a lower-than-average incidence of coronary heart disease (CHD). This correlation was misinterpreted as evidence that HRT protects women against CHD. Subsequent studies that controlled other factors related to CHD disproved this presumed causal connection. The studies found that women taking HRT were more likely to come from higher socio-economic groups, with better-than-average diets and exercise regimens. Rather than HRT causing lower CHD incidence, these studies concluded that HRT and lower CHD were both effects of higher socioeconomic status and related lifestyle factors.

COMMUNICATING RESULTS

The last step in a scientific investigation is communicating the results to other scientists. This is a very important step because it allows other scientists to try to repeat the investigation and see if they can produce the same results. If other researchers get the same results, it adds support to the hypothesis. If they get different results, it may disprove the hypothesis. When scientists communicate their results, they should describe their methods and point out any possible problems with the investigation. This allows other researchers to identify any flaws in the method or think of ways to avoid possible problems in future studies.

Repeating a scientific investigation and reproducing the same results is called **replication**. It is a cornerstone of scientific research.

Replication is not required for every investigation in science, but it is highly recommended for those that produce surprising or particularly consequential results. In some scientific fields, scientists routinely try to replicate their own investigations to ensure the reproducibility of the results before they communicate them.

Scientists may communicate their results in a variety of ways. The most rigorous way is to write up the investigation and results in the form of an article and submit it to a peer-reviewed scientific journal for publication. The editor of the journal provides copies of the article to several other scientists who work in the same field. These are the peers in the peer-review process. The reviewers study the article and tell the editor whether they think it should be published, based on the validity of the methods and significance of the study. The article may be rejected outright, or it may be accepted, either as is or with revisions. Only articles that meet high scientific standards are ultimately published.

REVIEW

1. Outline the steps of a typical scientific investigation.
2. What is a scientific hypothesis? What characteristics must a hypothesis have to be useful in science?
3. Explain how you could do a scientific investigation to answer this question: Which of the following surfaces in my home has the most bacteria: the house phone, TV remote, bathroom sink faucet, or outside door handle? Form a hypothesis and state what results would support it and what results would refute it.
4. Use the Table **1.5.1** above that shows data on the effect of mold on bacterial growth to answer the following questions
   A. Look at the areas of bacterial growth for the plates in just one group – either with mold (plates 1-5) or without mold (plates 6-10). Is there a variation within the group? What do you think could be possible sources of variation within the group?
   B. Compare the area of bacterial growth for plate 1 vs. plate 7. Does this appear to be more of a difference between the mold group vs. the no mold group than if you compared plate 5 vs. plate 6? Using these differences among the individual data points, explain why it is important to find the mean of each group when analyzing the data.
   C. Why do you think it would be important for other researchers to try to replicate the findings in this study?
5. A scientist is performing a study to test the effects of an anti-cancer drug in mice with tumors. They look in the cages and observes that the mice that received the drug for two weeks appear more energetic than those that did not receive the drug. At the end of the study, the scientist performs surgery on the mice to determine whether their tumors have shrunk. Answer the following questions about the experiment.
   A. Is the energy level of the mice treated with the drug a qualitative or quantitative observation?
   B. At the end of the study, the scientist measures the size of the tumors. Is this qualitative or quantitative data?
   C. Would the size of each tumor be considered raw data or descriptive statistics?
   D. The scientist determines the average decrease in tumor size for the drug-treated group. Is this raw data, descriptive statistics, or inferential statistics?
   E. The average decrease in tumor size in the drug-treated group is larger than the average decrease in the untreated group. Can the scientist assume that the drug shrinks tumors? If not, what do they need to do next?
6. Do you think results published in a peer-reviewed scientific journal are more or less likely to be scientifically valid than those in a self-published article or book? Why or why not
7. Explain why real science is usually “nonlinear”?

EXPLORE MORE

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1.6: CASE STUDY CONCLUSION- INHABITANTS AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: OUR INVISIBLE INHABITANTS

As you may recall, Wajiha's strep throat was caused by *Streptococcus pyogenes* bacteria, the species shown in the photomicrograph above. Wajiha took antibiotics to kill the *S. pyogenes*, but this also killed her "good" bacteria, throwing off the balance of microorganisms living inside of her, which resulted in diarrhea and a yeast infection.

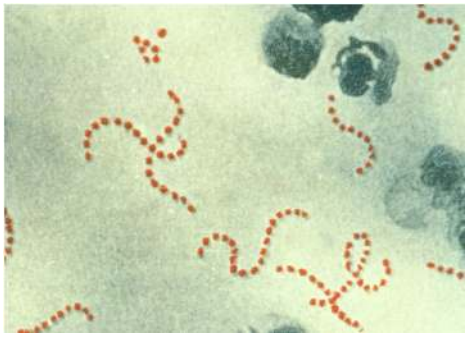


Figure **1.6.1**: Streptococcus pyogenes

After reading this chapter, you should now know that microorganisms such as the bacteria and yeast that live in humans are also similar to us in many ways. They are living organisms and therefore share the traits of homeostasis, organization, metabolism, growth, adaptation, response to stimuli, and reproduction with us. They, like us, contain genes, consist of cells, and have the ability to evolve. Wajiha's beneficial gut bacteria help digest her food as part of her metabolic processes. Wajiha got a yeast infection likely because the growth and reproductive rates of the yeast living on her body were not held in check by beneficial bacteria after she took antibiotics. You can see that there are many ways in which an understanding of the basic characteristics of life can directly apply to your own.

You also learned how living organisms are classified, from bacteria that are in the Bacteria domain, to yeast (fungus kingdom) and humans (animal kingdom) that are both in the Eukarya domain. You probably now recognize that *Streptococcus pyogenes* is the binomial nomenclature for this species and the fact that *Streptococcus* refers to the genus name.

As Wajiha's doctor told her, there are many different species of microorganisms living in the human digestive system. You should recognize this as a type of biodiversity called species diversity. This diversity is maintained in a balance, or homeostasis, that can be upset when one type of organism is killed — for instance, by antibiotics.

Wajiha's doctor advised her to complete the entire course of antibiotics because stopping too early would kill the bacteria that are most susceptible to the antibiotic while leaving the bacteria that are more resistant to the antibiotic alive. This difference in susceptibility to antibiotics is an example of genetic diversity. Over time, the surviving antibiotic-resistant bacteria will have increased survival and reproductive rates compared to the more susceptible bacteria, and the trait of antibiotic resistance will become more common in the population. In this way, the bacteria can evolve and become better adapted to their environment — at a major cost to our health because our antibiotics will no longer be effective. This issue of improper use of antibiotics leading to increased antibiotic resistance is a major concern of public health experts.

After reading the last section of this chapter, you know how humans are classified and some characteristics of humans and our near relatives. Beyond our more obvious features of big brains, intelligence, and the ability to walk upright, we also serve as a home to many different organisms that may be invisible to the naked eye but play a big role in maintaining our health.

CHAPTER SUMMARY

In this chapter, you learned about the basic principles of biology and how humans are situated among other living organisms. Specifically, you learned:

- To be classified as a living thing, most scientists agree that an object must exhibit seven characteristics, including:
  - Maintaining a more-or-less constant internal environment, which is called homeostasis.
  - Having multiple levels of the organization and consisting of one or more cells.
  - Using energy and being capable of metabolism.
  - The ability to grow and develop.
  - The ability to evolve adaptations to the environment.
  - The ability to detect and respond to environmental stimuli.
  - The ability to reproduce, which is the process by which living things give rise to offspring.
- Biodiversity refers to the variety of life that exists on Earth. It includes species diversity, genetic diversity within species, and ecosystem diversity.
- The formal biological definition of species is a group of actually or potentially interbreeding organisms. In reality, organisms are often classified into species on the basis of morphology.
- A system for classifying living things was introduced by Linnaeus in the 1700s. It includes taxa from the species (least inclusive) to the kingdom (most inclusive). Linnaeus also introduced a system of naming species, called binomial nomenclature.
- The domain, a taxon higher than the kingdom, was later added to the Linnaean system. Living things are generally grouped into three domains: Bacteria, Archaea, and Eukarya. Humans and other animal species are placed in the Eukarya domain.
- Modern systems of classification take into account phylogenies, or evolutionary histories of related organisms, rather than just morphological similarities and differences. These relationships

are often represented by phylogenetic trees or other tree-like diagrams.

- The human species, *Homo sapiens*, is placed in the primate order of the class of mammals, which are chordates in the animal kingdom.
- Traits humans share with other primates include five digits with nails and opposable thumbs; an excellent sense of vision including the ability to see in color and stereoscopic vision; a large brain, high degree of intelligence, and complex behaviors. Like most other primates, we also live in social groups. Many of our primate traits are adaptations to life in the trees.
- Within the primate order, our species is placed in the hominid family, which also includes chimpanzees, gorillas, and orangutans.
- The genus *Homo* first evolved about 2.8 million years ago. Early *Homo* species were fully bipedal but had small brains. All are now extinct.
- During the last 800,000 years, *Homo sapiens* evolved, with smaller faces, jaws, and front teeth but much bigger brains than earlier *Homo* species.

Now that you understand the basic principles of biology and some of the characteristics of living organisms, in the next chapter, you will learn about the molecules that make up living organisms and the chemistry that allows organisms to exist and function.

CHAPTER SUMMARY REVIEW

1. What are the seven traits of life?
2. A scientist is exploring in a remote area with many unidentified species. They find an unknown object that does not appear to be living. What is one way they could tell whether it is a dead organism that was once alive, versus an inanimate object that was never living?
3. Cows are dependent on bacteria living in their digestive systems to help break down cellulose in the plant material that the cows eat. Explain what characteristics these bacteria must have to be considered living organisms themselves, and not just part of the cow.
4. What is the basic unit of structure and function in living things?
5. Give one example of homeostasis that occurs in humans.
6. Can a living thing exist without using energy? Why or why not?
7. *True or False.* Evolution is a change in the characteristics of living things over time.
8. *True or False.* Only some living things have genes.
9. Give an example of a response to stimuli that occurs in a unicellular organism.
10. A scientist discovers two types of similar-looking insects that have not been previously identified. Answer the following questions about this discovery.
    A. What is one way they can try to determine whether the two types are the same species?
    B. If they are not the same species, what are some ways they can try to determine how closely related they are to each other?
    C. What is the name for a type of diagram they can create to demonstrate their evolutionary relationship to each other and to other insects?
    D. If they determine that the two types are different species but the same genus, create your own names for them using binomial nomenclature. You can be creative and make up the genus and species names, but be sure to put them in the format of binomial nomenclature.
    E. If they are the same species but have different colors, what kind of biodiversity does this most likely reflect?
    F. If they are the same species, but one type of insect has a better sense of smell for their limited food source than the other type, what do you think will happen over time? Assume the insects will experience natural selection.
11. Put the following taxa in order from the most specific to the most inclusive: phylum; species; kingdom; genus; family; domain; class; order
12. Humans are in the which domain?
13. Monkeys, apes, and humans are all in the:
    A. Same genus
    B. Same order
    C. Same class
    D. Both B and C
14. Amphibians, such as frogs, have a backbone but no hair. What is the most specific taxon that they share with humans?
15. Arboreal means:
    A. Living on the ground
    B. Living in the ocean
    C. Living in trees
    D. Living on grasslands
16. What is one characteristic of extinct *Homo* species that was larger than that of modern humans?
17. What is one characteristic of modern humans that is larger than that of extinct *Homo*species?
18. *True or False.* Most primates live in social groups.
19. *True or False.* Most other mammals have longer lifespans than primates.
20. *True or False.* Archaea are classified into the Bacteria domain.
21. How is the long period of dependency of infants on adults in primates related to learning?
22. Name one type of primate in the hominid family, other than humans.
23. Why do you think that scientists compare the bones of structures (such as the feet) of extinct *Homo* species to ours?
24. Some mammals other than primates also have their eyes placed in the front of their face, such as cats. How do you think the vision of a cat compares to that of a mouse, where the eyes are placed more at the sides?
25. Living sponges are animals. Are we in the same kingdom as sponges? Explain your answer.

ATTRIBUTIONS

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CHAPTER OVERVIEW

2: CHEMISTRY OF LIFE

This chapter provides the chemistry background needed to understand the human body, its functions, and its processes. The chapter describes biochemical compounds and reactions as well as the significance of water to life.

2.1: Case Study- Chemistry and Your Life
2.2: Elements and Compounds
2.3: Chemical Bonding
2.4: Biochemical Compounds
2.5: Carbohydrates
2.6: Lipids
2.7: Proteins
2.8: Nucleic Acids
2.9: Energy in Chemical Reactions
2.10: Chemical Reactions in Living Things
2.11: Biochemical Properties of Water
2.12: Acids and Bases
2.13: Case Study Conclusion- Diet and Chapter Summary

Thumbnail: 3D model of L-tryptophan. (Public Domain; Benjah-bmm27).

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2.1: CASE STUDY- CHEMISTRY AND YOUR LIFE

CASE STUDY: DIET DILEMMA

Mohinder is a college student who has watched their father suffer from complications of type 2 diabetes over the past few years. Mohinder likes to use gender-neutral pronouns, such as they, them, and their's. In type 2 diabetes, the hormone insulin does not transmit its signal sufficiently. Because insulin normally removes sugar from the bloodstream and brings it into the body's cells, diabetes causes blood sugar levels to not be regulated properly. This can cause damage to the cells of the body.



Figure **2.1.1**: Diabetes Detritus

Diabetes can be treated with insulin injections, as shown above, as well as dietary modifications, but sometimes complications can still occur. Mohinder's father has some nerve damage, or neuropathy, in his feet due to his diabetes. This made his feet numb and so he didn't notice when he got minor injuries to his feet, which led to some serious infections.

Mohinder is obese and knows that their weight plus a family history of diabetes increases their risk of getting diabetes themselves. They want to avoid the health issues that their father has suffered. Mohinder begins walking every day for exercise and starts to lose some weight. They also want to improve their diet in order to lose more weight, lower their risk of diabetes, and improve their general health, but they are overwhelmed with all the different dietary advice they read online and hear from their friends and family.

Mohinder's father tells them to limit refined carbohydrates, such as white bread and rice because that is what he does to help keep his blood sugar at an acceptable level. But Mohinder's friend tells them that eating a diet high in carbohydrates and low in fat is a good way to lose weight. Mohinder reads online that "eating clean" by eating whole, unprocessed foods and avoiding food with "chemicals" can help with weight loss. One piece of advice that everyone seems to agree on is that drinking enough water is good for overall health.

All of this dietary advice may sound confusing, but you can better understand health conditions such as diabetes and the role of diet and nutrition by understanding chemistry. Chemistry is so much more than reactions in test tubes in a lab — it is the atoms, molecules, and reactions that make us who we are and keep us alive and functioning properly. Our diets are one of the main ways our bodies take in raw materials that are needed for the important chemical reactions that take place inside of us.

CHAPTER OVERVIEW: CHEMISTRY OF LIFE

As you read this chapter, you will learn more about how chemistry relates to our lives, health, and the foods we eat. Specifically, you will learn:

- The nature of chemical substances, including elements and compounds and their component atoms and molecules.
- The types and mechanisms of the formation of chemical bonds.
- The structures and functions of biochemical compounds including carbohydrates, lipids, proteins, and nucleic acids such as DNA and RNA.
- What chemical reactions are, how energy is involved in chemical reactions, how enzymes assist in chemical reactions, and what some types of biochemical reactions in living organisms are.
- Properties of water and the importance of water for most biochemical processes.
- What pH is and why maintaining a proper pH in the body is important for biochemical reactions.

As you read the chapter, think about the following questions regarding Mohinder's situation and how diabetes and diet relate to the chemistry of life.

1. Why do you think Mohinder's father having diabetes increases his risk of getting diabetes?
2. What is the difference between refined (simple) carbohydrates and complex carbohydrates? Why are refined carbohydrates particularly problematic for people with diabetes?
3. Insulin is a peptide hormone. In which class of biochemical compounds would you categorize insulin?
4. Why is drinking enough water important for overall health? Can you drink too much water?
5. Sometimes "eating clean" is described as avoiding "chemicals" in food. Think about the definition of "chemicals" and how it relates to what we eat.

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2.2: ELEMENTS AND COMPOUNDS

WHAT ARE YOU MADE OF?

If you look at your hand, what do you see? Of course, you see skin, which consists of cells. But what are skin cells made of? Like all living cells, they are made of matter. In fact, all things are made of matter. **Matter** is anything that takes up space and has mass. Matter, in turn, is made up of chemical substances. A chemical substance is a matter that has a definite composition and the same composition throughout. A chemical substance may be either an element or a compound.



Figure **2.2.1**: Diversity and Unity

ELEMENTS AND ATOMS

An **element** is a pure substance. It cannot be broken down into other types of substances. Each element is made up of just one type of atom.

PERIODIC TABLE OF THE ELEMENTS

There are almost 120 known elements. As you can see in the Periodic Table of the Elements shown in Figure **2.2.3**, the majority of elements are metals. Examples of metals are iron (Fe) and copper (Cu). Metals are shiny and good conductors of electricity and heat. Nonmetal elements are far fewer in number. They include hydrogen (H) and oxygen (O). They lack the properties of metals. The element most important to life is Carbon (C). Find carbon in the table. What type of element is it, metal or nonmetal?

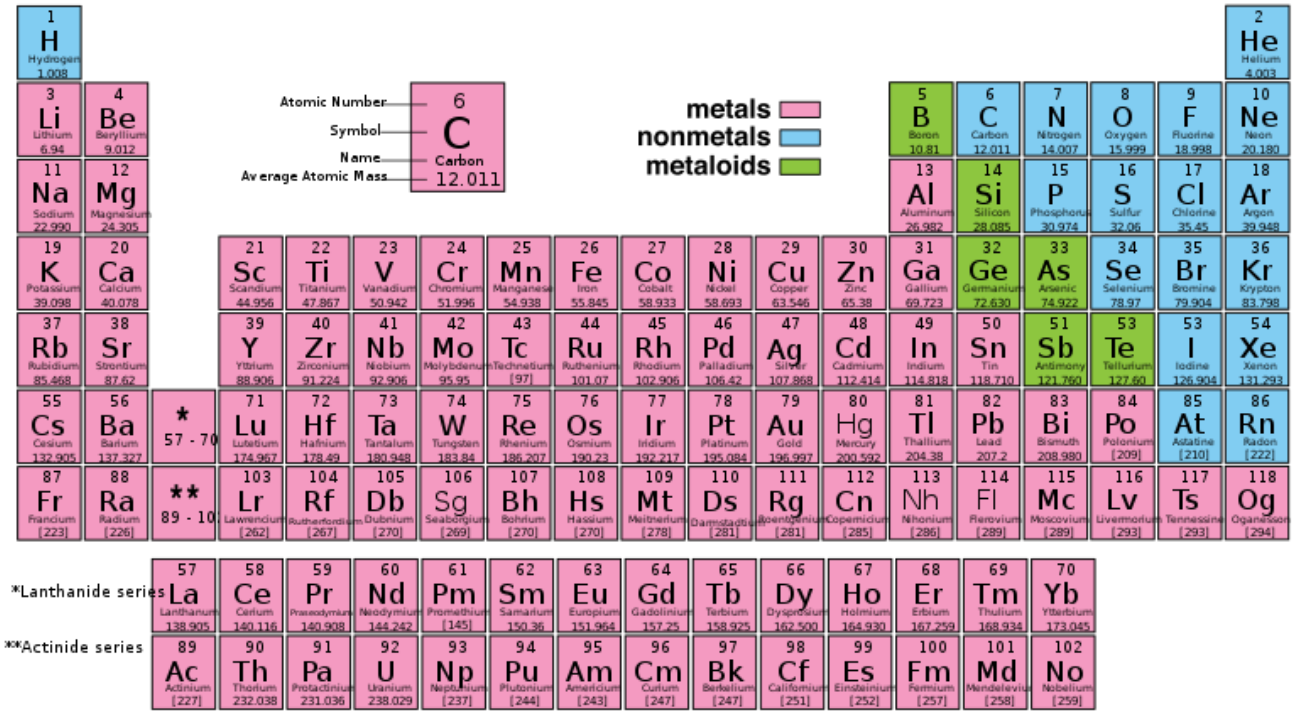


Figure **2.2.3**: Periodic Table of the Elements. The periodic table of the elements arranges elements in groups based on their properties. You may prefer to use an interactive periodic table or an accessible periodic table.

STRUCTURE OF AN ATOM

An **atom** is the smallest particle of an element that still has the properties of that element. Every substance is composed of atoms. Atoms are extremely small, typically about a ten-billionth of a meter in diameter. However, atoms do not have well-defined boundaries, as suggested by the atomic model shown in figure **2.2.2**. An atom is composed of many **subatomic particles.** We will only discuss **protons**, **neutrons**, and **electrons**.

Table 2.2.1: Subatomic Particles

Particle	Proton	Neutron	Electron
Electric Charge	+1	0	-1
Location	Nucleus	Nucleus	Outside the nucleus
Mass	1 amu	1 amu	~0 amu

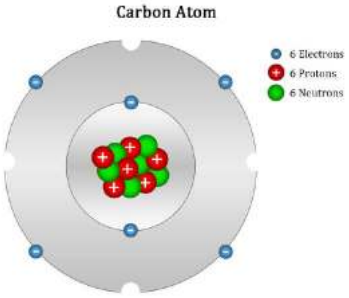


Figure 2.2.2: A model of a Carbon atom. Carbon has 6 protons and 6 neutrons (found in the nucleus). The image also shows the 6 electrons outside of the nucleus in 2 separate orbitals.

If the number of protons and electrons in an atom are equal, then an atom is electrically neutral because the positive and negative charges cancel out. If an atom has more or fewer electrons than protons, then it has an overall negative or positive charge, respectively, and it is called an **ion.**

The negatively charged electrons of an atom are attracted to the positively charged protons in the nucleus by a force called **electromagnetic force,** for which opposite charges attract. Electromagnetic force between protons in the nucleus causes these subatomic particles to repel each other because they have the same charge. However, the protons and neutrons in the nucleus are attracted to each other by a different force, called **nuclear force,** which is usually stronger than the electromagnetic force repelling the positively charged protons from each other.

COMPOUNDS AND MOLECULES

A **compound** is a unique substance that consists of two or more elements combined in fixed proportions. This means that the composition of a compound is always the same. The smallest particle of most compounds in living things is called a **molecule.** Consider water as an example. A molecule of water always contains one atom of oxygen and two atoms of hydrogen. The composition of water is expressed by the chemical formula H_2O. A model of a water molecule is shown in Figure 2.2.4. Notice that molecules can be drawn in different ways, but represent the same molecule. In this case, a molecule made of one oxygen and two hydrogens.

What causes the atoms of a water molecule to "stick" together? The answer is chemical bonds. A chemical bond is a force that holds together the atoms of molecules. Bonds in molecules involve atoms sharing electrons. New chemical bonds form when substances react with one another.

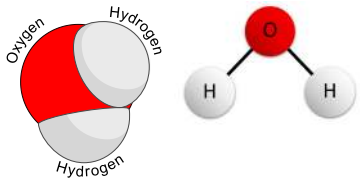


Figure 2.2.4: Water Molecule. A water molecule always has this composition, one atom of oxygen, and two atoms of hydrogen.

REVIEW

1. What is an element? Give three examples.
2. Define compound. Explain how compounds form.
3. Compare and contrast atoms and molecules.
4. The compound called water can be broken down into its constituent elements by applying an electric current to it. What ratio of elements is produced in this process?
5. Relate ions to elements and atoms.
6. What is the most important element of life?
7. Iron oxide is often known as rust — the reddish substance you might find on corroded metal. The chemical formula for this type of iron oxide is Fe2O3. Answer the following questions about iron oxide and briefly explain each answer.
   A. Is iron oxide an element or a compound?
   B. Would one particle of iron oxide be considered a molecule or an atom?
   C. Describe the relative proportion of atoms in iron oxide.
   D. What causes the Fe and O to stick together in iron oxide?
   E. Is iron oxide made of metal atoms, metalloid atoms, nonmetal atoms, or a combination of any of these?
8. Explain why ions have a positive or negative charge.
9. Name the three subatomic particles described in this section.

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2.3: CHEMICAL BONDING

CHEMICAL BONDING

When you think of bonding, you may not think of ions. Like most of us, you probably think of bonding between people. Like people, molecules bond — and some bonds are stronger than others. It's hard to break up a mother and baby, or a molecule made up of one oxygen and two hydrogen atoms! A chemical bond is a force of attraction between atoms or ions. Bonds form when atoms share or transfer valence electrons. Valence electrons are the electrons in the outer energy level of an atom that may be involved in chemical interactions. Valence electrons are the basis of all chemical bonds.



Figure **2.3.1**: Mother and daughter

WHY BONDS FORM

To understand why chemical bonds form, consider the common compound known as water, or H_2O. It consists of two hydrogen (H) atoms and one oxygen (O) atom. As you can see in the on the left side of the Figure **2.3.2** below, each hydrogen atom has just one electron, which is also its sole valence electron. The oxygen atom has six valence electrons. These are the electrons in the **outer energy level** of the oxygen atom.

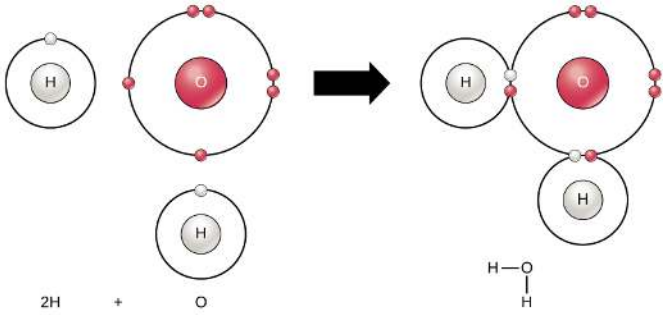


Figure **2.3.2**: Bonds between hydrogen and oxygen atoms in a water molecule. Electrons are drawn as spheres on the circle indicating an electron orbit. The nucleus is shown as the big sphere in the center of the atom.

In the water molecule on the right in Figure **2.3.2**, each hydrogen atom shares a pair of electrons with the oxygen atom. By sharing electrons, each atom has electrons available to fill its sole or outer energy level. The hydrogen atoms each have a pair of shared electrons, so their first and only energy level is full. The oxygen atom has a total of eight **valence electrons**, so its outer energy level is full. A full outer energy level is the most stable possible arrangement of electrons. It explains why elements form chemical bonds with each other.

TYPES OF CHEMICAL BONDS

Not all chemical bonds form in the same way as the bonds in water. There are actually four different types of chemical bonds that we will discuss here are non-polar covalent, polar covalent, hydrogen, and ionic bonding. Each type of bond is described below.

NON-POLAR COVALENT BONDS

For methane (CH_4) in Figure **2.3.3**, the carbon atom (with four electrons in its outermost valence energy shell) shares a single electron from each of the four hydrogens. Hydrogen has one valence electron in its first energy shell. Covalent bonding is prevalent in organic compounds. In fact, your body is held together by electrons shared by carbons and hydrogens! The electrons are equally shared in all directions; therefore, this type of covalent bond is referred to as non-polar.

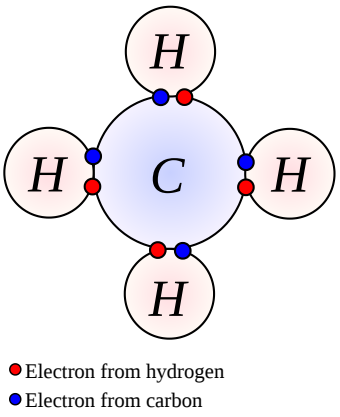


Figure **2.3.3**: Methane is formed when four hydrogens and one carbon covalently bond.

POLAR COVALENT BONDS AND HYDROGEN BONDS

A covalent bond is the force of attraction that holds together two nonmetal atoms that share a pair of electrons. One electron is provided by each atom, and the pair of electrons is attracted to the positive nuclei of both atoms. The water molecule represented in Figure **2.3.4** contains polar covalent bonds.

The attractive force between water molecules is a dipole interaction. The hydrogen atoms are bound to the highly electronegative oxygen atom (which also possesses two lone pair sets of electrons, making for a very polar bond. The partially positive hydrogen atom of one molecule is then attracted to the partially negative oxygen atom of a nearby water molecule as shown in Figure **2.3.4**).

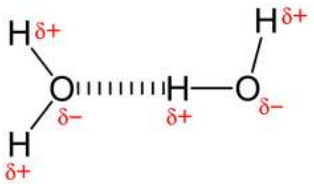


Figure **2.3.4**: A hydrogen bond in water occurs between the hydrogen atom of one water molecule and the lone pair of electrons on an oxygen atom of a neighboring water molecule

A **hydrogen bond** is an intermolecular and intramolecular attractive force in which a hydrogen atom that is covalently bonded to a highly **electronegative** atom is attracted to a lone pair of electrons on an atom or a partially negative atom in a neighboring polar molecule. Hydrogen bonds are also found intramolecularly in the tertiary and quaternary structures of protein and DNA strands.

Hydrogen bonding occurs only in molecules where hydrogen is covalently bonded to one of three elements: fluorine, oxygen, or nitrogen. These three elements are so electronegative that they withdraw the majority of the electron density in the covalent bond with hydrogen, leaving the H atom very electron-deficient. The H atom nearly acts as a bare proton, leaving it very attracted to lone pair electrons on a nearby atom.

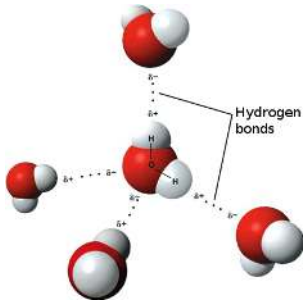


Figure **2.3.5**: Multiple hydrogen bonds occur simultaneously in water because of its bent shape and the presence of two hydrogen atoms per molecule.

The hydrogen bonding that occurs in water leads to some unusual, but very important properties. Most molecular compounds that have a mass similar to water are gases at room temperature. Because of the strong hydrogen bonds, water molecules are able to stay condensed in the liquid state. Figure **2.3.5** shows how the bent shape and two hydrogen atoms per molecule allow each water molecule to be able to hydrogen bond to two other molecules.

In the liquid state, the hydrogen bonds of water can break and reform as the molecules flow from one place to another. When water is cooled, the molecules begin to slow down. Eventually, when water is frozen to ice, the hydrogen bonds form a very specific network shown on the right side of Figure **2.3.6**. When water is liquid, the molecules are more motile and don't produce this rigid structure.

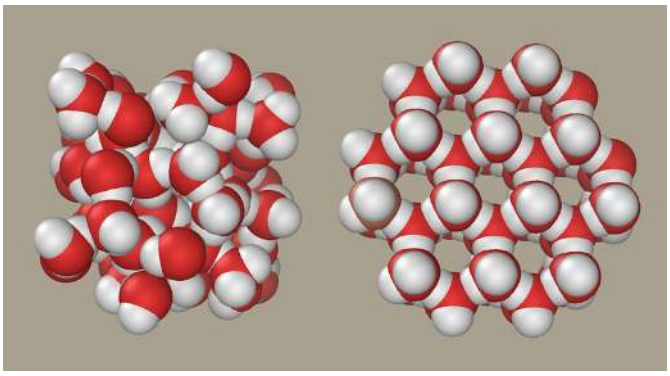


Figure **2.3.6**: When water freezes to ice, the hydrogen bonding network becomes more stable. Each oxygen atom has an approximately tetrahedral geometry – two covalent bonds and two hydrogen bonds.

IONIC BONDS

Electrons are transferred between atoms. An ion will give one or more electrons to another ion. Table salt, sodium chloride (NaCl), is a common example of an ionic compound. Note that sodium is on the left side of the periodic table and that chlorine is on the right side of the periodic table. In Figure **2.3.7**, an atom of lithium donates an electron to an atom of fluorine to form an ionic compound. This happens to full fill their outermost valence shell. The transfer of the electron gives the lithium ion a net charge of +1, and the fluorine ion a net charge of -1. These ions bond because they experience an attractive force due to the difference in sign of their charges.

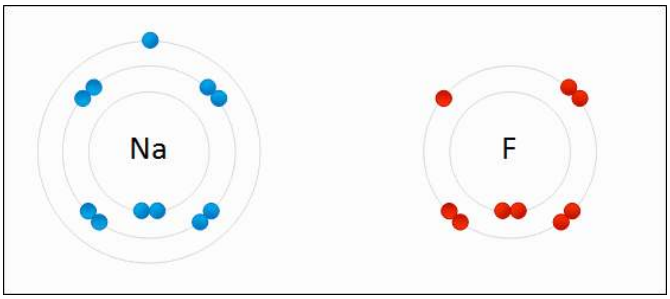


Figure **2.3.7**: Sodium (left) and fluorine (right) form an ionic compound called Sodium fluoride. The animation shows sodium (Na) losing an electron. This electron is taken by fluorine (F). This makes Na positively charged and F negatively charged. These ions are then attracted to each other.

REVIEW

1. How is a covalent bond different from an ionic bond?
2. Why is a hydrogen bond a relatively weak bond?
3. Diagram the polarity of a water molecule.
4. What is a chemical bond?
5. Explain why hydrogen and oxygen atoms are more stable when they form bonds in a water molecule.
6. How many valence electrons does sodium have? How many valence electrons does chlorine have? How does a chlorine atom bonds with sodium? What is the charge on a sodium ion? What about the chlorine ion?
7. When does covalent bonding occur? How does it work?
8. How many valence electrons does oxygen have?

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2.4: BIOCHEMICAL COMPOUNDS

CARBS GALORE

What do all these foods have in common? All of them consist mainly of large compounds called carbohydrates, often referred to as "carbs." Contrary to popular belief, carbohydrates are an important part of a healthy diet. They are also one of four major classes of biochemical compounds.



Figure **2.4.1**: Grain product food

CHEMICAL COMPOUNDS IN LIVING THINGS

The compounds found in living things are known as **biochemical compounds.** Biochemical compounds make up the cells and other structures of organisms and carry out life processes. Carbon is the basis of all biochemical compounds, so carbon is essential to life on Earth. Without carbon, life as we know it could not exist.

Why is carbon so basic to life? The reason is carbon's ability to form stable bonds with many elements, including itself. This property allows carbon to form a huge variety of very large and complex molecules. In fact, there are nearly 10 million carbon-based compounds in living things!

Most biochemical compounds are very large molecules called polymers. A **polymer** is built of repeating units of smaller compounds called **monomers.** Monomers are like the individual beads on a string of beads, and the whole string is the polymer. The strings of beads pictured below are simple models of polymers in biochemical compounds.



Figure **2.4.2**: A Fio de conta: Beads on a string are similar to the formation of polymers from repeating units called monomers.

CLASSES OF BIOCHEMICAL COMPOUNDS

Although there are millions of different biochemical compounds in Earth's living things, all biochemical compounds contain the elements carbon, hydrogen, and oxygen. Some contain only these elements; others contain additional elements as well. The vast number of biochemical compounds can be grouped into just four major classes: carbohydrates, lipids, proteins, and nucleic acids.

CARBOHYDRATES

Carbohydrates include sugars and starches. These compounds contain only the elements carbon, hydrogen, and oxygen. Functions of carbohydrates in living things include providing energy to cells, storing energy, and forming certain structures, such as the cell walls of plants. The monomer that makes up large carbohydrate compounds is called a monosaccharide. The sugar glucose, represented by the chemical model below, is a monosaccharide. It contains six carbon atoms (C) and several atoms of hydrogen (H) and oxygen (O). Thousands of glucose molecules can join together to form a polysaccharide such as starch.

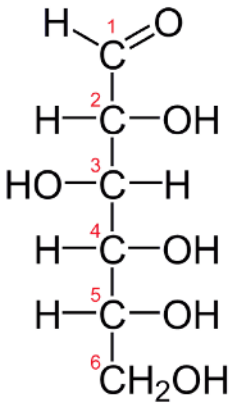


Figure **2.4.3**: Model of a monosaccharide (glucose) molecule. Glucose has 6 carbons forming a backbone. Each carbon has a total of 4 bonds. Each bond connects carbon to a carbon, hydrogen, or oxygen atom.

LIPIDS

Lipids include fats and oils. They contain primarily the elements carbon, hydrogen, and oxygen, although some lipids contain additional elements such as phosphorus. Functions of lipids in living

things include storing energy, forming cell membranes, and carrying messages. Lipids consist of repeating units that join together to form chains called fatty acids. Most naturally occurring fatty acids have an unbranched chain of an even number (generally from 4 to 28) of carbon atoms.

PROTEINS

Proteins include enzymes, antibodies, and many other important compounds in living things. They contain the elements carbon, hydrogen, oxygen, nitrogen, and sulfur. The functions of proteins are very numerous. They include helping cells keep their shape, making up muscles, speeding up chemical reactions, and carrying messages and materials. The monomers that make up large protein compounds are called amino acids. There are 23 different amino acids that combine into long chains (called polypeptides) to form the building blocks of a vast array of proteins in living things.

NUCLEIC ACIDS

Nucleic acids include the molecules DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). They contain the elements carbon, hydrogen, oxygen, nitrogen, and phosphorus. Their functions in living things are to encode instructions for making proteins, to help make proteins, and to pass the instructions from parents to offspring. The monomer that makes up nucleic acids is the nucleotide. All nucleotides are the same except for a component called a nitrogen base. There are four different nitrogen bases, and each nucleotide contains one of these four bases. The sequence of nitrogen bases in the chains of nucleotides in DNA and RNA makes up the code for protein synthesis, called the genetic code. The animation below represents the very complex structure of DNA, which consists of two chains of nucleotides.

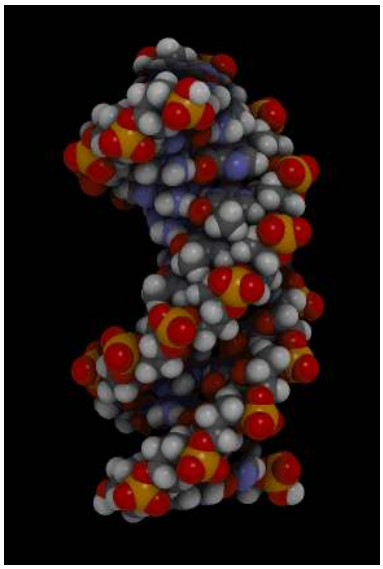


Figure **2.4.4**: This rotating DNA model shows the complexity of this two-stranded nucleic acid. There are many different atoms making the double helix structure.

REVIEW

1. Why is carbon so important to life on Earth?
2. What are the biochemical compounds?
3. Describe the diversity of biochemical compounds, and explain how they are classified.
4. Identify two types of carbohydrates. What are the main functions of this class of biochemical compounds?
5. What roles are played by lipids in living things?
6. The enzyme amylase is found in saliva. It helps break down starches in foods into simpler sugar molecules. What type of biochemical compound do you think amylase is?
7. Explain how DNA and RNA contain the genetic code.
8. What are the three elements present in every class of biochemical compound?
9. For each of the following terms (nucleic acid; amino acid; monosaccharide; protein; nucleotide; polysaccharide)
   A. Determine whether it is a monomer or a polymer.
   B. Match each monomer with its correct polymer.
   C. Identify which class of biochemical compound is represented by each monomer/polymer pair.
10. Is glucose a monomer or a polymer? Explain your answer.
11. What is one element contained in proteins and nucleic acids, but not in carbohydrates?
12. Describe the relationship between proteins and nucleic acids.
13. Why do you think it is important to eat a diet that contains a balance of carbohydrates, proteins, and fats?

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2.5: CARBOHYDRATES

THE CELLULOSE OF OUR LIVES

Where would we be without our jeans? They have been the go-to pants for many people for decades, and they are still as popular as ever. Jeans are made of denim, a type of cotton fabric. Cotton is a soft, fluffy fiber that grows in a protective case around the seeds of cotton plants. The fiber is almost pure cellulose. Cellulose is the single most abundant biochemical compound found in Earth's living things and one of several types of carbohydrates.



Figure 2.5.1: Body paint and jeans

WHAT ARE CARBOHYDRATES?

Carbohydrates are the most common class of biochemical compounds. They include sugars and starches. Carbohydrates are used to provide or store energy, among other uses. Like most biochemical compounds, carbohydrates are built of small repeating units, or monomers, which form bonds with each other to make larger molecules, called polymers. In the case of carbohydrates, the small repeating units are known as **monosaccharides.** Each monosaccharide consists of six carbon atoms, as shown in the model of the monosaccharide glucose below.

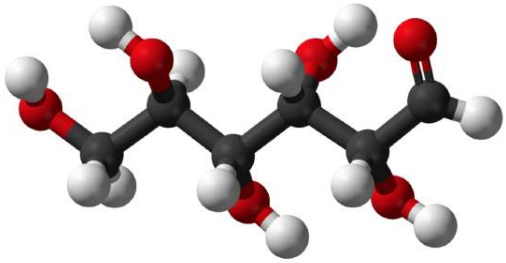


Figure 2.5.2: The six black balls in this model of the monosaccharide glucose represent carbon atoms. These six carbons make up the backbone in the center of glucose. The red balls are oxygen, and the white ones are hydrogen.

SUGARS

Sugars are the general name for sweet, short-chain, soluble carbohydrates, which are found in many foods. Their function in living things is to provide energy. The simplest sugars consist of a single monosaccharide. They include glucose, fructose, and galactose. **Glucose** is a simple sugar that is used for energy by the cells of living things. Fructose is a simple sugar found in fruits, and galactose is a simple sugar found in milk.

Other sugars contain two monosaccharide molecules and are called **disaccharides.** An example is sucrose or table sugar. It is composed of one fructose molecule and one glucose molecule. Other disaccharides include maltose (two glucose molecules) and lactose (one glucose molecule and one galactose molecule). Lactose occurs naturally in milk. Some people can't digest lactose. If they drink milk, it causes gas, cramps, and other unpleasant symptoms unless the milk has been processed to remove the lactose.

COMPLEX CARBOHYDRATES

The simple sugars form the foundation of more complex carbohydrates. The cyclic forms of two sugars can be linked together by means of a condensation reaction. The figure below shows how a glucose molecule and a fructose molecule combine to form a sucrose molecule. A hydrogen atom from one molecule and a hydroxyl group from the other molecule are eliminated as water, with a resulting covalent bond linking the two sugars together at that point.

Glucose and fructose combine to produce the disaccharide sucrose in a condensation reaction as shown in Figure 2.5.3. Sucrose, commonly known as table sugar, is an example of a disaccharide.

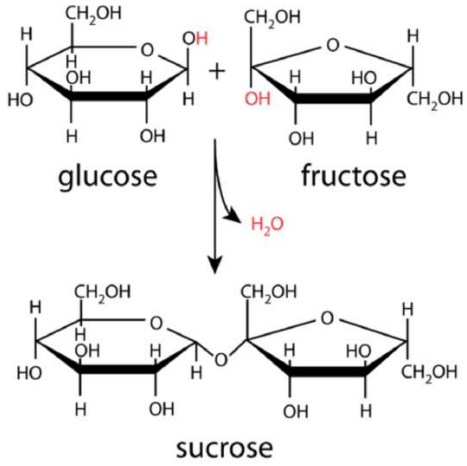


Figure 2.5.3: Glucose and fructose combine to produce the disaccharide sucrose in a condensation reaction. The diagram shows how water is produced when the reaction occurs. This is because the oxygen in glucose binds to the carbon in fructose. That removes an oxygen and two hydrogens from the new molecule.

A **disaccharide** is a carbohydrate formed by the joining of two monosaccharides. Other common disaccharides include lactose and maltose. Lactose, a component of milk, is formed from glucose and galactose, while maltose formed from two glucose molecules. During digestion, these disaccharides are hydrolyzed in the small intestine to form the component monosaccharides, which are then

absorbed across the intestinal wall and into the bloodstream to be transported to the cells.

Some carbohydrates consist of hundreds or even thousands of monosaccharides bonded together in long chains. These carbohydrates are called **polysaccharides** ("many saccharides"). Polysaccharides are also referred to as **complex carbohydrates.** Complex carbohydrates that are found in living things include starch, glycogen, cellulose, and chitin. Each type of complex carbohydrate has different functions in living organisms but they generally either store energy or make up certain structures of living things.



Figure **2.5.4**: (left) Potatoes are starch-filled tubers of potato plants. They are harvested by digging them up from underground. (center) Cotton fibers represent the purest natural form of cellulose, containing more than 90 percent of this polysaccharide. (right) The tough outer skeleton (exoskeleton) of this ten-lined beetle is made partly of the complex carbohydrate chitin.

STARCH

Starch is a complex carbohydrate that is made by plants to store energy. For example, the potatoes pictured below are packed full of starches that consist mainly of repeating units of glucose and other simple sugars. The leaves of potato plants make sugars by photosynthesis, and the sugars are carried to underground tubers where they are stored as starch. When we eat starchy foods such as potatoes, the starches are broken down by our digestive system to sugars, which provide our cells with energy. Starches are easily and quickly digested with the help of digestive enzymes such as amylase, which is found in the saliva. If you chew a starchy saltine cracker for several minutes, you may start to taste the sugars released as the starch is digested.

GLYCOGEN

Animals do not store energy as starch. Instead, animals store the extra energy as the complex carbohydrate glycogen. **Glycogen** is a polysaccharide of glucose. It serves as a form of energy storage in fungi as well as animals and is the main storage form of glucose in the human body. In humans, glycogen is made and stored primarily in the cells of the liver and the muscles. When energy is needed from either storage depot, the glycogen is broken down to glucose for use by cells. Muscle glycogen is converted to glucose for use by muscle cells, and liver glycogen is converted to glucose for use throughout the rest of the body. Glycogen forms an energy reserve that can be quickly mobilized to meet a sudden need for glucose, but one that is less compact than the energy reserves of lipids, which are the primary form of energy storage in animals.

Glycogen plays a critical part in the homeostasis of glucose levels in the blood. When blood glucose levels rise too high, excess glucose can be stored in the liver by converting it to glycogen. When glucose levels in the blood fall too low, glycogen in the liver can be broken down into glucose and released into the blood.

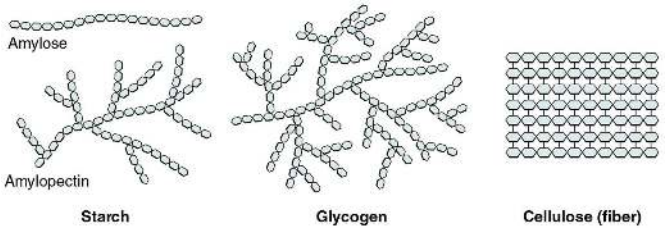


Figure **2.5.5**: Starch, Glycogen, and Cellulose have different arrangements of monosaccharides.

CELLULOSE

Cellulose is a polysaccharide consisting of a linear chain of several hundred to many thousands of linked glucose units. Cellulose is an important structural component of the cell walls of plants and many algae. Human uses of cellulose include the production of cardboard and paper, which consist mostly of cellulose from wood and cotton. The cotton fibers pictured below are about 90 percent cellulose.

Certain animals, including termites and ruminants such as cows, can digest cellulose with the help of microorganisms that live in their gut. Humans cannot digest cellulose, but it nonetheless plays an important role in our diet. It acts as a water-attracting bulking agent for feces in the digestive tract and is often referred to as "dietary fiber."

CHITIN

Chitin is a long-chain polymer of a derivative of glucose. It is found in many living things. For example, it is a component of the cell walls of fungi, the exoskeletons of arthropods such as crustaceans and insects (including the beetle pictured in Figure **2.5.7**), and the beaks and internal shells of animals such as squids and octopuses. The structure of chitin is similar to that of cellulose.

FEATURE: MY HUMAN BIOLOGY



Figure **2.5.6**: Beans are an excellent source of both soluble and insoluble fiber.

You probably know that you should eat plenty of fiber, but do you know how much fiber you need, how fiber contributes to good health, or which foods are good sources of fiber? Dietary fiber consists mainly of cellulose, so it is found primarily in plant-based foods, including fruits, vegetables, whole grains, and legumes. Dietary fiber can't be broken down and absorbed by your digestive system. Instead, it passes relatively unchanged through your gastrointestinal tract and is excreted in feces. That's how it helps keep you healthy.

The fiber in food is commonly classified as either soluble or insoluble fiber.

- Soluble fiber dissolves in water to form a gel-like substance as it passes through the gastrointestinal tract. Its health benefits include lowering blood levels of cholesterol and glucose. Good sources of soluble fiber include whole oats, peas, beans, and apples.
- Insoluble fiber does not dissolve in water. This type of fiber increases the bulk of feces in the large intestine and helps keep food wastes moving through, which may help prevent or correct constipation. Good sources of insoluble fiber include whole wheat, wheat bran, beans, and potatoes.

How much fiber do you need for good health? That depends on your age and gender. The Institute of Medicine recommends the daily fiber intake for adults shown in the table below. Most dietitians further recommend a ratio of about 3 parts insoluble fiber to 1 part soluble fiber each day. Most fiber-rich foods contain both types of fiber, so it usually isn't necessary to keep track of the two types of fiber as long as your overall fiber intake is adequate.

Use food labels and online fiber counters to find out how much total fiber you eat in a typical day. Are you consuming enough fiber for good health? If not, consider ways to increase your intake of this important substance. For example, substitute whole grains for refined grains, eat more legumes such as beans, and try to consume at least five servings of fruits and vegetables each day.

Table **2.5.1**: Recommended Daily Fiber Intake for Males and Females

Gender	Age 50 or Younger	Age 51 or Older
Male	38 grams	30 grams
Female	25 grams	21 grams

SUMMARY

- Carbohydrates are the most common class of biochemical compounds. The basic building block of carbohydrates is the monosaccharide, which consists of six carbon atoms.
- Sugars are sweet, short-chain, soluble carbohydrates that are found in many foods and supply us with energy. Simple sugars, such as glucose, consist of just one monosaccharide. Some sugars, such as sucrose, or table sugar, consist of two monosaccharides and are called disaccharides.
- Complex carbohydrates, or polysaccharides, consist of hundreds or even thousands of monosaccharides. They include starch, glycogen, cellulose, and chitin. They generally either store energy or form structures, such as cell walls, in living things.
- Starch is a complex carbohydrate that is made by plants to store energy. Potatoes are a good food source of dietary starch, which is readily broken down to its component sugars during digestion.
- Glycogen is a complex carbohydrate that is made by animals and fungi to store energy. Glycogen plays a critical part in the homeostasis of blood glucose levels in humans.
- Cellulose is the single most common biochemical compound in living things. It forms the cell walls of plants and certain algae. Like most other animals, humans cannot digest cellulose, but it makes up most of the crucial dietary fiber in the human diet.
- Chitin is a complex carbohydrate, similar to cellulose, that makes up organic structures such as the cell walls of fungi and the exoskeletons of insects and other arthropods.

REVIEW

1. What are carbohydrates? Describe their structure.
2. Compare and contrast sugars and complex carbohydrates.
3. Identify the four main types of complex carbohydrates and their functions.
4. If you chew on a starchy food such as a saltine cracker for several minutes, it may start to taste sweet. Explain why.
5. *True or False.* Glucose is mainly stored by lipids in the human body.
6. Put the following carbohydrates in order from smallest to largest: cellulose; fructose; sucrose
7. Name three carbohydrates that contain glucose as a monomer.
8. Jeans are made of tough, durable cotton. Explain how you think this fabric gets its tough qualities, based on what you know about the structure of carbohydrates.
9. Which do you think is faster to digest — simple sugars or complex carbohydrates? Explain your answer.
10. *True or False.* Cellulose is broken down in the human digestive system into glucose molecules.
11. Which type of fiber dissolves in water? Which type does not dissolve in water?
12. What are the similarities and differences between muscle glycogen and liver glycogen?
13. Which carbohydrate is used directly by the cells of living things for energy?
14. Which of the following is *not* a complex carbohydrate?

A. chitin
B. starch
C. disaccharide
D. none of the above

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2.6: LIPIDS

YUM!

It glistens with fat, from the cheese to the steak. You may never have visited Philadelphia, but you probably know about its famous gastronomic delight, the Philly cheesesteak, pictured here. Both cheese and steak are typically high-fat foods, so this sandwich is definitely not recommended if you are following a low-fat diet. We need some fats in our diet for good health, but too much of a good thing can be harmful to our health, no matter how good it tastes. What are fats? And why do we have such a love-hate relationship with them? Read on to find out.



Figure **2.6.1**: Philly Cheesesteak Sandwich

LIPIDS AND FATTY ACIDS

Fats are actually a type of lipid. **Lipids** are a major class of biochemical compounds that includes oils as well as fats. Organisms use lipids to store energy and for many other uses.

Lipid molecules consist mainly of repeating units called **fatty acids.** There are two types of fatty acids: saturated fatty acids and unsaturated fatty acids. Both types consist mainly of simple chains of carbon atoms bonded to one another and to hydrogen atoms. The two types of fatty acids differ in how many hydrogen atoms they contain.

SATURATED FATTY ACIDS

In saturated fatty acids, carbon atoms are bonded to as many hydrogen atoms as possible. All the carbon-to-carbon atoms share just single bonds between them. This causes the molecules to form straight chains, as shown in Figure **2.6.2**. The straight chains can be packed together very tightly, allowing them to store energy in a compact form. Saturated fatty acids have relatively high melting points, explaining why they are solids at room temperature. Animals use saturated fatty acids to store energy.

UNSATURATED FATTY ACIDS

In **unsaturated fatty acids**, some carbon atoms are not bonded to as many hydrogen atoms as possible. Instead, they form double or even triple bonds with other carbon atoms. This causes the chains to bend (see Figure **2.6.2**). The bent chains cannot be packed together very tightly. Unsaturated fatty acids have relatively low melting points, which explains why they are liquids at room temperature. Plants use unsaturated fatty acids to store energy.

Monounsaturated fatty acids contain one less hydrogen atom than the same-length saturated fatty acid chain. Monounsaturated fatty acids are liquids at room temperature but start to solidify at refrigerator temperatures. Good food sources of monounsaturated fats include olive and peanut oils and avocados.

Polyunsaturated fatty acids contain at least two fewer hydrogen atoms than the same-length saturated fatty acid chain. Polyunsaturated fatty acids are liquids at room temperature and remain in the liquid state in the refrigerator. Good food sources of polyunsaturated fats include safflower and soybean oils and many nuts and seeds.

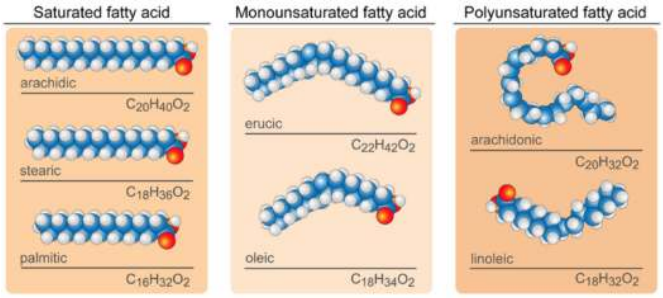


Figure **2.6.2**: Fatty Acids models. The blue balls, white balls, and red balls represent carbon, hydrogen, and oxygen, respectively. Saturated fatty acids, such as arachidic, stearic and palmitic, have straight chains. Unsaturated fatty acids have bent chains. Monounsaturated fatty acids, such as erucic and oleic have a single double bond between carbons creating a single bend in the chain. Polyunsaturated fatty acids, such as arachidoic and linoleic, have multiple carbon-carbon double bonds creating multiple bends.

TYPES OF LIPIDS

Lipids may consist of fatty acids alone, or they may contain other molecules as well. For example, some lipids contain alcohol or phosphate groups. Types of lipids include triglycerides, phospholipids, and steroids. Each type has different functions in living things.

TRIGLYCERIDES

Triglycerides are formed by combining a molecule of glycerol with three fatty acid molecules. Glycerol (also called glycerine) is a simple compound known as a sugar alcohol. It is a colorless, odorless liquid that is sweet tasting and nontoxic. Triglycerides are the main constituent of body fat in humans and other animals. They are also found in fats derived from plants. There are many different types of triglycerides, with the main division being between those that contain saturated fatty acids and those that contain unsaturated fatty acids.

In the human bloodstream, triglycerides play an important role in metabolism as energy sources and transporters of dietary fat. They contain more than twice as much energy as carbohydrates, the other major source of energy in the diet. When you eat, your body converts any calories it doesn't need to use right away into triglycerides, which are stored in your fat cells. When you need energy between meals, hormones trigger the release of some of these stored triglycerides back into the bloodstream.

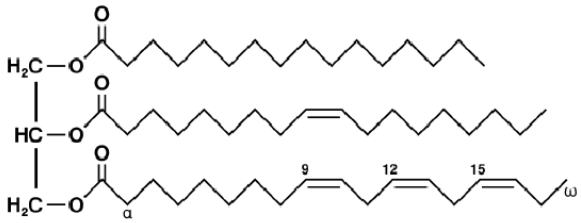


Figure **2.6.3**: Triglyceride Molecule. The left part of this triglyceride molecule represents glycerol. Each of the three long chains on the right represents a different fatty acid. From top to bottom, the fatty acids are palmitic acid, oleic acid, and alpha-linolenic acid. These fatty acids are shown in Figure **2.6.2**. The chemical formula for this triglyceride is $C_{55}H_{98}O_6$. KEY: H=hydrogen, C=carbon, O=oxygen.

PHOSPHOLIPIDS

Phospholipids are a major component of the cell membranes of all living things. Each phospholipid molecule has a "tail" consisting of two long fatty acids and a "head" consisting of a phosphate group and glycerol molecule (see diagram below). The phosphate group is a small negatively charged molecule. The phospholipid head is **hydrophilic** or attracted to water. The fatty acid tail of the phospholipid is **hydrophobic** or repelled by water. These properties allow phospholipids to form a two-layer, or bilayer, cell membrane.

As shown in the diagram below, a phospholipid bilayer forms when many phospholipid molecules line up tail to tail, forming an inner and outer surface of hydrophilic heads. The hydrophilic heads point toward both the watery extracellular space and the watery intracellular space (lumen) of the cell.

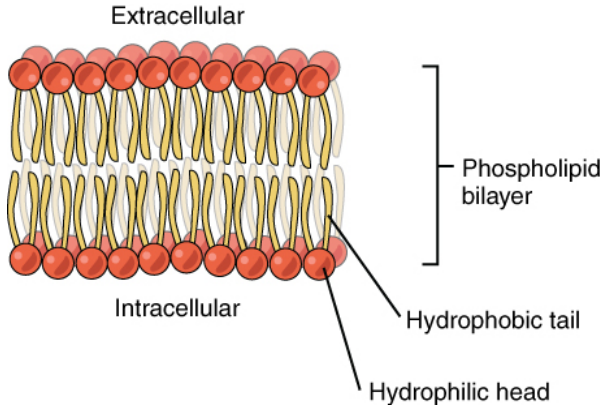


Figure **2.6.4**: The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads contact the fluid inside and outside of the cell.

STEROIDS

Steroids are lipids with a ring structure. Each steroid has a core of seventeen carbon atoms arranged in four rings of five or six carbons each (see model pictured below). Steroids vary by the other components attached to this four-ring core. Hundreds of steroids are found in plants, animals, and fungi, but most steroids have one of just two principal biological functions: some steroids, such as cholesterol, are important components of cell membranes; many other steroids are hormones, which are messenger molecules. In humans, steroid hormones include cortisone, a fight-or-flight hormone; and the sex hormones estrogen and testosterone.

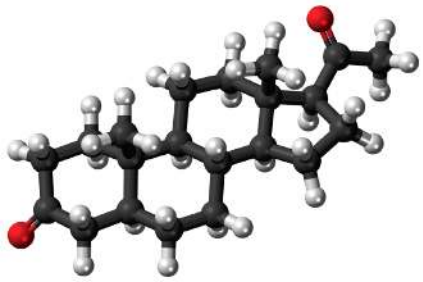


Figure **2.6.5**: Each steroid molecule consists of a four-ring core of 17 carbon atoms (black balls in the model). The red balls are representing oxygen and the white balls are representing hydrogen in the model. The components of the molecule may vary and determine the steroid's function.

FEATURE: MY HUMAN BODY

During a routine checkup with your family doctor, your blood was collected for a lipid profile. The results are back, and your triglyceride level is 180 mg/dL. Your doctor says this is a little high. A blood triglyceride level of 150 mg/dL or lower is considered normal. Higher levels of triglycerides in the blood have been linked to increased risk of atherosclerosis, heart disease, and stroke.

If a blood test reveals that you have high triglycerides, the levels can be lowered through healthy lifestyle choices and/or prescription medications. Healthy lifestyle choices to control triglyceride levels include:

- losing weight. If you are overweight, losing even 5 or 10 pounds may help lower your triglyceride level.
- cutting back on calories. Extra calories are converted to triglycerides and stored as fat, so reducing your calories should also reduce your triglyceride level.
- avoiding sugary and refined foods. Simple carbohydrates, such as sugars and foods made with white flour, can increase triglyceride levels.
- choosing healthier fats. Trade saturated fats found in animal foods for healthier unsaturated fats found in plants and oily fish. For example, substitute olive oil for butter and salmon for red meat.
- limiting alcohol consumption. Alcohol is high in calories and sugar and has a strong effect on triglyceride levels.
- exercising regularly. Aim for at least 30 minutes of physical activity on most or all days of the week to lower triglyceride levels.

If healthy lifestyle changes aren't enough to bring down high triglyceride levels, drugs prescribed by your doctor are likely to help.

REVIEW

1. What are lipids?
2. Compare and contrast saturated and unsaturated fatty acids.
3. Identify three major types of lipids, and describe differences in their structures.
4. How do triglycerides play an important role in human metabolism?
5. Explain how phospholipids form cell membranes.
6. What is cholesterol, and what is its major function?
7. Give three examples of steroid hormones in humans.
8. Which type of fatty acid do you think is predominant in the steak and cheese of the cheesesteak shown above? Explain your answer.
9. Which type of fat would be the most likely to stay liquid in colder temperatures — bacon fat, olive oil, or soybean oil? Explain your answer.
10. Why do you think that the shape of the different types of fatty acid molecules affects how easily they solidify?
11. High cholesterol levels in the bloodstream can cause negative health effects but explain why we wouldn't want to get rid of *all* the cholesterol in our bodies.
12. Name two types of lipids that are part of the cell membrane.
13. *True or False.* Fatty acids are made up of triglycerides.
14. Which type of lipid often functions as chemical messenger molecules?

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2.7: PROTEINS

PROTEIN SHAKE

Drinks like this shake contain a lot of protein. Such drinks are popular with people who want to build muscle because muscle tissue consists mainly of protein. Making up muscles is just one of a plethora of functions of this amazingly diverse class of biochemicals.



Figure 2.7.1: Protein shake

WHAT ARE PROTEINS?

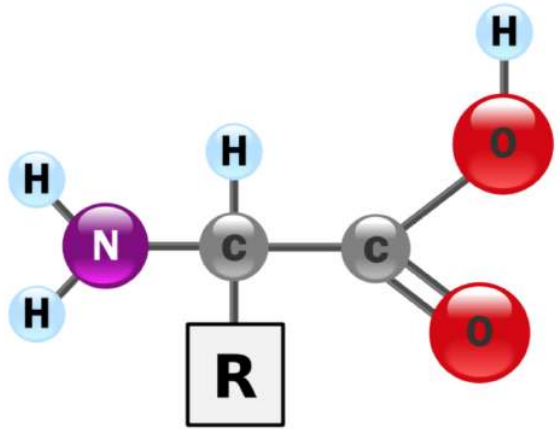


Figure 2.7.2: General Structure of Amino Acids. This model shows the general structure of all amino acids. Only the side chain, R, varies from one amino acid to another. For example, in the amino acid glycine, the side chain is simply hydrogen (H). In glutamic acid, in contrast, the side chain is CH_2CH_2COOH CH2CH2COOH. Variable side chains give amino acids different chemical properties. The order of amino acids, together with the properties of the amino acids, determines the shape of the protein, and the shape of the protein determines the function of the protein. KEY: H = hydrogen, N = nitrogen, C = carbon, O = oxygen, R = variable side chain.

Proteins are organic compounds that contain carbon, hydrogen, oxygen, nitrogen, and, in some cases, sulfur. These compounds have many essential functions within the cell (see below). Proteins are made of smaller units called **amino acids**. There are 20 different common amino acids needed to make proteins. All amino acids have the same basic structure, which is shown in Figure 2.7.3. Only the side chain (labeled R in the figure) differs from one amino acid to another. These side chains can vary in size from just one hydrogen atom in glycine to a large heterocyclic group in tryptophan. The variable side chain gives each amino acid unique properties. The side chains can also characterize the amino acid as (1) nonpolar or hydrophobic, (2) neutral (uncharged) but polar, (3) acidic, with a net negative charge, and (4) basic, with a net positive charge at neutral pH.

Proteins can differ from one another in the number and sequence (order) of amino acids. It is because of the side chains of the amino acids that proteins with different amino acid sequences have different shapes and different chemical properties. Small proteins can contain just a few hundred amino acids. Yeast proteins average 466 amino acids. The largest known proteins are the titins, found in muscle, which are composed of over 27,000 amino acids.

PROTEIN STRUCTURE

Amino acids join together to form a molecule called a dipeptide. The –OH from the carboxyl group of one amino acid combines with a hydrogen atom from the amino group of the other amino acid to produce water. This is called a **condensation reaction** - a reaction in which two molecules combine to form a single molecule with a release of water. Figure 2.7.3) shows this process. The top part of the image shows two amino acids; note the -OH in amino acid 1 and the -H in amino acid two are highlighted. These are the atoms that will be removed from the amino acids to form water. This allows a covalent bond forms between the carboxyl carbon of one amino acid and the amine nitrogen of the second amino acid. This reaction forms a molecule called a dipeptide and the carbon-nitrogen covalent bond is called a **peptide bond**. When repeated numerous times, a lengthy molecule called a **polypeptide** is eventually produced. Very lengthy polypeptides with functional configuration are called **proteins.**

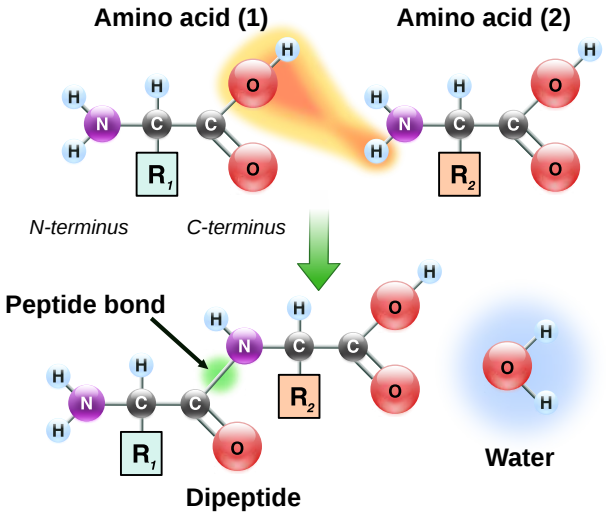


Figure 2.7.3: Amino acids join together to form a molecule called a dipeptide. The C–N bond is called a peptide bond. The order of amino acids is by convention shown with the free amino group on the left and the free carboxyl group on the right.

Proteins may have up to four levels of structure, from primary to quaternary, as described and shown in the diagram below, giving them the potential for tremendous diversity:

- A protein's primary structure is the sequence of amino acids in its polypeptide chain(s). This sequence of amino acids determines the higher levels of protein structure and is encoded in genes.
- A protein's secondary structure consists of regularly repeating local structures stabilized by hydrogen bonding between the carboxylic and amino groups of the backbone. The most common secondary structures include the alpha-helix and beta-sheet. Because secondary structures are local, many regions of different secondary structures can be present in the same protein molecule.
- A protein's tertiary structure refers to the overall three-dimensional shape of a single protein molecule. It is determined by the spatial relationship of non-covalent and covalent bonds between the "R" groups of distant amino acids in a polypeptide. The tertiary structure is what controls the basic function of the protein.
- Not all proteins have a final, quaternary structure. This is a structure formed by several protein molecules that function together as a single protein complex.

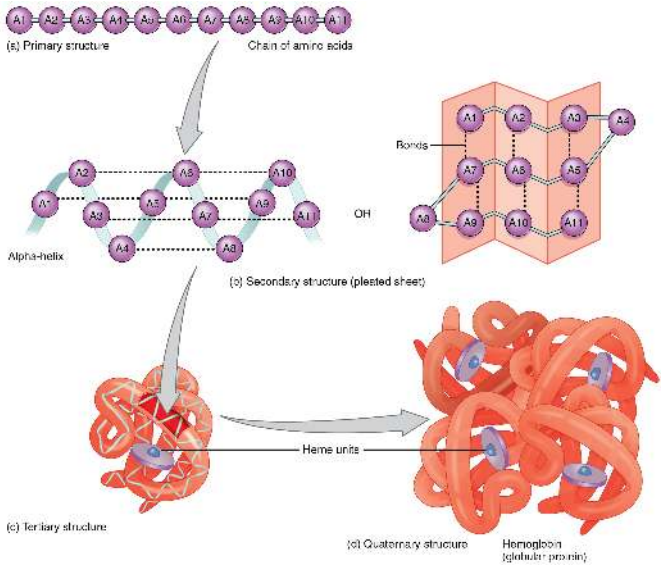


Figure **2.7.4**: The levels of structure of a protein called hemoglobin.

FUNCTIONS OF PROTEINS

The diversity of protein structures explains how this class of biochemical compounds can play so many important roles in living things. What are the roles of proteins?

- Some proteins have structural functions. They may help cells keep their shape or make up muscle tissues.
- Many proteins are enzymes that speed up chemical reactions in cells. Enzymes are usually highly specific and accelerate only one or a few chemical reactions. Thousands of different biochemical reactions are known to be catalyzed by enzymes, including most of the reactions involved in metabolism. A reaction without an enzyme might take millions of years to complete, whereas, with the proper enzyme, it may take just a few milliseconds!
- Other proteins are antibodies. These are proteins that bind to specific foreign substances, such as proteins on the surface of bacterial cells. This targets the cells for destruction.
- Still, other proteins carry messages or materials. For example, a protein called myoglobin is an oxygen-binding protein found in the muscle tissues of most mammals including humans. You can see a model of the tertiary structure of myoglobin in the figure below.

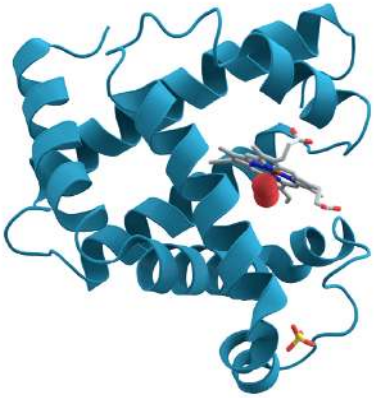


Figure **2.7.5**: Myoglobin is a protein found in the muscle tissues of most mammals. It binds with oxygen to supply the cells with this element. The modle shows the 3D structure of the protein.

The chief characteristic of proteins that allows their diverse set of functions is their ability to bind other molecules specifically and tightly. For example, myoglobin can bind specifically and tightly with oxygen. The region of a protein responsible for binding with another molecule is known as the **binding site.** This site is often a depression on the molecular surface, determined largely by the tertiary structure of the protein.

PROTEIN CONSUMPTION, DIGESTION, AND SYNTHESIS

Proteins are necessary for the diets of humans and other animals. We cannot make all the different amino acids we need, so we must obtain some of them from the foods we consume. Through the process of digestion, we break down the proteins in food into free amino acids that can then be used to synthesize our own proteins. Protein synthesis from amino acid monomers takes place in all cells and is controlled by genes. Once new proteins are synthesized, they generally do not last very long before they are degraded and their amino acids are recycled. A protein's lifespan is generally just a day or two in mammalian cells.

REVIEW

1. What are proteins?
2. How do two amino acids combine together to make a dipeptide?
3. Outline the four levels of protein structure.
4. Identify four functions of proteins.

5. Explain why proteins can take on so many different functions in living things.
6. What is the role of proteins in the human diet?
7. Can you have a protein with both an alpha helix and a beta-sheet? Why or why not?
8. If there is a mutation in a gene that causes a different amino acid to be encoded than the one that is usually encoded in that position within the protein, would that affect:
   A. The primary structure of the protein? Explain your answer.
   B. The higher structures (secondary, tertiary, quaternary) of the protein? Explain your answer.
   C. The function of the protein? Explain your answer.
9. What is the region of a protein responsible for binding to another molecule called? Which level/s of protein structure create this region?
10. Arrange the following in order from the smallest to the largest level of organization:
11. peptide; protein; amino acid; polypeptide
12. *True or False.* You can tell the function of all proteins from their quaternary structure.
13. Explain what the reading means when it says that amino acids are "recycled."

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2.8: NUCLEIC ACIDS

WHO'S WHO?

Identical twins show clearly the importance of genes in making us who we are. Genes, in turn, would not be possible without nucleic acids.



Figure **2.8.1**: Twins

Nucleic acids are the class of biochemical compounds that includes DNA and RNA. These molecules are built of small monomers called **nucleotides**. Many nucleotides bind together to form a chain called a **polynucleotide**. The nucleic acid **DNA** (deoxyribonucleic acid) consists of two polynucleotide chains. The nucleic acid **RNA** (ribonucleic acid) consists of just one polynucleotide chain.

STRUCTURE OF NUCLEIC ACIDS

Each nucleotide consists of three smaller molecules:

1. a sugar molecule (the sugar deoxyribose in DNA and the sugar ribose in RNA).
2. a phosphate group.
3. a nitrogenous base.

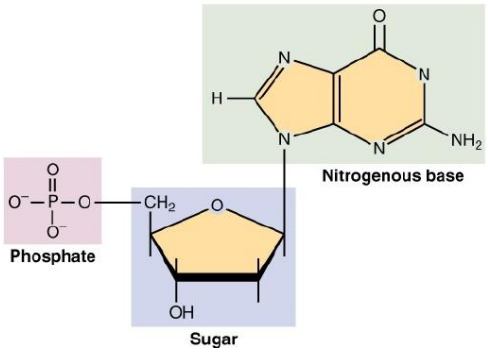


Figure **2.8.2**: Nucleotides consist of a sugar, a nitrogenous base, and a phosphate group

Nucleotides are connected to form DNA as shown in Figure **2.8.3**. The sugar molecule of one nucleotide binds to the phosphate group of the next nucleotide. These two molecules alternate to form the backbone of the nucleotide chain. The nitrogen bases in a nucleic acid stick out from the backbone. There are four different nitrogenous bases: cytosine, adenine, guanine, and either thymine (in DNA) or uracil (in RNA). In DNA, hydrogen bonds form between bases on the two nucleotide chains and hold the chains together. Each type of base binds with just one other type of base: cytosine always bonds with guanine, and adenine always bonds with thymine. These pairs of bases are called **complementary base pairs**.

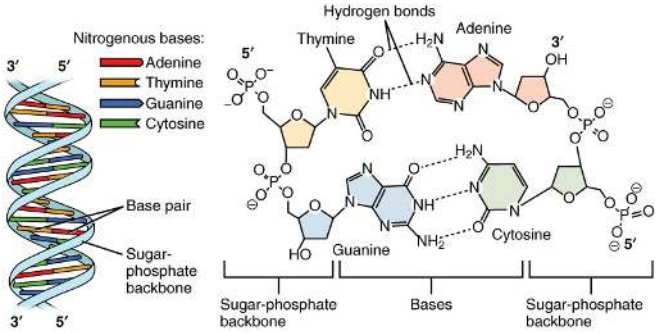


Figure **2.8.3**: Nucleic Acid

The hydrogen bonding of complementary bases causes DNA molecules automatically to take their well-known shape, called a double helix, which is shown in the animation in Figure **2.8.4**. A double helix is like a spiral staircase. The double helix shape forms naturally and is very strong, making the two polynucleotide chains difficult to break apart.

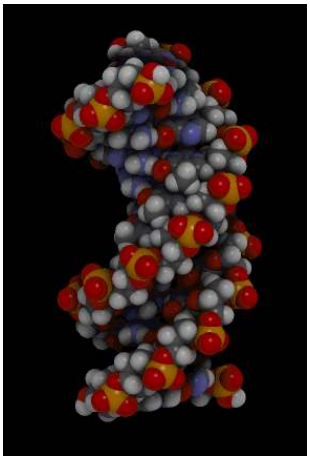


Figure **2.8.4**: DNA molecule

ROLES OF NUCLEIC ACIDS

The DNA of cells is organized into structures called chromosomes as shown in Figure **2.8.5**. The letters A, T, G, and C stand for the bases adenine, thymine, guanine, and cytosine. The sequence of these four bases in DNA is a code that carries instructions for making proteins. The DNA helix is wrapped around proteins called histones to form nucleosomes. These are then further structured into chromatin and, finally, chromosomes. Human cells have 46 chromosomes; other organisms have different numbers of chromosomes.

DNA makes up genes, and the sequence of bases in DNA makes up the genetic code. Between "starts" and "stops," the code carries instructions for the correct sequence of amino acids in a protein. The information in DNA is passed from parent cells to daughter cells whenever cells divide. The information in DNA is also passed from

parents to offspring when organisms reproduce. This is how inherited characteristics are passed from one generation to the next.

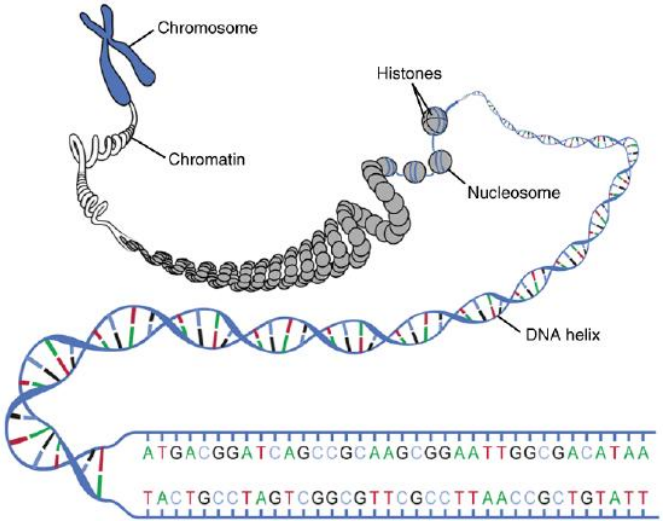


Figure **2.8.5**: The organization of a chromosome

FEATURE: HUMAN BIOLOGY IN THE NEWS

Look at the Neanderthals in Figure **2.8.6**. The image is an artist's reconstruction of these close human relatives, who seem to have disappeared from Europe some 50,000 years ago. The consensus that Neandertals were brutish and went extinct when overtaken by modern humans is undergoing revision as we learn more about these interesting members of the genus *Homo*.



Figure **2.8.6**: Neanderthals were stocky and barrel-chested, but DNA evidence shows that they mated with modern humans thousands of years ago.

Several years ago, scientists were able to extract DNA from fossilized bones of Neanderthals (see Figure **2.8.7**). When the Neanderthal DNA was compared with modern human DNA, researchers discovered similarities in the DNA of Neanderthals and modern European-derived peoples that suggest modern humans mated with Neanderthals. Some experts now think that Neanderthals didn't go extinct but were simply incorporated into the much larger population of *Homo sapiens*.



Figure **2.8.7**. A scientist works to extract DNA from a fossilized Neanderthal bone

New research published in *Science* early in 2016 shows that our inherited Neanderthal DNA may be more than just an interesting curiosity or useful evidence of our evolutionary past. These bits of DNA may actually be affecting our health today. In the research reported in *Science*, scientists looked for Neanderthal DNA sequences in the DNA from an electronic database compiled from health records of almost 30,000 modern American adults. The scientists found that certain segments of Neanderthal DNA are especially common in people who have particular medical conditions, such as depression and increased amounts of blood clotting. Other bits of Neanderthal DNA seems to boost the immune response to certain parasites and other pathogens.

Most of the Neanderthal DNA segments that have persisted into our modern gene pool were probably beneficial in prehistoric times. Now, however, they may increase the risk of disease because our lifestyles and environments have changed so much since then. For example, an increase in blood clotting would have helped prevent life-threatening bleeding from injuries or childbirth in the past, but today it may increase the risk of blood clots and strokes in older people with sedentary lifestyles. Even immune-boosting bits of Neanderthal DNA may now do more harm than good for Americans who live in environments where there are far fewer parasites. They may make our immune systems overactive and cause allergies and autoimmune disorders.

REVIEW

1. What are the nucleic acids?
2. How does RNA differ in structure from DNA?
3. Describe a nucleotide. Explain how nucleotides bind together to form a polynucleotide.
4. What role do nitrogen bases in nucleotides play in the structure and function of DNA?
5. What is the role of RNA?
6. Explain why Mark and Scott Kelly look so similar, using what you learned about nucleic acids in this article.
7. *True or False.* A, C, G, and T represent the bases in RNA.
8. *True or False.* The two polynucleotide chains of RNA twist into a double helix shape.
9. *True or False.* Cytosine always binds to guanine in DNA.
10. If part of a chain of DNA has the sequence of bases: ATTG, what is the corresponding sequence of bases that it binds to on the other chain?

11. Arrange the following in order from the smallest to the largest level of organization: DNA; nucleotide; polynucleotide
12. As part of the DNA replication process, the two polynucleotide chains are separated from each other, but each individual chain remains intact. Which bonds are broken in this process?
    A. Bonds between adjacent sugars and phosphate groups
    B. Bonds within nucleotides
    C. Bonds between complementary bases
    D. Bonds between adenine and guanine
13. Adenine, guanine, cytosine, and thymine are:
    A. Nucleotides
    B. Nitrogenous bases
    C. Sugars in DNA and RNA
    D. Phosphate groups
14. Some diseases and disorders are caused by genes. Explain why these genetic disorders can be passed down from parents to their children.

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2.9: ENERGY IN CHEMICAL REACTIONS

SLOW BURN

These old iron chains give off a small amount of heat as they rust. The rusting of iron is a chemical process. It occurs when iron and oxygen undergo a chemical reaction similar to burning or combustion. The chemical reaction that occurs when something burns gives off energy. You can feel the heat, and you may be able to see the light of flames. The rusting of iron is a much slower process, but it still gives off energy. It's just that it releases energy so slowly you can't detect a temperature change.



Figure **2.9.1**: Rusty chain

WHAT IS A CHEMICAL REACTION?

A **chemical reaction** is a process that changes some chemical substances into others. A substance that starts a chemical reaction is called a **reactant,** and a substance that forms as a result of a chemical reaction is called a **product.** During the reaction, the reactants are used to create the products.

Another example of a chemical reaction is the burning of methane gas, shown in Figure **2.9.2**. In this chemical reaction, the reactants are methane (CH_4) and oxygen (O_2), and the products are carbon dioxide (CO_2) and water (H_2O). As this example shows, a chemical reaction involves the breaking and forming of chemical bonds. Chemical bonds are forces that hold together the atoms of a molecule. Bonds occur when atoms share electrons. When methane burns, for example, bonds break within the methane and oxygen molecules, and new bonds form in the molecules of carbon dioxide and water.



Figure **2.9.2**: Flames from methane burning

CHEMICAL EQUATIONS

Chemical reactions can be represented by chemical equations. A **chemical equation** is a symbolic way of showing what happens during a chemical reaction. For example, the burning of methane can be represented by the chemical equation:

$$CH_4 + 2\,O_2 \rightarrow CO_2 + 2\,H_2O \qquad (2.9.1)$$

The arrow in a chemical equation separates the reactants from the products and shows the direction in which the reaction proceeds. If the reaction could occur in the opposite direction as well, two arrows pointing in opposite directions would be used. The number 2 in front of O_2 and H_2O shows that two oxygen molecules and two water molecules are involved in the reaction. If just one molecule is involved, no number is placed in front of the chemical symbol.

ROLE OF ENERGY IN CHEMICAL REACTIONS

Matter rusting or burning are common examples of chemical changes. Chemical changes involve chemical reactions in which some substances, called reactants, change at the molecular level to form new substances, called products. All chemical reactions involve energy. However, not all chemical reactions release energy, as rusting and burning do. In some chemical reactions, energy is absorbed rather than released.

EXERGONIC REACTIONS

A chemical reaction that releases energy is called an **exergonic reaction**. This type of reaction can be represented by a general chemical equation:

$$\text{Reactants} \rightarrow \text{Products} + \text{Energy} \qquad (2.9.2)$$

Besides rusting and burning, examples of exothermic reactions include chlorine combining with sodium to form table salt. The decomposition of organic matter also releases energy because of exergonic reactions. Sometimes, on a chilly morning, you can see steam rising from a compost pile because of these chemical reactions (see Figure **2.9.3**). Exergonic chemical reactions also take place in the cells of living things. In a chemical process similar to combustion, called cellular respiration, the sugar glucose is "burned" to provide cells with energy.



Figure **2.9.3**: This compost pile is steaming because it is much warmer than the chilly air around it. The heat comes from all the exothermic chemical reactions taking place inside the compost as it decomposes.

ENDERGONIC REACTIONS

A chemical reaction that absorbs energy is called an **endergonic reaction**. This type of reaction can also be represented by a general chemical equation:

$$\text{Reactants} + \text{Energy} \rightarrow \text{Products} \qquad (2.9.3)$$

Did you ever use a chemical cold pack like the one in the picture below? The pack cools down because of an endergonic reaction. When a tube inside the pack is broken, it releases a chemical that reacts with water inside the pack. This reaction absorbs heat energy and quickly cools down the contents of the pack.



Figure **2.9.4**: This pack gets cold due to an endergonic reaction

Many other chemical processes involve endergonic reactions. For example, most cooking and baking involve the use of energy to produce chemical reactions. You can't bake a cake or cook an egg without adding heat energy. Arguably, the most important endergonic reactions occur during photosynthesis. When plants produce sugar by photosynthesis, they take in light energy to power the necessary endergonic reactions. The sugar they produce provides plants and virtually all other living things with glucose for cellular respiration.

ACTIVATION ENERGY

All chemical reactions need energy to get started. Even reactions that release energy need a boost of energy in order to begin. The energy needed to start a chemical reaction is called **activation energy**. Activation energy is like the push a child needs to start going down a playground slide. The push gives the child enough energy to start moving, but once she starts, she keeps moving without being pushed again. Activation energy is illustrated in Figure **2.9.5**.

Why do all chemical reactions need energy to get started? In order for reactions to begin, reactant molecules must bump into each other, so they must be moving, and movement requires energy. When reactant molecules bump together, they may repel each other because of intermolecular forces pushing them apart. Overcoming these forces so the molecules can come together and react also takes energy.

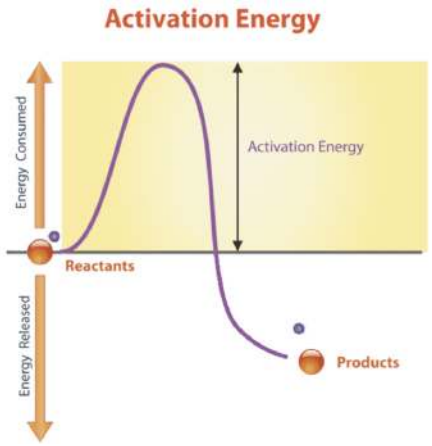


Figure **2.9.5**: This diagram of activation energy shows the reactants on the far left and the products on the right. Notice that the reactants are at a higher energy level than the products, so this reaction releases energy overall. But the reaction consumes energy to get started - this is the activation energy for the reaction.

REVIEW

1. What is a chemical reaction?
2. Identify reactants and products in a chemical reaction.
3. List three examples of common changes that involve chemical reactions.
4. Define a chemical bond.
5. What is a chemical equation? Give an example.
6. Our cells use glucose ($C_6H_{12}O_6$) to obtain energy in a chemical reaction called cellular respiration. In this reaction, six oxygen molecules (O_2) react with one glucose molecule. Answer the following questions about this reaction.
   A. How many oxygen atoms are in one molecule of glucose?
   B. Write out what the reactant side of this equation would look like.
   C. How many oxygen atoms are in the reactants in total? Explain how you calculated your answer.
   D. How many oxygen atoms are in the products in total? Is it possible to answer this question without knowing what the products are? Why or why not?
7. Answer the following questions about the equation you saw above: $CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O$
   A. Can carbon dioxide (CO_2) become transformed into methane (CH_4) and oxygen (O_2) in this reaction? Why or why not?

B. How many molecules of carbon dioxide (CO_2) are produced in this reaction?

8. Is the evaporation of liquid water into water vapor a chemical reaction? Why or why not
9. Why do bonds break in the reactants during a chemical reaction?
10. Contrast endergonic and exergonic chemical reactions. Give an example of each.
11. Define activation energy.
12. Explain why all chemical reactions require activation energy.
13. Heat is a form of _____ .
14. In which type of reaction is heat added to the reactants?
15. In which type of reaction is heat produced?
16. If there was no heat energy added to an endothermic reaction, would that reaction occur? Why or why not?
17. If there was no heat energy added to an exothermic reaction, would that reaction occur? Why or why not?
18. Explain why a chemical cold pack feels cold when activated.
19. Explain why cellular respiration and photosynthesis are “opposites” of each other.
20. Explain how the sun indirectly gives our cells energy.

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2.10: CHEMICAL REACTIONS IN LIVING THINGS

ASSEMBLY LINE

We stay alive because millions of different chemical reactions are taking place inside our bodies all the time. Each of our cells is like the busy auto assembly line pictured here. Raw materials, half-finished products, and waste materials are constantly being used, produced, transported, and excreted. The "workers" on the cellular assembly line are mainly enzymes. These are the proteins that make biochemical reactions happen.



Figure **2.10.1**: Assembly line

WHAT ARE BIOCHEMICAL REACTIONS?

Chemical reactions that take place inside living things are called **biochemical reactions.** The sum of all the biochemical reactions in an organism is referred to as **metabolism**. Metabolism includes both exothermic (heat-releasing) chemical reactions and endothermic (heat-absorbing) chemical reactions.

CATABOLIC REACTIONS

Exergonic reactions in organisms are called **catabolic reactions**. These reactions break down molecules into smaller units and release energy. An example of a catabolic reaction is the breakdown of glucose during cellular respiration, which releases energy that cells need to carry out life processes.

ANABOLIC REACTIONS

Endergonic reactions in organisms are called **anabolic reactions**. These reactions absorb energy and build bigger molecules from smaller ones. An example of an anabolic reaction is the joining of amino acids to form a protein. Which type of reactions — catabolic or anabolic — do you think occur when your body digests food?

ENZYMES

Most biochemical reactions in organisms need help in order to take place. Why is this the case? For one thing, temperatures are usually too low inside living things for biochemical reactions to occur quickly enough to maintain life. The concentrations of reactants may also be too low for them to come together and react. Where do the biochemical reactions get the help they need to proceed? The help comes from enzymes.

An **enzyme** is a protein that speeds up a biochemical reaction. It is a biological catalyst. An enzyme generally works by reducing the amount of activation energy needed to start the reaction. Figure **2.10.2** shows the activation energy needed for glucose to combine with oxygen to produce carbon dioxide and water. The overall reaction releases energy, but an initial activation energy is needed to start the process. The activation energy without an enzyme is much higher than the activation energy when an enzyme is used.

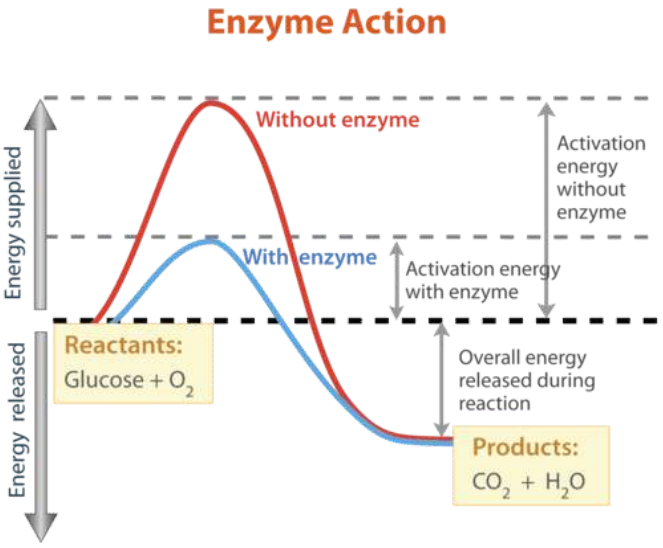


Figure **2.10.2**: Enzyme Action. This graph shows what happens when glucose combines with oxygen. An enzyme speeds up the reaction by lowering the activation energy. Compare the activation energy needed with and without the enzyme.

HOW WELL ENZYMES WORK

Enzymes are involved in most biochemical reactions, and they do their jobs extremely well. A typical biochemical reaction that would take several days or even several centuries to occur without an enzyme is likely to occur in just a split second with the proper enzyme! Without enzymes to speed up biochemical reactions, most organisms could not survive. Enzymes are substrate-specific. The substrate of an enzyme is the specific substance it affects (Figure **2.10.3**). Each enzyme works only with a particular substrate, which explains why there are so many different enzymes. In addition, for an enzyme to work, it requires specific conditions, such as just the right temperature and pH. Some enzymes work best under acidic conditions, for example, while others work best in neutral environments.

ENZYME-DEFICIENCY DISORDERS

There are hundreds of known inherited metabolic disorders in humans. In most of them, a single enzyme is either not produced by the body at all or is produced in a form that doesn't work. The missing or defective enzyme is like an absentee worker on the cell's assembly line. The absence of the normal enzyme means that toxic chemicals build-up or an essential product isn't made. Generally, the normal enzyme is missing because the individual with the disorder

inherited two copies of a gene mutation, which may have occurred originally many generations in the past.

Any given inherited metabolic disorder is generally quite rare in the general population. However, there are so many different metabolic disorders that a total of 1 in 1,000 to 2,500 newborns can be expected to have one. In certain ethnic populations, such as Ashkenazi Jews (Jews of central and eastern European ancestry), the rate of certain inherited metabolic disorders is much higher.

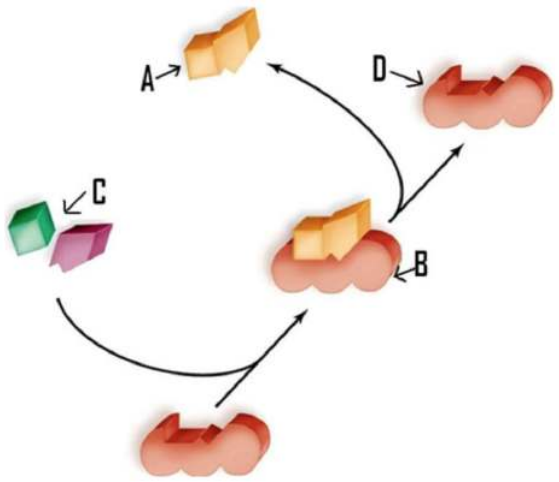


Figure **2.10.3**: The figure shows how enzymes convert substrates into products. the substrate (A) binds at the activation site of the enzyme(D) and makes a substrate-enzyme complex (B). Then, the enzyme converts the substrate into the product (C) by breaking or making bonds between the atoms of the substrate.

FEATURE: RELIABLE SOURCES

The most common of all known enzyme-deficiency disorders is glucose-6-phosphate-dehydrogenase, or G6PD, deficiency. In the U.S., the disorder occurs most often in African-American males. The enzyme G6PD is needed to prevent the abnormal breakdown of red blood cells. Without the enzyme, red blood cells break down prematurely and anemia results.

Choose one of the following topics about G6PD deficiency:

- genetic basis
- signs and symptoms
- diagnosis and treatment
- worldwide distribution

For the topic, you chose, go online to learn more about it. Find at least three sources of additional information that you think are reliable. Compare the information provided by the different sources, and identify any discrepancies among them. Do additional online research as needed to try to find a reliable consensus view of the discrepant issue.

REVIEW

1. What are biochemical reactions?
2. Define metabolism.
3. Compare and contrast catabolic and anabolic reactions.
4. Explain the role of enzymes in biochemical reactions.
5. What are enzyme-deficiency disorders?
6. True or False. Metabolism is one specific type of catabolism.
7. True or False. Biochemical reactions include catabolic and anabolic reactions.
8. Explain why the relatively low temperature of living things, as well as the low concentration of reactants, would cause biochemical reactions to occur very slowly in the body without enzymes.
9. Answer the following questions about what happens after you eat a sandwich.
   A. Pieces of the sandwich go into your stomach, where there are digestive enzymes that break down the food. Which type of metabolic reaction is this? Explain your answer.
   B. Through the process of digestion, part of the sandwich is broken down to glucose, which is then further broken down to release energy that your cells can use. Is this an exergonic or endergonic reaction? Explain your answer.
   C. The proteins in the cheese, meat, and bread in the sandwich are broken down into their component amino acids. Then your body uses those amino acids to build new proteins. Which kind of metabolic reaction is represented by the building of these new proteins? Explain your answer.
10. Explain why your body doesn't just use one or two enzymes for all of its biochemical reactions.
11. What is the specific substance that enzyme affects in a biochemical reaction called?
12. An enzyme is a biological
    A. catabolism
    B. form of activation energy
    C. catalyst
    D. reactant

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2.11: BIOCHEMICAL PROPERTIES OF WATER

THE BLUE MARBLE

It's often called the "water planet," and it's been given the nickname "the blue marble." You probably just call it "home." Almost three-quarters of our home planet is covered by water, and without it, life as we know it could not exist on Earth. Water, like carbon, has a special role in living things. It is needed by all known forms of life. Although water consists of simple molecules, each containing just three atoms, its structure gives it unique properties that help explain why it is vital to all living organisms.



Figure **2.11.1**: Planet Earth

CHEMICAL STRUCTURE AND PROPERTIES OF WATER

You are probably already familiar with many of the water's properties. For example, you no doubt know that water is tasteless, odorless, and transparent. In small quantities, it is also colorless. However, when a large amount of water is observed, as in a lake or the ocean, it is actually light blue in color. The blue hue of the water is an intrinsic property and is caused by selective absorption and scattering of white light. These and other properties of water depend on its chemical structure.

The transparency of water is important for organisms that live in water. Because water is transparent, sunlight can pass through it. Sunlight is needed by water plants and other water organisms for photosynthesis.

CHEMICAL STRUCTURE OF WATER

Each molecule of water consists of one atom of oxygen and two atoms of hydrogen, so it has the chemical formula H_2O. The arrangement of atoms in a water molecule, shown in Figure **2.11.2**, explains many of the water's chemical properties. In each water molecule, the nucleus of the oxygen atom (with 8 positively charged protons) attracts electrons much more strongly than the hydrogen nuclei (with only one positively charged proton). This results in a negative electrical charge near the oxygen atom (due to the "pull" of the negatively charged electrons toward the oxygen nucleus) and a positive electrical charge near the hydrogen atoms. A difference in electrical charge between different parts of a molecule is called **polarity**. A **polar molecule** is a molecule in which part of the molecule is positively charged, and part of the molecule is negatively charged.

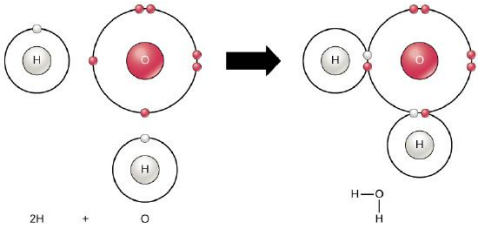


Figure **2.11.2**: This model is an atomic diagram of water, showing the two hydrogen atoms and an oxygen atom in the center.

WATER IS A GOOD SOLVENT

Water is considered a very good solvent in biochemical reactions. Figure **2.11.3** illustrates how water dissolves salts. Table salt (NaCl) consists of a positively charged sodium ion and a negatively charged chloride ion. The oxygen of water is attracted to the positive Na ion. The hydrogens of water are attracted to the negative Cl ion.

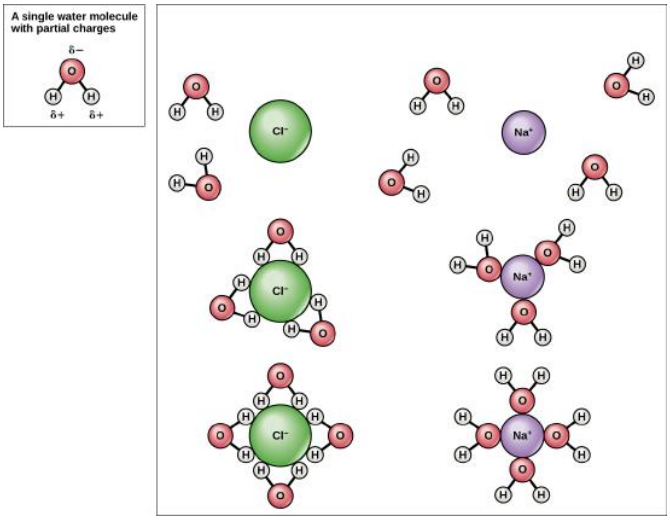


Figure **2.11.3**: This diagram shows the positive and negative parts of a water molecule. It also depicts how a charge, such as on an ion (Na or Cl, for example) can interact with a water molecule.

HYDROGEN BONDING

Opposite electrical charges attract one another. Therefore, the positive part of one water molecule is attracted to the negative parts of other water molecules. Because of this attraction, bonds form between hydrogen and oxygen atoms of adjacent water molecules, as demonstrated in Figure **2.11.4**. This type of bond always involves a hydrogen atom, so it is called a **hydrogen bond**.

Hydrogen bonds can also form within a single large organic molecule. For example, hydrogen bonds that form between different parts of a protein molecule bend the molecule into a distinctive shape, which is important for the protein's functions. Hydrogen bonds also hold together the two nucleotide chains of a DNA molecule.

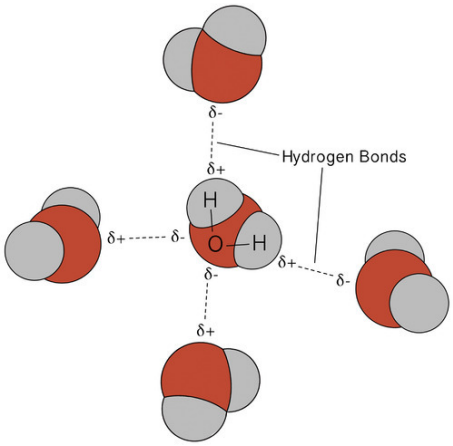


Figure **2.11.4**: Hydrogen bonds form between positively and negatively charged parts of water molecules. The bonds hold the water molecules together. How do you think this might affect water's properties?

STICKY, WET WATER

Water has some unusual properties due to its hydrogen bonds. One property is **cohesion**, the tendency for water molecules to stick together. The cohesive forces between water molecules are responsible for the phenomenon known as **surface tension**. The molecules at the surface do not have other like molecules on all sides of them, and consequently, they cohere more strongly with those directly associated with them on the surface. For example, if you drop a tiny amount of water onto a very smooth surface, the water molecules will stick together and form a droplet rather than spread out over the surface. The same thing happens when water slowly drips from a leaky faucet. The water doesn't fall from the faucet as individual water molecules but as droplets of water. The tendency of water to stick together in droplets is also illustrated by the dew drops in Figure **2.11.5**.



Figure **2.11.5**: Droplets of dew cling to a spider web, demonstrating cohesion, the tendency of water molecules to stick together because of hydrogen bonds.

Another important physical property of water is **adhesion**. In terms of water, adhesion is the bonding of a water molecule to another substance, such as the sides of a leaf's veins. This process happens because hydrogen bonds are special in that they break and reform with great frequency. This constant rearranging of hydrogen bonds allows a percentage of all the molecules in a given sample to bond to another substance. This grip-like characteristic that water molecules form causes **capillary action**, the ability of a liquid to flow against gravity in a narrow space. An example of capillary action is when you place a straw into a glass of water. The water seems to climb up the straw before you even place your mouth on the straw. The water has created hydrogen bonds with the surface of the straw, causing the water to adhere to the sides of the straw. As the hydrogen bonds keep interchanging with the straw's surface, the water molecules interchange positions, and some begin to ascend the straw.

Adhesion and capillary action are necessary to the survival of most organisms. It is the mechanism that is responsible for water transport in plants through roots and stems, and in animals through small blood vessels.

Hydrogen bonds also explain why water's boiling point (100°C) is higher than the boiling points of similar substances without hydrogen bonds. Because of water's relatively high boiling point, most water exists in a liquid state on Earth. Liquid water is needed by all living organisms. Therefore, the availability of liquid water enables life to survive over much of the planet.

Furthermore, water has a high specific heat because it takes a lot of energy to raise or lower the temperature of the water. As a result, water plays a very important role in temperature regulation. Since cells are made up of water, this property helps to maintain homeostasis.

THE DENSITY OF ICE AND WATER

The **melting point** of water is 0°C. Below this temperature, water is a solid (ice). Unlike most chemical substances, water in a solid state has a lower density than water in a liquid state. This is because water expands when it freezes. Again, hydrogen bonding is the reason. Hydrogen bonds cause water molecules to line up less efficiently in ice than in liquid water. As a result, water molecules are spaced farther apart in ice, giving ice a lower density than liquid water. A substance with lower density floats on a substance with higher density. This explains why ice floats on liquid water, whereas many other solids sink to the bottom of liquid water.

In a large body of water, such as a lake or the ocean, the water with the greatest density always sinks to the bottom. Water is most dense at about 4°C. As a result, the water at the bottom of a lake or the ocean usually has a temperature of about 4°C. In climates with cold winters, this layer of 4°C water insulates the bottom of a lake from freezing temperatures. Lake organisms such as fish can survive the winter by staying in this cold but unfrozen water at the bottom of the lake.

REVIEW

1. Describe the structure of a water molecule. What is polarity, and why is water polar?
2. Explain how the internal polarity of the water molecule makes it a good solvent.
3. Explain how hydrogen bonds cause molecules of liquid water to stick together.
4. What is capillary action? Give an example.
5. What property of water helps to maintain homeostasis and how?

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2.12: ACIDS AND BASES

DANGER! BATTERY ACID!

You probably know that car batteries like this one contain dangerous chemicals such as strong acids. Strong acids can hurt you if they come into contact with your skin or eyes. Therefore, it may surprise you that your life depends on acids. Many acids are inside your body, and some are as strong as battery acid. Acids are needed for digestion and some forms of energy production. Genes are made of nucleic acids, proteins of amino acids, and lipids of fatty acids.



Figure **2.12.1**: Car battery

WATER AND SOLUTIONS

Acids such as battery acid are solutions. A **solution** is a mixture of two or more substances with the same composition. Many solutions are a mixture of water and some other substance. Not all solutions are acids. Some are bases, and some are neither acids nor bases. You need to know more about pure water to understand acids and bases.

In pure water (such as distilled water), a tiny fraction of water molecules naturally breaks down to form ions. An ion is an electrically charged atom or molecule. The chemical equation represents the breakdown of water:

$$2H_2O \rightarrow H_3O^+ + OH^- \qquad (2.12.1)$$

The products of this reaction are a hydronium ion (H_3O^+) and a hydroxide ion (OH^-). The hydroxide ion, which has a negative charge, forms when a water molecule gives up a positively charged hydrogen ion (H^+). The hydronium ion, which has a positive charge, forms when another water molecule accepts the hydrogen ion.

ACIDITY AND PH

The concentration of hydronium ions in a solution is known as **acidity.** The concentration of hydronium ions in pure water is very low; only about 1 in 10 million water molecules naturally breaks down to form a hydronium ion. As a result, pure water is essentially neutral. Acidity is measured on a scale called **pH**. Pure water has a pH of 7, so the point of neutrality on the pH scale is 7.

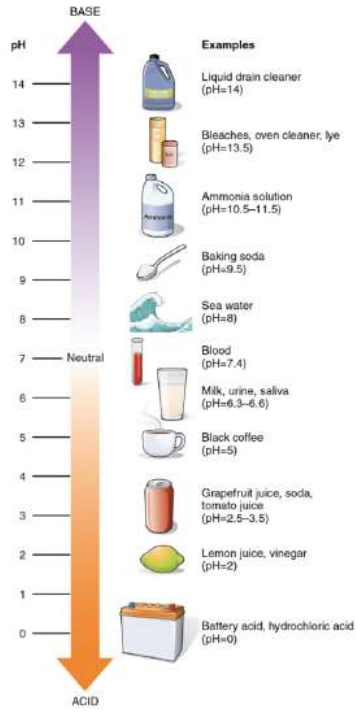


Figure **2.12.2**: This pH scale shows the acidity of many common substances. The lower the pH value, the more acidic a substance is.

Examples of pH

- Liquid drain cleaner has a pH = 14
- Bleaches, oven cleaner, lye have a pH = 13.5
- Ammonia solution has a pH = 10.5 - 11.5
- Baking soda has a pH = 9.5
- Sea water has a pH = 8
- Blood has a pH = 7.4
- Milk, urine, saliva have a pH = 6.3 - 6.6
- Black coffee has a pH = 5
- Grapefruit juice, soda, and tomato juice have a pH = 2.5 - 3.5
- Lemon juice, vinegar have a pH = 2
- Battery acid, hydrochloric acid have a pH = 0

ACIDS

A solution with a higher concentration of hydronium ions than pure water has a pH lower than 7. A solution with a pH lower than 7 is called an **acid**. As the hydronium ion concentration increases, the pH value decreases. Therefore, the more acidic a solution is, the lower its pH value is. Did you ever taste vinegar? Like other acids, it tastes sour. Stronger acids can be harmful to organisms. For example, stomach acid would eat through the stomach if not lined with a layer of mucus. Strong acids can also damage materials, even hard materials such as glass.

BASES

A solution with a lower concentration of hydronium ions than pure water has a pH higher than 7. This solution is called a **base**. Bases, such as baking soda, have a bitter taste. Like strong acids, strong

bases can harm organisms and damage materials. For example, lye can burn the skin, and bleach can remove the color from clothing.

ACIDS, BASES, AND ENZYMES

Many acids and bases in living things provide the pH that enzymes need. Enzymes are biological catalysts that must work effectively for biochemical reactions to occur. Most enzymes can do their job only at a certain level of acidity. Cells secrete acids and bases to maintain the proper pH for enzymes to do their work.

Every time you digest food, acids, and bases work in your digestive system. Consider the enzyme pepsin, which helps break down proteins in the stomach. Pepsin needs an acidic environment to do its job. The stomach secretes the hydrochloric acid that allows pepsin to work. When stomach contents enter the small intestine, the acid must be neutralized. This is because enzymes in the small intestine need a basic environment to work. An organ called the pancreas secretes a base named bicarbonate into the small intestine, and this base neutralizes the acid.

FEATURE: MY HUMAN BODY

Do you ever have heartburn? The answer is probably "yes." More than 60 million Americans have heartburn at least once a month, and more than 15 million suffer from it daily. Knowing more about heartburn may help you prevent it or know when to seek medical treatment.

Heartburn doesn't have anything to do with the heart, but it does cause a burning sensation in the vicinity of that organ. Normally, the acid secreted into the stomach remains in the stomach where it is needed to allow pepsin to do its job of digesting proteins. A long tube called the esophagus carries food from the mouth to the stomach. A sphincter, or valve, between the esophagus and stomach, opens to allow swallowed food to enter the stomach. Then, it closes to prevent stomach contents from flowing back into the esophagus. If this sphincter is weak or relaxes inappropriately, stomach contents flow into the esophagus. Because stomach contents are usually acidic, this causes a burning sensation known as heartburn. People who are prone to heartburn and suffer from it often may be diagnosed with GERD, which stands for gastroesophageal reflux disease.

GERD—as well as occasional heartburn—can often be improved by dietary and other lifestyle changes that decrease the amount and acidity of reflux from the stomach into the esophagus.

- Some foods and beverages seem to contribute to GERD, so these should be avoided. They include chocolate, fatty foods, peppermint, coffee, and alcoholic beverages.
- Decreasing portion size and eating the last meal of the day at least a couple of hours before bedtime may reduce the risk of reflux.
- Smoking weakens the lower esophageal sphincter, so quitting the habit may help control reflux.
- GERD is often associated with being overweight, and losing weight brings improvement.
- Some people are helped by sleeping with the head of the bed elevated. This allows gravity to help control the backflow of acids from the stomach into the esophagus.

REVIEW

1. What is the solution?
2. Define acidity.
3. Explain how acidity is measured.
4. Compare and contrast acids and bases.
5. The stomach secretes hydrochloric acid to provide an acidic environment for the enzyme pepsin. What is the pH of this acid? How strong of an acid is it compared with other acids?
6. *True or False*. Strong bases are gentle and cannot hurt you, unlike strong acids.
7. *True or False*. The lower the pH, the higher the concentration of hydronium ions.
8. Define an ion.
9. Identify the ions in the following equation and explain why they are ions:

$$2H_2O \rightarrow H_3O^+ + OH^- \qquad (2.12.2)$$

10. Explain why the pancreas secretes bicarbonate into the small intestine.
11. Do you think pepsin would work in the small intestine? Why or why not?
12. How does the pH of the stomach compare to the small intestine? It is
    A. the same as
    B. not as important as the pH of
    C. higher than
    D. lower than
13. You may have mixed vinegar and baking soda and noticed that they bubble and react with each other.
    A. Explain why this happens.
    B. Explain what happens to the pH of this solution after you mix the vinegar and baking soda.
14. Pregnancy hormones can cause the lower esophageal sphincter to relax. What effect do you think this has on pregnant women? Explain your answer.

ATTRIBUTIONS

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2.13: CASE STUDY CONCLUSION- DIET AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: DIET DILEMMA

After reading this chapter, you should be able to see numerous connections between chemistry, human life, and health. In Mohinder's situation, chemistry is involved in the reasons why their father has diabetes, why their personal risk of getting diabetes is high, and the different dietary changes they are considering.



Figure **2.13.1**: Fruits and yogurt

For instance, type 2 diabetes is caused mainly by a lack of response in the body to the hormone insulin, which causes problems in the regulation of blood sugar, or glucose. Insulin is a peptide hormone, and as you have learned, peptides are chains of amino acids. Therefore, insulin is in the class of biochemical compounds called proteins. Mohinder is at increased risk of diabetes partly because there is a genetic component to the disease. DNA, which is a type of chemical compound called a nucleic acid, is passed down from parents to their offspring and carries the instructions for the production of proteins in units called genes. If there is a problem in a gene (or genes) that contributes to the development of a disease, such as type 2 diabetes, this can get passed down to the offspring and may raise that child's risk of getting the disease.

But genetics is only part of the reason why Mohinder is at an increased risk of diabetes. Obesity itself is a risk factor and one that can be shared in families due to shared lifestyle factors such as poor diet and lack of exercise, in addition to genetics. Consumption of too many refined carbohydrates, such as white bread and soda, also may contribute to obesity and the development of diabetes. As you probably now know, these simple carbohydrates are more easily and quickly broken down in the digestive system to glucose than larger complex carbohydrate molecules, such as those found in vegetables and whole grains. This can lead to dramatic spikes in blood sugar levels, which is particularly problematic for people with diabetes because they have trouble maintaining their blood sugar at a safe level. You can understand why Mohinder's father limits the consumption of refined carbohydrates, and in fact, some scientific studies have shown that avoiding refined carbohydrates may actually help reduce the risk of getting diabetes in the first place.

Mohinder's friend recommended eating a low fat and high carbohydrate diet to lose weight, but you can see that which *type* of carbohydrate — simple or complex — is an important consideration. Eating lots of white bread and rice may not help Mohinder reduce their risk of diabetes! But a healthy diet that helps them lose weight may lower their risk of diabetes since obesity itself is a factor. Which specific diet will work best to help them lose weight probably depends on a variety of factors including their biology, lifestyle, and food preferences. Mohinder should consult with their doctor about their diet and exercise plan so that their specific situation can be taken into account and monitored by a medical professional.

Drinking enough water is usually good advice for everyone, especially if it replaces sugary drinks like soda. You now know that water is important for many of the chemical reactions that take place in the body.

Finally, you probably now realize that "chemicals" do not have to be scary, toxic substances. All matter consists of chemicals, including you, water, and healthy fresh fruits and vegetables, like the ones pictured above. When people advocate "clean eating" and avoiding "chemicals" in food, they are usually referring to avoiding synthetic, or man-made, chemical additives such as preservatives. This can be a healthy way to eat because it involves eating a variety of whole, fresh, unprocessed foods. But there is no reason to be scared of chemicals in general – they are simply molecules and how they react depends on what they are, what other molecules are present, and the environmental conditions surrounding them.

CHAPTER SUMMARY

By now, you should have a good understanding of the basics of the chemistry of life. Specifically, you have learned:

- All matter consists of chemical substances. A chemical substance has a definite and consistent composition and may be either an element or a compound.
- An element is a pure substance that cannot be broken down into other types of substances.
  - An atom is the smallest particle of an element that still has the properties of that element. Atoms, in turn, are composed of subatomic particles, including negative electrons, positive protons, and neutral neutrons. The number of protons in an atom determines the element it represents.
  - Atoms have equal numbers of electrons and protons so they have no charge. Ions are atoms that have lost or gained electrons so they have either a positive or negative charge. Atoms with the same number of protons but different numbers of neutrons are called isotopes.
  - There are almost 120 known elements. The majority of the elements are metals. A smaller number are nonmetals, including carbon, hydrogen, and oxygen.
- A compound is a substance that consists of two or more elements in a unique composition. The smallest particle of a compound is called a molecule. Chemical bonds hold together the atoms of molecules. We discussed four types of bonds, polar covalent bond, hydrogen bond, non-polar covalent bond, and ionic bond.

- In an ionic bond, an atom gives away one or more electrons to another atom.
- In a covalent bond, two atoms share one or more electrons. The equal sharing of electrons gives rise to a non- polar covalent bond, and unequal sharing of electrons gives rise to a polar covalent bond.
- The polar molecules make hydrogen bonds between them and within themselves.
- A chemical bond is a force of attraction between atoms or ions. Bonds form when atoms share or transfer valence electrons.
- Atoms form chemical bonds to achieve a full outer energy level, which is the most stable arrangement of electrons.

- Compounds can form only in chemical reactions, and they can break down only in other chemical reactions.
- Biochemical compounds are carbon-based compounds found in living things. They make up cells and other structures of organisms and carry out life processes. Most biochemical compounds are large molecules called polymers that consist of many repeating units of smaller molecules called monomers.
- There are millions of different biochemical compounds, but all of them fall into four major classes: carbohydrates, lipids, proteins, and nucleic acids.
- Carbohydrates are the most common class of biochemical compounds. They provide cells with energy, store energy, and make up organic structures such as the cell walls of plants. The basic building block of carbohydrates is the monosaccharide.
  - Sugars are short-chain carbohydrates that supply us with energy. Simple sugars, such as glucose, consist of just one monosaccharide. Some sugars, such as sucrose, or table sugar, consist of two monosaccharides and are called disaccharides. Disaccharides are formed with the condensation reaction.
  - Complex carbohydrates, or polysaccharides, consist of hundreds or even thousands of monosaccharides. They include starch, glycogen, cellulose, and chitin.
    - Starch is made by plants to store energy and is readily broken down to its component sugars during digestion.
    - Glycogen is made by animals and fungi to store energy and plays a critical part in the homeostasis of blood glucose levels in humans.
    - Cellulose is the most common biochemical compound in living things. It forms the cell walls of plants and certain algae. Humans cannot digest cellulose, but it makes up most of the crucial dietary fiber in the human diet.
    - Chitin makes up organic structures such as the cell walls of fungi and the exoskeletons of insects and other arthropods.
- Lipids include fats and oils. They store energy, form cell membranes, and carry messages.
  - Lipid molecules consist mainly of repeating units called fatty acids. Fatty acids may be saturated or unsaturated, depending on the proportion of hydrogen atoms they contain. Animals store fat as saturated fatty acids; plants store fat as unsaturated fatty acids.
  - Types of lipids include triglycerides, phospholipids, and steroids.
    - Triglycerides contain glycerol (an alcohol) in addition to fatty acids. Humans and other animals store fat as triglycerides in fat cells.
    - Phospholipids contain phosphate and glycerol in addition to fatty acids. They are the main component of cell membranes in all living things.
    - Steroids are lipids with a four-ring structure. Some steroids, such as cholesterol, are important components of cell membranes. Many other steroids are hormones.
- Proteins include enzymes, antibodies, and numerous other important compounds in living things. They have many functions including helping cells keep their shape, making up muscles, speeding up chemical reactions, and carrying messages and materials.
  - Proteins are made up of small monomer molecules called amino acids.
  - A peptide bond is formed between two amino acids when they come together in a condensation synthesis reaction. Long chains of amino acids form polypeptides. The sequence of amino acids in polypeptides makes up the primary structure of proteins. Secondary structure refers to configurations such as helices and sheets within polypeptide chains. Tertiary structure is a protein's overall three-dimensional shape, which controls the molecule's basic function. A quaternary structure forms if multiple protein molecules join together and function as a complex.
  - The chief characteristic that allows proteins' diverse functions is their ability to bind specifically and tightly with other molecules.
- Nucleic acids include DNA and RNA. They encode instructions for making proteins, helping make proteins, and passing the encoded instructions from parents to offspring.
  - Nucleic acids are built of monomers called nucleotides, which bind together in long chains to form polynucleotides. DNA consists of two polynucleotides, and RNA consists of one polynucleotide.
  - Each nucleotide consists of a sugar molecule, phosphate group, and a nitrogen base. Sugars and phosphate groups of adjacent nucleotides bind together to form the "backbone" of the polynucleotide. Bonds between complementary bases hold together the two polynucleotide chains of DNA and cause it to take on its characteristic double helix shape.
  - DNA makes up genes, and the sequence of nitrogen bases in DNA makes up the genetic code for the synthesis of proteins. RNA helps synthesize proteins in cells. The genetic code in DNA is also passed from parents to offspring during

reproduction, explaining how inherited characteristics are passed from one generation to the next.

- A chemical reaction is a process that changes some chemical substances into others. A substance that starts a chemical reaction is called a reactant, and a substance that forms in a chemical reaction is called a product. During the chemical reaction, bonds break in reactants and new bonds form in products.
- Chemical reactions can be represented by chemical equations. According to the law of conservation of mass, mass is always conserved in a chemical reaction, so a chemical equation must be balanced, with the same number of atoms of each type of element in the products as in the reactants.
- Many chemical reactions occur all around us each day, such as iron rusting and organic matter rotting, but not all changes are chemical processes. Some changes, such as ice melting or paper being torn into smaller pieces, are physical processes that do not involve chemical reactions and the formation of new substances.
- All chemical reactions involve energy and need activation energy to begin. Exergonic reactions release energy. Endergonic reactions absorb energy.
- Biochemical reactions are chemical reactions that take place inside living things. The sum of all the biochemical reactions in an organism is referred to as metabolism. Metabolism includes catabolic reactions, which are exothermic reactions, and anabolic reactions, which are endothermic reactions.
- Most biochemical reactions need a biological catalyst called an enzyme to speed up the reaction by reducing the amount of activation energy needed for the reaction to begin. Most enzymes are proteins that affect just one specific substance, called the enzyme's substrate.
- Water is a polar molecule; therefore, water molecules make hydrogen bonds between them. Due to this property water exists as a liquid over a wide range of temperatures and dissolves many substances. These properties depend on water's polarity, which causes water molecules to "stick" together.
- Organisms need water to dissolve many substances and for most biochemical processes, including photosynthesis and cellular respiration.
- A solution is a mixture of two or more substances that has the same composition throughout. Many solutions consist of water and one or more dissolved substances.
- Acidity is a measure of the hydronium ion concentration in a solution. Pure water has a very low concentration and a pH of 7, which is the point of neutrality on the pH scale. Acids have a higher hydronium ion concentration than pure water and a pH lower than 7. Bases have a lower hydronium ion concentration than pure water and a pH higher than 7.
- Many acids and bases in living things are secreted to provide the proper pH for enzymes to work properly.

Now that you understand the chemistry of the molecules that make up living things, in the next chapter you will learn how these molecules make up the basic unit of structure and function in living organisms — cells — and will be able to understand some of the crucial chemical reactions that occur within cells.

CHAPTER SUMMARY REVIEW

1. The four major classes of biochemical compounds are carbohydrates, lipids, proteins, and nucleic acids. For each of the substances below, identify which of these classes includes the substance.
   A. Enzymes
   B. Fructose
   C. DNA
   D. RNA
   E. Steroids
2. The chemical formula for the complex carbohydrate glycogen is C24H42O21.
   A. What are the elements in glycogen?
   B. How many atoms are in one molecule of glycogen?
   C. Is glycogen an ion? Why or why not?
   D. Is glycogen a monosaccharide or polysaccharide? Besides memorizing this fact, how would you know this based on the information in the question?
   E. What is the function of glycogen in the human body?
3. What is the difference between an ion and a polar molecule? Give an example of each in your explanation.
4. Define monomer and polymer.
5. For each of the following polymers, identify the name of its monomers.
   A. RNA
   B. Protein
   C. Complex carbohydrate
6. What is the difference between a protein and a polypeptide?
7. People with diabetes have trouble controlling the level of glucose in their bloodstream. Knowing this, why do you think it is often recommended that people with diabetes limit their consumption of carbohydrates?
8. Identify each of the following reactions as endergonic or exergonic.
   A. Cellular respiration
   B. Photosynthesis
   C. Catabolic reactions
   D. Anabolic reactions
9. Pepsin is an enzyme in the stomach that helps us digest protein. Answer the following questions about pepsin.
   A. What is the substrate for pepsin?
   B. How does pepsin work to speed the reaction of protein digestion?
   C. Given what you know about the structure of proteins, what do you think are some of the products of the reaction that pepsin catalyzes?
   D. The stomach is normally acidic. What do you think would happen to the activity of pepsin and the effect on protein

digestion if the pH is raised significantly?

10. What defines a neutral pH? What is the numerical value of a neutral pH?
11. *True or False.* Unsaturated fatty acids have straight chains.
12. *True or False.* The DNA code carries instructions for the correct sequence of nucleic acids in a protein.
13. *True or False.* Phospholipids make up cell membranes.
14. The function of proteins can include
    A. helping cells keep their shape
    B. helping to destroy foreign substances
    C. speeding up biochemical reactions
    D. all of the above
15. Which of the following is not part of a nucleotide?
    A. nitrogen base
    B. cellulose molecule
    C. sugar molecule
    D. phosphate group
16. The "push" needed to start a chemical reaction is the
    A. enzymatic energy
    B. endothermic energy
    C. activation energy
    D. reactant energy

ATTRIBUTIONS

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CHAPTER OVERVIEW

3: CELLS

This chapter outlines the discovery of cells and cell theory. It identifies ways in which all cells are alike and ways in which they vary. The chapter describes in detail important cell structures and their functions; and it explains how cells obtain energy, grow, and divide.

3.1: Case Study- The Importance of Cells
3.2: Discovery of Cells and Cell Theory
3.3: Variation in Cells
3.4: Plasma Membrane
3.5: Cytoplasm and Cytoskeleton
3.6: Cell Organelles
3.7: Cell Transport
3.8: Active Transport and Homeostasis
3.9: Cellular Respiration
3.10: Fermentation
3.11: Case Study Conclusion- Tired and Chapter Summary

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3.1: CASE STUDY- THE IMPORTANCE OF CELLS

CASE STUDY: MORE THAN JUST TIRED

We all get tired sometimes, especially if we have been doing a lot of physical activity. But for Jasmin, a 34-year-old former high school track star who is now a recreational runner, her tiredness was going far beyond what she thought should be normal for someone who is generally in good physical shape. She was experiencing extreme fatigue after her runs, as well as muscle cramping, spasms, and an unusual sense of heaviness in her legs. At first, she chalked it up to getting older, but her exhaustion and pain worsened to the point where this former athlete could no longer run for more than a few minutes at a time. She also began to experience other unusual symptoms, such as blurry vision and vomiting for no apparent reason.



Figure **3.1.1**: Exhausted

Concerned, she went to her doctor. Her doctor ran many tests and consulted with several specialists. After several months, Jasmin is finally diagnosed with a mitochondrial disease. Jasmin is surprised. She has an 8-year-old niece with a mitochondrial disease, but her niece's symptoms started when she was very young, and included seizures and learning disabilities. How can Jasmin have the same disease but different symptoms? Why did she not have problems until adulthood while her niece had symptoms at an early age? And what are mitochondria anyway?

CHAPTER OVERVIEW: CELLS

As you will learn in this chapter, mitochondria are important structures within our cells. This chapter will describe cells, which are the basic unit of structure and function in all living organisms. Specifically, you will learn:

- How cells were discovered, their common structures, and the principles of cell theory.
- The importance of size and shape in the functions of cells.
- The differences between eukaryotic cells (such as those in humans and other animals) and prokaryotic cells (such as bacteria).
- The structures and functions of parts of cells including mitochondria, the plasma membrane, cytoplasm, cytoskeleton, nucleus, ribosomes, Golgi apparatus, endoplasmic reticulum, vesicles, and vacuoles.
- How the processes of passive and active transport move substances into and out of cells and help maintain homeostasis.
- How organisms obtain the energy needed for life, including how the sugar glucose is broken down to produce ATP through the processes of aerobic cellular respiration and anaerobic respiration.

As you read this chapter, think about the following questions related to Jasmin's disease:

1. What are mitochondria? What is their structure, function, and where did they come from during evolution?
2. Why are fatigue and "exercise intolerance," such as Jasmin's extreme exhaustion after running, common symptoms of mitochondrial diseases?
3. Why do you think Jasmin has symptoms that affect so many different parts of her body including her legs, eyes, and digestive system?

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3.2: DISCOVERY OF CELLS AND CELL THEORY

A BIG BLUE CELL

What is this incredible object? Would it surprise you to learn that it is a human cell? The cell is actually too small to see with the unaided eye. It is visible here in such detail because it is being viewed with a very powerful microscope. Cells may be small in size, but they are extremely important for life. Like all other living things, you are made of cells. Cells are the basis of life, and without cells, life as we know it would not exist. You will learn more about these amazing building blocks of life when you read this section.

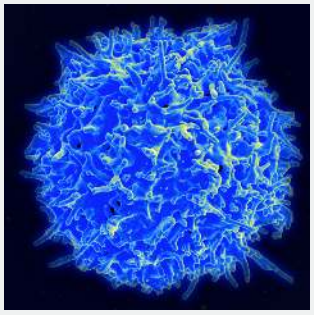


Figure **3.2.1**: Healthy human T-cell

If you look at a living matter with a microscope — even a simple light microscope — you will see that it consists of cells. **Cells** are the basic units of the structure and function of living things. They are the smallest units that can carry out the processes of life. All organisms are made up of one or more cells, and all cells have many of the same structures and carry out the same basic life processes. Knowing the structure of cells and the processes they carry out is necessary to understanding life itself.

DISCOVERY OF CELLS

The first time the word *cell* was used to refer to these tiny units of life was in 1665 by a British scientist named Robert Hooke. Hooke was one of the earliest scientists to study living things under a microscope. The microscopes of his day were not very strong, but Hooke was still able to make an important discovery. When he looked at a thin slice of cork under his microscope, he was surprised to see what looked like a honeycomb. Hooke made the drawing in the figure below to show what he saw. As you can see, the cork was made up of many tiny units, which Hooke called cells.

Soon after Robert Hooke discovered cells in cork, Anton van Leeuwenhoek in Holland made other important discoveries using a microscope. Leeuwenhoek made his own microscope lenses, and he was so good at it that his microscope was more powerful than other microscopes of his day. In fact, Leeuwenhoek's microscope was almost as strong as modern light microscopes. Using his microscope, Leeuwenhoek was the first person to observe human cells and bacteria.

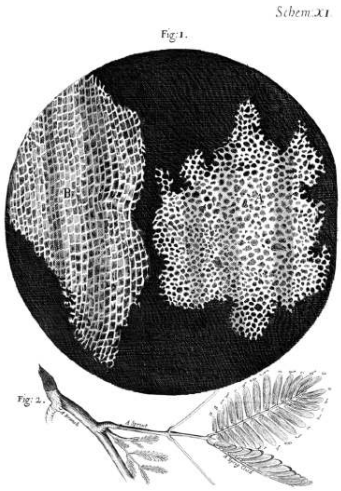


Figure **3.2.2**: Robert Hooke sketched these cork cells as they appeared under a simple light microscope.

CELL THEORY

By the early 1800s, scientists had observed the cells of many different organisms. These observations led two German scientists, named Theodor Schwann and Matthias Jakob Schleiden, to propose that cells are the basic building blocks of all living things. Around 1850, a German doctor named Rudolf Virchow was studying cells under a microscope when he happened to see them dividing and forming new cells. He realized that living cells produce new cells through division. Based on this realization, Virchow proposed that living cells arise only from other living cells.

The ideas of all three scientists — Schwann, Schleiden, and Virchow — led to **cell theory**, which is one of the fundamental theories unifying all of biology. Cell theory states that:

- All organisms are made of one or more cells.
- All the life functions of organisms occur within cells.
- All cells come from already existing cells.

SEEING INSIDE CELLS

Starting with Robert Hooke in the 1600s, the **microscope** opened up an amazing new world — the world of life at the level of the cell. As microscopes continued to improve, more discoveries were made about the cells of living things. However, by the late 1800s, light microscopes had reached their limit. Objects much smaller than cells, including the structures inside cells, were too small to be seen with even the strongest light microscope.

Then, in the 1950s, a new type of the microscope was invented. Called the electron microscope, it used a beam of electrons instead of light to observe extremely small objects. With an electron microscope, scientists could finally see the tiny structures inside cells. In fact, they could even see individual molecules and atoms. The electron microscope had a huge impact on biology. It allowed scientists to study organisms at the level of their molecules and led

to the emergence of the field of cell biology. With the electron microscope, many more cell discoveries were made. Figure **3.2.3** shows how the cell structures called **organelles** appear when scanned by an electron microscope.

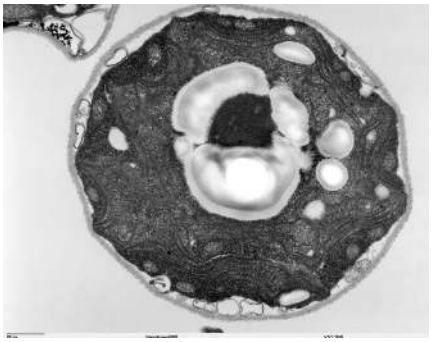


Figure **3.2.3**: An electron microscope produced this image of the structures inside a cell.

STRUCTURES SHARED BY ALL CELLS

Although cells are diverse, all cells have certain parts in common. These parts include a plasma membrane, cytoplasm, ribosomes, and DNA.

1. The **plasma membrane** (also called the cell membrane) is a thin coat of phospholipids that surrounds a cell. It forms the physical boundary between the cell and its environment, so you can think of it as the "skin" of the cell.
2. **Cytoplasm** refers to all of the cellular material inside the plasma membrane. The Cytoplasm is made up of a watery substance called cytosol and contains other cell structures such as ribosomes.
3. **Ribosomes** are structures in the cytoplasm where proteins are made.
4. **DNA** is a nucleic acid found in cells. It contains the genetic instructions that cells need to make proteins.

These parts are common to all cells, from organisms as different as bacteria and human beings. How did all known organisms come to have such similar cells? The similarities show that all life on Earth has a common evolutionary history.

REVIEW

1. Describe cells.
2. Explain how cells were discovered.
3. Outline how cell theory developed.
4. Identify structures shared by all cells.
5. *True or False.* Cork is not a living organism.
6. *True or False.* Some organisms are made of only one cell.
7. *True or False.* Ribosomes are found outside of the cytoplasm of a cell.
8. Proteins are made on _____ .
9. What are the differences between a light microscope and an electron microscope?
10. The first microscopes were made around
    A. 1965
    B. 1665
    C. 1950
    D. 1776
11. Which of these scientists made each of the following discoveries? (Anton van Leeuwenhoek; Robert Hooke; Rudolf Virchow)
    A. Observed some of the first cells and first used the term "cell"
    B. Observed the first human cells
    C. Observed cells dividing
12. Robert Hooke sketched what looked like honeycombs, or repeated circular or square units when he observed plant cells under a microscope.
    A. What is each unit?
    B. Of the shared parts of all cells, what makes up the outer surface of each unit?
    C. Of the shared parts of all cells, what makes up the inside of each unit?

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3.3: VARIATION IN CELLS

BACTERIA ATTACK!

Figure **3.3.1** shows a bacterial cell (colored green) attacking human red blood cells. The bacterium causes a disease called relapsing fever. The bacterial and human cells look very different in size and shape. Although all living cells have certain things in common — such as a plasma membrane and cytoplasm — different types of cells, even within the same organism, may have their own unique structures and functions. Cells with different functions generally have different shapes that suit them for their particular job. Cells vary not only in shape but also in size, as this example shows. In most organisms, however, even the largest cells are no bigger than the period at the end of this sentence. Why are cells so small?



Figure **3.3.1**: Bacterial cell attacking a human red blood cell

EXPLAINING CELL SIZE

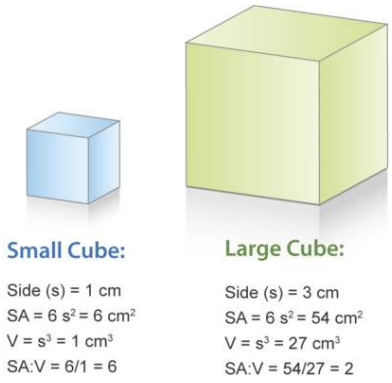


Figure **3.3.2**: Surface Area to Volume Comparison. A larger cube has a smaller surface area (SA) to volume (V) ratio than a smaller cube. This also holds true for cells and limits how large they can be.

Table **3.3.1**: Characteristics of small and large cubes

Characteristic	Small Cube	Large Cube
sides (S)	$1cm$	$3cm$
Surface Area (SA)	$6S^2 = 6 \times 1^2 = 6cm^2$	$6S^2 = 6 \times 3^2 = 54cm^2$
Volume (V)	$S^3 = 1^3 = 1cm^3$	$S^3 = 3^3 = 27cm^3$
SA:V	$SA/V = 6/1 = 6$	$SA/V = 54/27 = 2$

Most organisms, even very large ones, have microscopic cells. Why don't cells get bigger instead of remaining tiny and multiplying? What limits cell size?

The answers to these questions are clear once you know how a cell functions. To carry out life processes, a cell must be able to quickly pass substances into and out of the cell. For example, it must be able to pass nutrients and oxygen into the cell and waste products out of the cell. Anything that enters or leaves a cell must cross its outer surface. It is this need to pass substances across the surface that limits how large a cell can be.

Look at the two cubes in Figure **3.3.2**. As this figure and table show, a larger cube has less surface area relative to its volume than a smaller cube. This relationship also applies to cells; a larger cell has less surface area relative to its volume than a smaller cell. A cell with a larger volume also needs more nutrients and oxygen and produces more wastes. Because all of these substances must pass through the surface of the cell, a cell with a large volume will not have enough surface area to allow it to meet its needs. The larger the cell is, the smaller its ratio of surface area to volume, and the harder it will be for the cell to get rid of its wastes and take in necessary substances. This is what limits the size of the cell.

CELL FORM AND FUNCTION

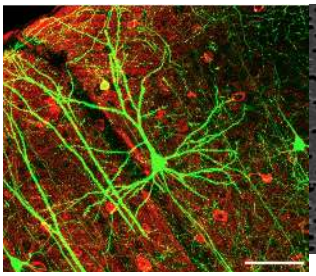


Figure **3.3.3**: Human nerve cell

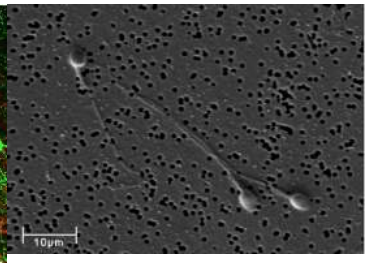


Figure **3.3.4**: Human sperm cells

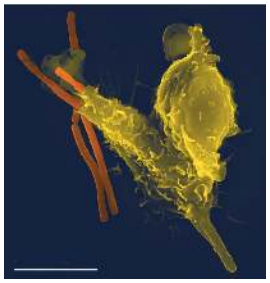


Figure **3.3.5**: Human white blood cell

Cells with different functions often have different shapes. The cells in Figure **3.3.3** - Figure **3.3.5** are just a few examples of the many different shapes that human cells may have. Each type of cell in the figure has characteristics that help it do its job. For example, the job of the nerve cell is to carry messages to other cells. The nerve cell has many long extensions that reach out in all directions, allowing it to pass messages to many other cells at once. Do you see the tail of each tiny sperm cell? Its tail helps a sperm cell "swim" through fluids in the female reproductive tract in order to reach an egg cell. The white blood cell has the job of destroying bacteria and other pathogens. Figure **3.3.5** shows the large white blood cell (in yellow) engulfing and destroying bacteria (in orange).

CELLS WITH AND WITHOUT A NUCLEUS

There is a basic cell structure that is present in many but not all living cells: the nucleus. The nucleus of a cell is a structure in the cytoplasm that is surrounded by a membrane (the nuclear membrane) and contains DNA. Based on whether or not they have a nucleus, there are two basic types of cells: prokaryotic cells and eukaryotic cells.

PROKARYOTIC CELLS

Prokaryotic cells are cells without a nucleus. The DNA in prokaryotic cells is in the cytoplasm rather than enclosed within a nuclear membrane. Prokaryotic cells are found in single-celled organisms, such as the bacterium represented by the model below. Organisms with prokaryotic cells are called **prokaryotes**. They were the first type of organisms to evolve and are still the most common organisms today.

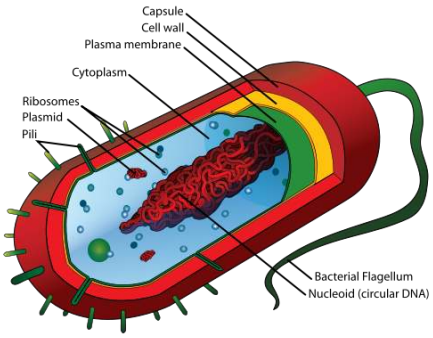


Figure **3.3.6**: Prokaryotic Cell. This diagram shows the structure of a typical prokaryotic cell, a bacterium. Like other prokaryotic cells, this bacterial cell lacks a nucleus but has other cell parts, including a plasma membrane, cytoplasm, ribosomes, and DNA.

Table **3.3.2**: Prokaryotic cell structures

Cell Structure	Description
Flagellum	Long projection(s) outside of the cell in some bacteria; aids in the motility
Pili	Small projections outside of the cell; aid in attachment
Capsule	A thick protective layer outside the cell wall of some bacteria
Cell wall	Outer layer of bacterial cells; more chemically complex than eukaryotic cell walls
Plasma Membrane	Phospholipid bilayer marking the outside of the cytoplasm
Cytoplasm	The fluid portion of the cell
Ribosome	Involved in protein synthesis
Nucleoid	Circular DNA found in the cytoplasm
Plasmid	Small loops of DNA found in some bacteria

EUKARYOTIC CELLS

Eukaryotic cells are cells that contain a nucleus. A typical eukaryotic cell is represented by the model below. Eukaryotic cells are usually larger than prokaryotic cells. They are found in some single-celled and all multicellular organisms. Organisms with eukaryotic cells are called **eukaryotes**, and they range from fungi to people.

Besides a nucleus, eukaryotic cells also contain other organelles. An **organelle** is a structure within the cytoplasm that performs a specific job in the cell. Organelles called mitochondria, for example, provide energy to the cell, and organelles called vacuoles store substances in the cell. Organelles allow eukaryotic cells to carry out more functions than prokaryotic cells can.

Table **3.3.3**: Eukaryotic cell structures

Structure	Location	Description
Flagellum	Outside the cell	A projection used for locomotion in some eukaryotic cells
Plasma Membrane	Outer layer of cell	Phospholipid bilayer enclosing the cytoplasm
Cytoplasm	Bound by the plasma membrane	Entire region between the plasma membrane and the nuclear envelope, consisting of organelles suspended in the gel-like cytosol, the cytoskeleton, and various chemicals
Golgi Vesicles (Golgi Apparatus)	Cytoplasm	A series of stacked membranes that sorts, tags, and packages lipids and proteins for distribution
Ribosomes	free-floating or on rough ER	Involved in protein synthesis
Rough Endoplasmic Reticulum	Cytoplasm	Interconnected membranous structures that are studded with ribosomes and engage in protein modification and phospholipid synthesis
Smooth Endoplasmic Reticulum	Cytoplasm	Interconnected membranous structures that have few or no ribosomes on its cytoplasmic surface and synthesize carbohydrates, lipids, and steroid hormones; detoxifies certain chemicals (like pesticides, preservatives, medications, and environmental pollutants), and stores calcium ions
Mitochondria	Cytoplasm	(singular = mitochondrion) cellular organelles responsible for carrying out cellular respiration, resulting in producing ATP, the cell's main energy-carrying molecule
Peroxisome	Cytoplasm	The small, round organelle that contains hydrogen peroxide, and detoxifies many poisons
Lysosome	Cytoplasm	Organelle in an animal cell that functions as the cell's digestive component; it breaks down proteins, polysaccharides, lipids, nucleic acids, and even worn-out organelles
Secretory Vesicle	Cytoplasm	Small, membrane-bound sac that functions in cellular storage and transport; its membrane is capable of fusing with the plasma membrane and the membranes of the endoplasmic reticulum and Golgi apparatus
Centrosome (with 2 centrioles)	Cytoplasm	Region in animal cells made of two centrioles that serve as an organizing center for microtubules
Actin Filaments	Cytoskeleton	The cytoskeleton's narrowest element; it provides rigidity and shape to the cell and enables cellular movements
Intermediate Filaments	Cytoskeleton	Cytoskeletal component, comprised of several fibrous protein intertwined strands, that bears tension, supports cell-cell junctions, and anchors cells to extracellular structures
Microtubules	Cytoskeleton	The cytoskeleton's widest element; provides a track along which vesicles move through the cell, pulls replicated chromosomes to opposite ends of a dividing cell, and is the structural element of centrioles
Cytoskeleton	Throughout cell	Protein fiber network that collectively maintains the cell's shape, secures some organelles in specific positions and allows cytoplasm and vesicles to move within the cell
Nucleus	Cytoplasm	Cell organelle that houses the cell's DNA and directs ribosome and protein synthesis
Nuclear Pore	Nucleus	Pores in the nuclear envelope allow substances to enter and exit the nucleus.
Nuclear Envelope	Nucleus	Double-membrane structure that constitutes the nucleus' outermost portion
Chromatin	Nucleus	Protein-DNA complex that serves as the chromosomes' building material
Nucleolus	Nucleus	Darkly staining body within the nucleus that is responsible for assembling ribosome subunits

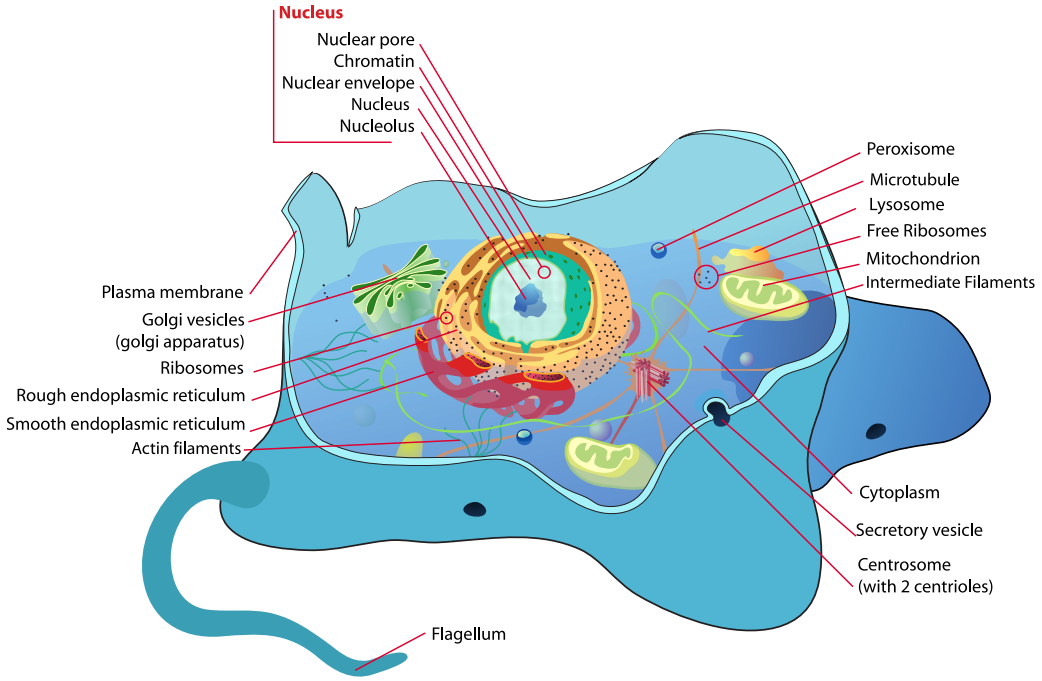


Figure **3.3.7**: Eukaryotic Cell. Compare and contrast the eukaryotic cell shown here with the prokaryotic cell. What similarities and differences can you identify?

REVIEW

1. Explain why most cells are very small.
2. Discuss variations in the form and function of cells.
3. Compare and contrast prokaryotic and eukaryotic cells.
4. *True or False.* Prokaryotic cells do not have mitochondria.
5. *True or False.* Prokaryotic cells do not have DNA.
6. *True or False.* All single-celled organisms are prokaryotes.
7. Which was the first type of organism to evolve – eukaryotes or prokaryotes? Based on their structures, does this make sense to you? Explain your answer.
8. Do human cells have organelles? Explain your answer.
9. Which are usually larger – prokaryotic or eukaryotic cells? What do you think this means for their relative ability to take in needed substances and release wastes? Discuss your answer.
10. DNA in eukaryotes is enclosed within the _____ _____.
11. Name three different types of cells in humans.
12. Which organelle provides energy in eukaryotic cells?
13. What is the function of a vacuole in a cell?

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3.4: PLASMA MEMBRANE

A BAG FULL OF JELL-O

This simple, cut-away model of an animal cell (Figure **3.4.1**) shows that a cell resembles a plastic bag full of Jell-O. Its basic structure is a plasma membrane filled with cytoplasm. Like Jell-O containing mixed fruit, the cytoplasm of the cell also contains various structures, such as a nucleus and other organelles. Your body is made up of trillions of cells, but all of them perform the same basic life functions. They all obtain and use energy, respond to the environment, and reproduce. How do your cells carry out these basic functions and keep themselves — and you — alive? To answer these questions, you need to know more about the structures that make up cells, starting with the plasma membrane.



Figure **3.4.1**: Animal cell model

The plasma membrane is a structure that forms a barrier between the cytoplasm inside the cell and the environment outside the cell. Without the plasma membrane, there would be no cell. The membrane also protects and supports the cell and controls everything that enters and leaves it. It allows only certain substances to pass through while keeping others in or out. To understand how the plasma membrane controls what passes into or out of the cell, you need to know its basic structure.

PHOSPHOLIPID BILAYER

The **plasma membrane** is composed mainly of **phospholipids**, which consist of fatty acids and alcohol. The phospholipids in the plasma membrane are arranged in two layers, called a **phospholipid bilayer**, with a hydrophobic, or water-hating, interior and a hydrophilic, or water-loving, exterior. Each phospholipid molecule has a head and two tails. The head “loves” water (hydrophilic) and the tails “fear” water (hydrophobic). The water-fearing tails are on the interior of the membrane, whereas the water-loving heads point outwards, toward either the cytoplasm or the fluid that surrounds the cell. The polar head group and fatty acid chains are attached by a 3-carbon glycerol unit. Figure **3.4.2** shows a single phospholipid next to a phospholipid bilayer.

Molecules that are hydrophobic can easily pass through the plasma membrane if they are small enough because they are water-hating like the interior of the membrane. Molecules that are hydrophilic, on the other hand, cannot pass through the plasma membrane — at least not without help — because they are water-loving like the exterior of the membrane.

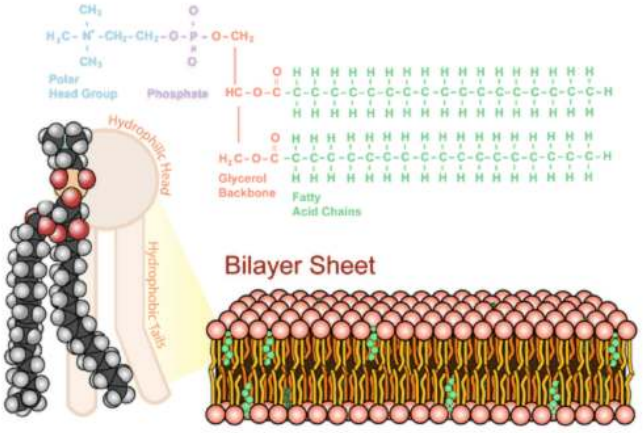


Figure **3.4.2**: Phospholipid and a phospholipid Bilayer.

OTHER MOLECULES IN THE PLASMA MEMBRANE

The plasma membrane also contains other molecules, primarily other lipids and proteins. The green molecules in Figure **3.4.2**, for example, are the lipid cholesterol. Molecules of the steroid lipid cholesterol help the plasma membrane keep its shape. (Figure **3.4.3**) shows the cholesterol molecules as yellow structures within the center of the phospholipid bilayer. Other structures shown in (Figure **3.4.3**):

- Protein channels. These span the full membrane and have a space within them because they are used to transport materials into or out of the cell.
- Transmembrane proteins. The root "trans" explains that these span (go "across") the membrane. Transmembrane proteins can have a variety of functions.
- Peripheral proteins. These are found only on one side of the membrane. They can be found on either the cytoplasmic side or the outside of the membrane.
- Glycoproteins. These consist of a protein in the plasma membrane with chains of carbohydrates projecting out of the cell.
- Glycolipids. These are chains of carbohydrates attached directly to a lipid in the membrane. Both glycoproteins and glycolipids act as labels to identify the cell.
- Filaments of cytoskeleton are found along the cytoplasmic side of the membrane and provide a scaffolding for the membrane.

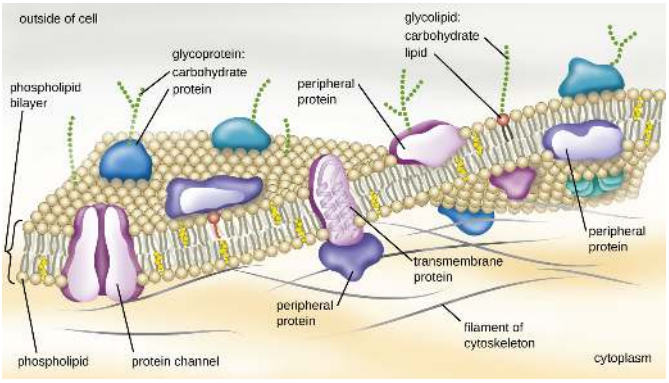


Figure **3.4.3**: The figure illustrates the major components of the phospholipid bilayer.

ADDITIONAL FUNCTIONS OF THE PLASMA MEMBRANE

The plasma membrane may have extensions, such as whip-like **flagella** or brush-like **cilia**, that give it other functions. In single-celled organisms, like those shown below, these membrane extensions may help the organisms move. In multicellular organisms, the extensions have different functions. For example, the cilia on human lung cells sweep foreign particles and mucus toward the mouth and nose.

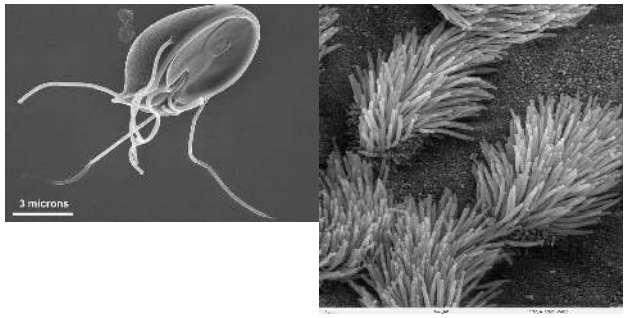


Figure **3.4.4**: Flagella of Giardia (left) and cilia of human respiratory mucosa (right). Flagella and cilia are extensions of the plasma membrane of many cells.

FEATURE: MY HUMAN BODY

If you smoke and need another reason to quit, here's a good one. We usually think of lung cancer as a major disease caused by smoking. But smoking can have devastating effects on the body's ability to protect itself from repeated, serious respiratory infections, such as bronchitis and pneumonia.

Cilia are microscopic, hair-like projects on cells that line the respiratory, reproductive, and digestive systems. Cilia in the respiratory system line most of your airways where they have the job of trapping and removing dust, germs, and other foreign particles before they can make you sick. Cilia secrete mucus that traps particles, and they move in a continuous wave-like motion that sweeps the mucus and particles upward toward the throat, where they can be expelled from the body. When you are sick and cough up phlegm, that's what you are doing.

Smoking prevents cilia from performing these important functions. Chemicals in tobacco smoke paralyze the cilia so they can't sweep mucus out of the airways and they also inhibit the cilia from producing mucus. Fortunately, these effects start to wear off soon after the last exposure to tobacco smoke. If you stop smoking, your cilia will return to normal. Even if prolonged smoking has destroyed cilia, they will regrow and resume functioning in a matter of months after you stop smoking.

REVIEW

1. What are the general functions of the plasma membrane?
2. Describe the phospholipid bilayer of the plasma membrane.
3. Identify other molecules in the plasma membrane, and state their functions.
4. Why do some cells have plasma membrane extensions such as flagella and cilia?
5. Explain why hydrophilic molecules cannot easily pass through the cell membrane. What type of molecule in the cell membrane might help hydrophilic molecules pass through it?
6. Which part of a phospholipid molecule in the plasma membrane is made of fatty acid chains? Is this part hydrophobic or hydrophilic?
7. The two layers of phospholipids in the plasma membrane are called a phospholipid _____.
8. *True or False.* The flagella on your lung cells sweep foreign particles and mucus toward your mouth and nose.
9. *True or False.* Small hydrophobic molecules can easily pass through the plasma membrane.
10. *True or False.* The side of the cell membrane that faces the cytoplasm is hydrophilic.
11. Steroid hormones can pass directly through cell membranes. Why do you think this is the case?
12. Some antibiotics work by making holes in the plasma membrane of bacterial cells. How do you think this kills the cells?
13. What is the name of the long, whip-like extensions of the plasma membrane that helps some single-celled organisms move?

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3.5: CYTOPLASM AND CYTOSKELETON

A PEEK INSIDE THE CELL

Figure **3.5.1** may look like a colorful work of abstract art or maybe an ultra-modern carpet design, but it's neither. It is actually a model of the interior of a cell. It's an artist's representation of what you might see if you could take a peek inside one of these basic building blocks of living things. A cell's interior is obviously a crowded and busy space. It contains cytoplasm, dissolved substances, and many structures; and it's a hive of countless biochemical activities all going on at once.

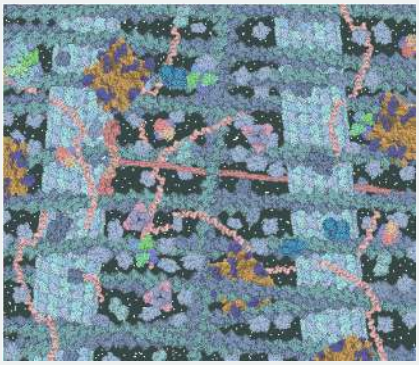


Figure **3.5.1**: Picture of cytosol, showing microtubules (light blue), actin filaments (dark blue), ribosomes (yellow and purple), soluble proteins (light blue), kinesin (red), small molecules (white) and RNA (pink).

CYTOPLASM

The **cytoplasm** is a thick, usually colorless solution that fills each cell and is enclosed by the cell membrane. Cytoplasm presses against the cell membrane, filling out the cell and giving it its shape. Sometimes cytoplasm acts like a watery solution and sometimes it takes on a more gel-like consistency. In eukaryotic cells, the cytoplasm includes all of the material inside the cell but outside the nucleus, which contains its own watery substance called **nucleoplasm**. All of the organelles in eukaryotic cells, such as the endoplasmic reticulum and mitochondria, are located in the cytoplasm. The cytoplasm helps to keep them in place. It is also the site of most metabolic activities in the cell, and it allows materials to pass easily throughout the cell.

The portion of the cytoplasm surrounding organelles is called cytosol, which is the liquid part of the cytoplasm. It is composed of about 80 percent water and also contains dissolved salts, fatty acids, sugars, amino acids, and proteins such as enzymes. These dissolved substances are needed to keep the cell alive and carry out metabolic processes. For example, enzymes dissolved in cytosol break down larger molecules into smaller products that can then be used by organelles of the cell. Waste products are also dissolved in the cytosol before they are taken in by vacuoles or expelled from the cell.

Though prokaryotic cells do not have organelles (they do have ribosomes), they still have cytoplasm. It is within the cytoplasm that most cellular activities occur, including the many metabolic pathways that occur within organelles, such as photosynthesis and aerobic respiration.

CYTOSKELETON

Although cytoplasm may appear to have no form or structure, it is actually highly organized. A framework of protein scaffolds called the **cytoskeleton** provides the cytoplasm and the cell with structure. The cytoskeleton consists of thread-like filaments and tubules that criss-cross the cytoplasm. You can see these filaments and tubules in the cells in Figure **3.5.2**. As its name suggests, the cytoskeleton is like a cellular “skeleton.” It helps the cell maintain its shape and also helps to hold cell structures such as organelles in place within the cytoplasm.

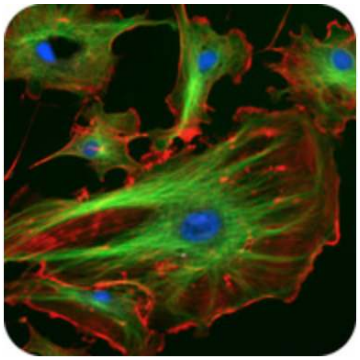


Figure **3.5.2**: Cytoskeleton. The cytoskeleton gives the cell an internal structure, like the frame of a house. In this photograph, actin filaments and tubules of the cytoskeleton are green and red, respectively. The blue dots are cell nuclei.

The eukaryotic cytoskeleton is made up of a network of long, thin protein fibers. These threadlike proteins continually rebuild to adapt to the cell's constantly changing needs. Three main kinds of cytoskeleton fibers are microtubules, intermediate filaments, and microfilaments (Table **3.5.1**).

- **Microtubules** are the thickest of the cytoskeleton structures. They are most commonly made of filaments which are polymers of alpha and beta-tubulin and radiate outwards from an area near the nucleus called the centrosome. Two forms of tubulin form dimers (pairs) which come together to form the hollow cylinders. The cylinders are twisted around each other to form the microtubules. Microtubules help the cell keep its shape. They hold organelles in place and allow them to move around the cell, and they form the mitotic spindle during cell division. Microtubules also make up parts of cilia and flagella, the organelles that help a cell move.
- **Microfilaments** are made of two thin **actin** chains that are twisted around one another. Microfilaments are mostly concentrated just beneath the cell membrane, where they support the cell and help the cell keep its shape. Microfilaments form cytoplasmatic extensions, such as **microvilli** and pseudopodia, which allow certain cells to move. The actin and myosin protein interact to cause a contraction in muscle cells. Microfilaments

are found in almost every cell and are numerous in muscle cells and in cells that move by changing shape, such as phagocytes (white blood cells that search the body for bacteria and other invaders).

- **Intermediate filaments (IF)** differ in make-up from one cell type to another. The IF may be composed of **vimentin**, **keratin**, **desmin**, or **lamin**. Each cell type can have a unique combination of IFs. For example, intermediate filaments made of keratin are found in skin, hair, and nail cells. IFs organize the inside structure of the cell by holding organelles and providing strength. They are also structural components of the nuclear envelope. Intermediate filaments made of the protein keratin are found in skin, hair, and nail cells.

Table **3.5.1**: Cytoskeleton Structure

Characteristic	Microtubules	Intermediate Filaments	Microfilaments
Fiber Diameter	About 25 nm	8 to 11 nm	Around 7 nm
Protein Composition	Tubulin with two subunits, alpha, and beta-tubulin	One of the different types of proteins such as lamin, vimentin, desmin, and keratin	Actin
Shape	Hollow cylinders made of two protein chains twisted around each other	Protein fiber coils twisted into each other	Two actin chains twisted around one another
Main Functions	Organelle and vesicle movement; form mitotic spindles during cell reproduction; cell motility (in cilia and flagella)	Organize cell shape; positions organelles in cytoplasm structural support of the nuclear envelope and sarcomeres; involved in cell-to-cell and cell-to-matrix junctions	Keep cellular shape; allows movement of certain cells by forming cytoplasmatic extensions or contraction of actin fibers; involved in some cell-to-cell or cell-to-matrix junctions

FEATURE: HUMAN BIOLOGY IN THE NEWS

News about an important study of the cytoplasm of eukaryotic cells appeared early in 2016. Researchers in Dresden, Germany discovered that when cells are deprived of adequate nutrients, they may essentially shut down and become dormant. Specifically, when cells do not get enough nutrients, they shut down their metabolism, their energy level drops, and the pH of their cytoplasm decreases. Their normally liquid cytoplasm also assumes a solid state. The cells appear dead and as though a kind of rigor mortis has set in. The researchers think that these changes protect the sensitive structures inside the cells and allow the cells to survive difficult conditions. If nutrients are returned to the cells, they can emerge from their dormant state unharmed. They will continue to grow and multiply when conditions improve.

This important basic science research was carried out on a nonhuman organism: one-celled fungi called yeasts. Nonetheless, it may have important implications for humans because yeasts have eukaryotic cells with many of the same structures as human cells. Yeast cells appear to be able to "trick" death by shutting down all life processes in a controlled way. Researchers hope to learn with the continued research on whether human cells can be taught this "trick" as well.

REVIEW

1. Describe the composition of cytoplasm.
2. What are some of the functions of cytoplasm?
3. Outline the structure and functions of the cytoskeleton.
4. Is the cytoplasm made of cells? Why or why not?
5. Name two types of cytoskeletal structures.
6. *True or False.* The cytoplasm is usually green.
7. *True or False.* The nucleus of a cell is filled with cytoplasm.
8. In Figure **3.5.2** of the different cytoskeletal structures above (shown in red and green), what do you notice about these different structures?
9. Describe one example of a metabolic process that occurs in the cytosol.
10. In eukaryotic cells, all of the material inside of the cell but outside of the nucleus is called the _____.
11. What is the liquid part of the cytoplasm called?
12. What chemical substance makes up most of the cytosol?
13. When yeast cells deprived of nutrients go dormant, their cytoplasm assumes a solid-state. What effect do you think a solid cytoplasm would have on normal cellular processes? Explain your answer.
14. What is the difference between cytoplasm and cytosol?
15. Name the three main parts of the cytoskeleton.
16. List two functions of the eukaryotic cytoskeleton

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3.6: CELL ORGANELLES

RIBOSOME REVIEW

Figure **3.6.1** represents an important structure in living cells. It is a component of a ribosome, the cell structure where proteins are synthesized. Large ribosomal subunit (50S) of *Haloarcula marismortui*, facing the 30S subunit. The ribosomal proteins are shown in blue, the rRNA in ochre (a shade of brown and yellow), the active site in red. All living cells contain ribosomes, whether they are prokaryotic or eukaryotic cells. However, only eukaryotic cells also contain a nucleus and several other types of organelles.

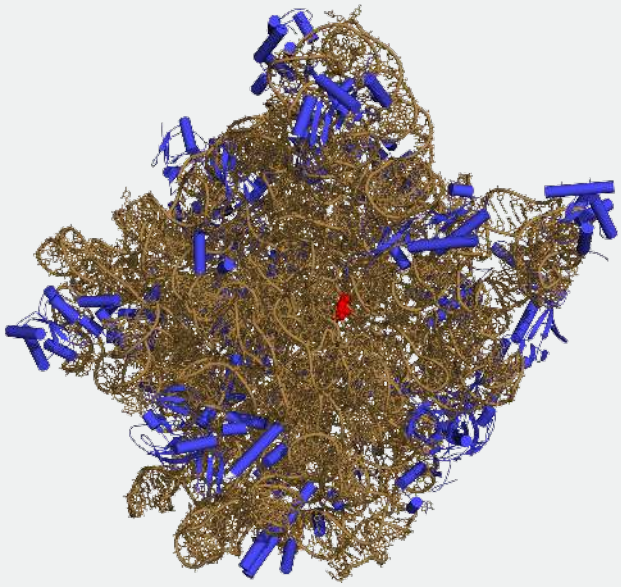


Figure **3.6.1**: Ribosomal subunit

An organelle is a structure within the cytoplasm of a eukaryotic cell that is enclosed within a membrane and performs a specific job. Organelles are involved in many vital cell functions. Organelles in animal cells include the nucleus, mitochondria, endoplasmic reticulum, Golgi apparatus, vesicles, and vacuoles. Ribosomes are not enclosed within a membrane but are still commonly referred to as organelles in eukaryotic cells.

THE NUCLEUS

The nucleus is the largest organelle in a eukaryotic cell and is considered to be the cell's control center. It contains most of the cell's DNA, which makes up chromosomes and is encoded with the genetic instructions for making proteins. The function of the nucleus is to regulate gene expression, including controlling which proteins the cell makes. In addition to DNA, the nucleus contains a thick liquid called nucleoplasm that is similar in composition to the cytosol found in the cytoplasm outside the nucleus (Figure **3.6.2**). Most eukaryotic cells contain just a single nucleus, but some types of cells, such as red blood cells, contain no nucleus. A few other types of cells, such as muscle cells, contain multiple nuclei.

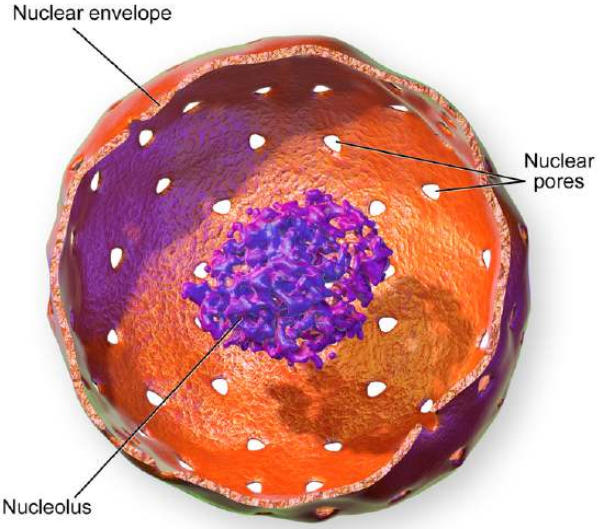


Figure **3.6.2**: This closeup of a cell nucleus shows that it is surrounded by a structure called the nuclear envelope, which contains tiny perforations, or pores. The nucleus also contains a dense center called the nucleolus.

As you can see from the model in Figure **3.6.2**, the membrane enclosing the nucleus is called the **nuclear envelope**. This is actually a double membrane that encloses the entire organelle and isolates its contents from the cellular cytoplasm. Tiny holes, called **nuclear pores**, allow large molecules to pass through the nuclear envelope with the help of special proteins. Large proteins and RNA molecules must be able to pass through the nuclear envelope so proteins can be synthesized in the cytoplasm and the genetic material can be maintained inside the nucleus. The **nucleolus** shown in the model below is mainly involved in the assembly of ribosomes. After being produced in the nucleolus, ribosomes are exported to the cytoplasm where they are involved in the synthesis of proteins.

MITOCHONDRIA

The **mitochondrion** (plural, **mitochondria)** is an organelle that makes energy available to the cell (Figure **3.6.3**). This is why mitochondria are sometimes referred to as the power plants of the cell. They use energy from organic compounds such as glucose to make molecules of **ATP (adenosine triphosphate)**, an energy-carrying molecule that is used almost universally inside cells for energy.

Scientists think that mitochondria were once free-living organisms because they contain their own DNA. They theorize that ancient prokaryotes infected (or were engulfed by) larger prokaryotic cells, and the two organisms evolved a symbiotic relationship that benefited both of them. The larger cells provided the smaller prokaryotes with a place to live. In return, the larger cells got extra energy from the smaller prokaryotes. Eventually, the smaller prokaryotes became permanent guests of the larger cells, as organelles inside them. This theory is called the **endosymbiotic theory**, and it is widely accepted by biologists today

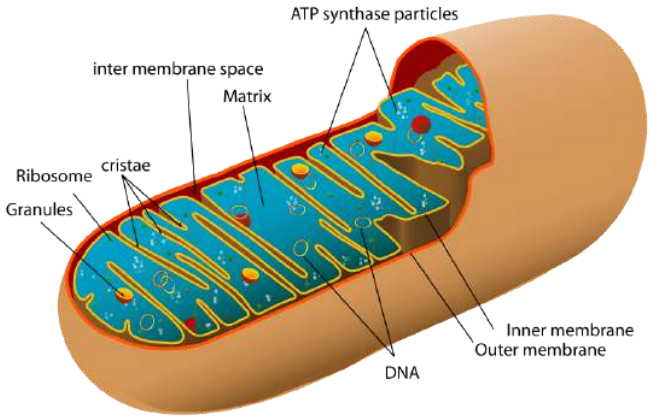


Figure **3.6.3**: Mitochondria, organelles specialized to carry out aerobic respiration, contain an inner membrane folded into cristae, which form two separate compartments: the inner membrane space and the matrix. The Krebs Cycle takes place in the matrix. The electron transport chain is embedded in the inner membrane and uses both compartments to make ATP by chemiosmosis. Mitochondria have their own DNA and ribosomes, resembling those of prokaryotic organisms.

MITOCHONDRIAL COMPARTMENTS

The double membrane nature of the mitochondria results in five distinct compartments, each with an important role in cellular respiration. These compartments are:

1. the outer mitochondrial membrane,
2. the intermembrane space (the space between the outer and inner membranes),
3. the inner mitochondrial membrane,
4. the cristae (formed by infoldings of the inner membrane), and
5. the matrix (space within the inner membrane).

ENDOPLASMIC RETICULUM

The *endoplasmic reticulum* **(ER)** (plural, reticuli) is a network of phospholipid membranes that form hollow tubes, flattened sheets, and round sacs. These flattened, hollow folds and sacs are called *cisternae*. The ER has two major functions:

- Transport: Molecules, such as proteins, can move from place to place inside the ER, much like on an intracellular highway.
- Synthesis: Ribosomes that are attached to the ER, similar to unattached ribosomes, make proteins. Lipids are also produced in the ER.

There are two types of endoplasmic reticulum, rough endoplasmic reticulum (RER) and smooth endoplasmic reticulum (SER):

- **Rough endoplasmic reticulum** is studded with ribosomes, which gives it a “rough” appearance. These ribosomes make proteins that are then transported from the ER in small sacs called transport vesicles. The transport vesicles pinch off the ends of the ER. The rough endoplasmic reticulum works with the Golgi apparatus to move new proteins to their proper destinations in the cell. The membrane of the RER is continuous with the outer layer of the nuclear envelope.
- **Smooth endoplasmic reticulum** does not have any ribosomes attached to it, and so it has a smooth appearance. SER has many different functions, some of which include lipid synthesis, calcium ion storage, and drug detoxification. The smooth endoplasmic reticulum is found in both animal and plant cells and it serves different functions in each. The SER is made up of tubules and vesicles that branch out to form a network. In some cells, there are dilated areas like the sacs of RER. Smooth endoplasmic reticulum and RER form an interconnected network.

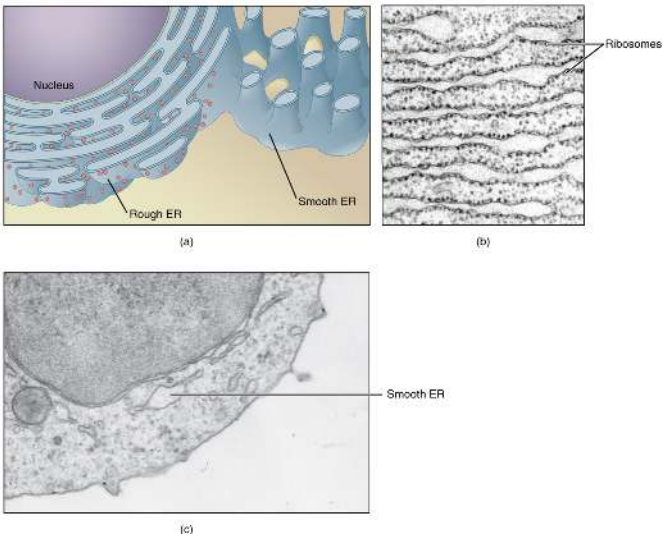


Figure **3.6.4**: The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function (source: mouse tissue). (b) Rough ER is studded with numerous ribosomes, which are sites of protein synthesis (source: mouse tissue). EM × 110,000. (c) Smooth ER synthesizes phospholipids, steroid hormones, regulates the concentration of cellular Ca^{2+}, metabolizes some carbohydrates, and breaks down certain toxins.

GOLGI APPARATUS

The **Golgi apparatus** (Figure **3.6.5**) is a large organelle that processes proteins and prepares them for use both inside and outside the cell. It was identified in 1898 by the Italian physician Camillo Golgi. The Golgi apparatus modifies, sorts, and packages different substances for secretion out of the cell, or for use within the cell. The Golgi apparatus is found close to the nucleus of the cell where it modifies proteins that have been delivered in transport vesicles from the Rough Endoplasmic Reticulum. It is also involved in the transport of lipids around the cell. Pieces of the Golgi membrane pinch off to form vesicles that transport molecules around the cell. The Golgi apparatus can be thought of as similar to a post office; it packages and labels "items" and then sends them to different parts of the cell. The Golgi apparatus tends to be larger and more numerous in cells that synthesize and secrete large quantities of materials; for example, the plasma B cells and the antibody-secreting cells of the immune system have prominent Golgi complexes.

The Golgi apparatus manipulates products from the Rough Endoplasmic Reticulum (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.

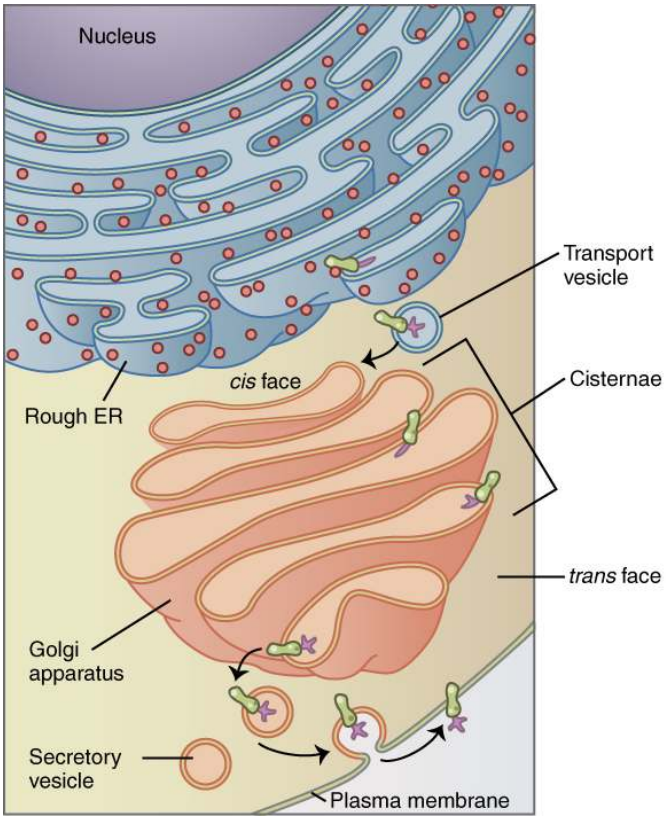


Figure **3.6.5**: The rough ER is continuous with the nuclear envelope and has ribosomes on it's surface. The ribosomes produce proteins such as the one shown which remains bound to the membrane of the rough ER. The membrane of the rough ER pinches off to form a transport vesicle containing the protein. The vesicle fuses with the cis face of the Golgi apparatus. The protein is now found on the membrane of the Golgi apparatus and travels along the cisternae. Once it reaches the trans face of the Golgi apparatus, it gets packaged into a secretory vesicle that sends the protein to the plasma membrane.

The stack of **cisternae** has four functional regions: the **cis-Golgi network**, medial-Golgi, endo-Golgi, and trans-Golgi network. Vesicles from the ER fuse with the network and subsequently progress through the stack from the cis- to the **trans-Golgi network**, where they are packaged and sent to their destination. Each cisterna includes special Golgi enzymes which modify or help to modify proteins that travel through it. Proteins may be modified by the addition of a carbohydrate group (glycosylation) or phosphate group (phosphorylation). These modifications may form a signal sequence on the protein, which determines the final destination of the protein. For example, the addition of mannose-6-phosphate signals the protein for lysosomes.

VESICLES AND VACUOLES

Both **vesicles** and **vacuoles** are sac-like organelles that store and transport materials in the cell. Vesicles are much smaller than vacuoles and have a variety of functions. The vesicles that pinch off from the membranes of the ER and Golgi apparatus store and transport protein and lipid molecules. You can see an example of this type of transport vesicle in the figure above. Some vesicles are used as chambers for biochemical reactions. Other vesicles include:

- Lysosomes, which use enzymes to break down foreign matter and dead cells.
- Peroxisomes, which use oxygen to break down poisons.
- Transport vesicles, transport contents between organelle as well as between cell exterior and interior.

CENTRIOLES

Centrioles are organelles involved in cell division. The function of centrioles is to help organize the chromosomes before cell division occurs so that each daughter cell has the correct number of chromosomes after the cell divides. Centrioles are found only in animal cells and are located near the nucleus. Each centriole is made mainly of a protein named **tubulin**. The centriole is cylindrical in shape and consists of many microtubules, as shown in the model pictured below.

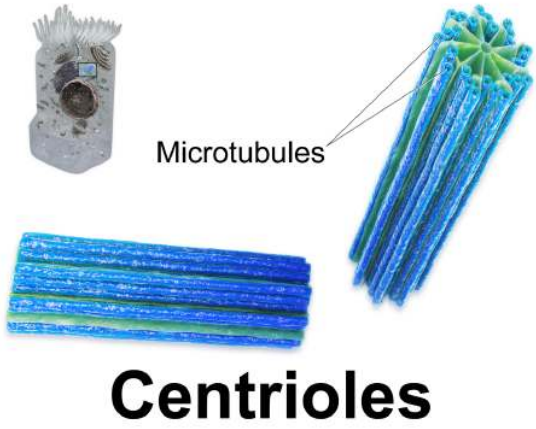


Figure **3.6.6**: Centrioles are tiny cylinders near the nucleus, enlarged here to show their tubular structure.

RIBOSOMES

Ribosomes are small structures where proteins are made. Although they are not enclosed within a membrane, they are frequently considered organelles. Each ribosome is formed of two subunits, like the one pictured at the top of this section. Both subunits consist of proteins and RNA. RNA from the nucleus carries the genetic code, copied from DNA, which remains in the nucleus. At the ribosome, the genetic code in RNA is used to assemble and join together amino acids to make proteins. Ribosomes can be found alone or in groups within the cytoplasm as well as on the RER.

REVIEW

1. Define organelle.
2. Describe the structure and function of the nucleus.
3. Explain how the nucleus, ribosomes, rough endoplasmic reticulum, and Golgi apparatus work together to make and transport proteins.
4. Why are mitochondria referred to as the power plants of the cell?
5. What roles are played by vesicles and vacuoles?
6. Why do all cells need ribosomes, even prokaryotic cells that lack a nucleus and other cell organelles?
7. Explain endosymbiotic theory as it relates to mitochondria. What is one piece of evidence that supports this theory?
8. Lysosomes and peroxisomes are types of:
   A. A. Organelles
   B. B. Vesicles
   C. C. Vacuoles
   D. D. Both A and B
9. Which of the following organelles fits best with each description of function? Choose only one organelle for each answer: Golgi apparatus, centrioles, nucleolus, nucleus, rough endoplasmic reticulum
   A. a. Contains the genetic instructions for the production of proteins
   B. b. Organizes chromosomes before cell division
   C. c. Provides a framework for ribosomes
   D. d. Packages and labels proteins
   E. e. Assembles ribosomes
10. *True or False*. All eukaryotic cells have a nucleus.
11. *True or False*. The outer surface of the nucleus of a eukaryotic cell is not completely solid.

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3.7: CELL TRANSPORT

LETTING IN THE LIGHT

Look at the big windows and glass doors in this house. Imagine all the light they must let in on a sunny day. Now imagine living in a house that has walls without any windows or doors. Nothing could enter or leave. Or imagine living in a house with holes in the walls instead of windows and doors. Things could enter or leave, but you couldn't control what came in or went out. Only if a house has walls with windows and doors that can be opened or closed you can control what enters or leaves. For example, windows and doors allow you to let in light and the family dog and keep out rain and bugs.



Figure **3.7.1**: A house with windows

TRANSPORT ACROSS MEMBRANES

If a cell were a house, the plasma membrane would be walls with windows and doors. Moving things in and out of the cell is an important role of the plasma membrane. It controls everything that enters and leaves the cell. There are two basic ways that substances can cross the plasma membrane: passive transport, which requires no energy; and active transport, which requires energy. Passive transport is explained in this section and Active transport is explained in the next section, Active Transport and Homeostasis. Various types of cell transport are summarized in the concept map in Figure **3.7.2**.

TRANSPORT WITHOUT ENERGY

Passive transport occurs when substances cross the plasma membrane without any input of energy from the cell. No energy is needed because the substances are moving from an area where they have a higher concentration to an area where they have a lower concentration. Water solutions are very important in biology. When water is mixed with other molecules this mixture is called a **solution**. Water is the **solvent** and the dissolved substance is the **solute**. A solution is characterized by the solute. For example, water and sugar would be characterized as a sugar solution. More the particles of a solute in a given volume, the higher the concentration. The particles of solute always move from an area where it is more concentrated to an area where it is less concentrated. It's a little like a ball rolling down a hill. It goes by itself without any input of extra energy.

The different categories of cell transport are outlined in Figure **3.7.2**. Cell transport can be classified as follows:

- Passive Transport which includes
  - Simple Diffusion
  - Osmosis
  - Facilitated Diffusion
- Active Transport can involve either a pump or a vesicle
  - Pump Transport can be
    - primary
    - secondary
  - Vesicle Transport can involve
    - Exocytosis
    - Endocytosis which includes
      - Pinocytosis
      - Phagocytosis
      - Receptor-Mediated Endocytosis

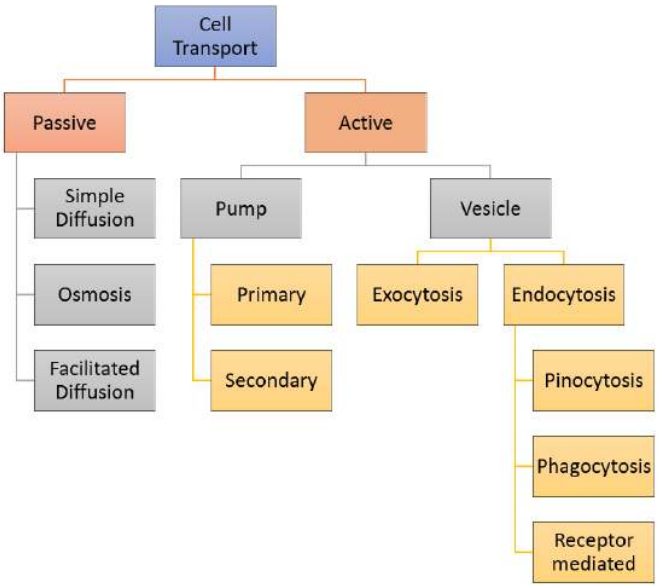


Figure **3.7.2**: The Cell Transport Concept Map illustrates various types of cell transports that happen at the plasma membrane

SIMPLE DIFFUSION

Diffusion Although you may not know what diffusion is, you have experienced the process. Can you remember walking into the front door of your home and smelling a pleasant aroma coming from the kitchen? It was the diffusion of particles from the kitchen to the front door of the house that allowed you to detect the odors. **Diffusion** is defined as the net movement of particles from an area of greater concentration to an area of lesser concentration.

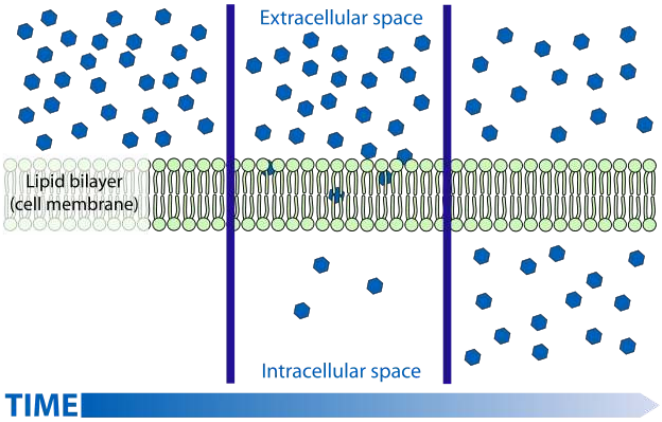


Figure **3.7.3**. Simple diffusion shows as a timeline with the outside of the cell (extracellular space) separated from the inside of the cell (intracellular space) by the cell membrane. In the beginning of the timeline there are many molecules outside of the cell and none inside. Over time, they diffuse into the cell until there is an equal amount outside and inside.

The molecules in a gas, a liquid, or a solid are in constant motion due to their kinetic energy. Molecules are in constant movement and collide with each other. These collisions cause the molecules to move in random directions. Over time, however, more molecules will be propelled into the less concentrated area. Thus, the net movement of molecules is always from more tightly packed areas to less tightly packed areas. Many things can diffuse. Odors diffuse through the air, salt diffuses through water and nutrients diffuse from the blood to the body tissues. This spread of particles through the random motion from an area of high concentration to an area of lower concentration is known as diffusion. This unequal distribution of molecules is called a concentration gradient. Once the molecules become uniformly distributed, a dynamic equilibrium exists. The equilibrium is said to be dynamic because molecules continue to move, but despite this change, there is no net change in concentration over time. Both living and nonliving systems experience the process of diffusion. In living systems, diffusion is responsible for the movement of a large number of substances, such as gases and small uncharged molecules, into and out of cells.

OSMOSIS

Osmosis is a specific type of diffusion; it is the passage of water from a region of high water concentration through a semi-permeable membrane to a region of low water concentration. Water moves in or out of a cell until its concentration is the same on both sides of the plasma membrane.

Semi-permeable membranes are very thin layers of material that allow some things to pass through them but prevent other things from passing through. Cell membranes are an example of semi-permeable membranes. Cell membranes allow small molecules such as oxygen, water carbon dioxide, and oxygen to pass through but do not allow larger molecules like glucose, sucrose, proteins, and starch to enter the cell directly.

The classic example used to demonstrate osmosis and osmotic pressure is to immerse cells into sugar solutions of various concentrations. There are three possible relationships that cells can encounter when placed into a sugar solution. Figure **3.7.4** shows what happens in osmosis through the semi-permeable membrane of the cells.

A. The concentration of solute in the solution can be **greater than** the concentration of solute in the cells. This cell is described as being in a **hypertonic solution** (hyper = greater than normal). The net flow or water will be out of the cell.
B. The concentration of solute in the solution can be **equal to** the concentration of solute in cells. In this situation, the cell is in an **isotonic solution** (iso = equal or the same as normal). The amount of water entering the cell is the same as the amount leaving the cell.
C. The concentration of solute in the solution can be **less than** the concentration of solute in the cells. This cell is in a **hypotonic solution** (hypo = less than normal). The net flow of water will be into the cell.

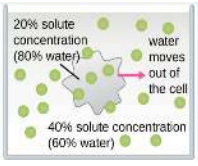


Figure **3.7.4.*A***: **Hypertonic solution.** A solution that has a higher solute concentration than another solution. Water particles will move out of the cell, causing crenation.

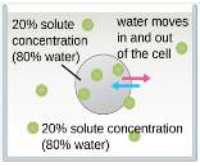


Figure **3.7.4.*B***: **Isotonic solution.** A solution that has the same solute concentration as another solution. There is no net movement of water particles, and the overall concentration on both sides of the cell membrane remains constant.

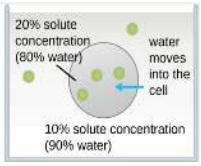


Figure **3.7.4.*C***: **Hypotonic solution.** A solution that has a lower solute concentration than another solution. Water particles will move into the cell, causing the cell to expand and eventually lyse.

Figure **3.7.5** demonstrates the specific outcomes of osmosis in red blood cells.

A. **Hypertonic solution.** The red blood cell will appear to shrink as the water flows out of the cell and into the surrounding environment.
B. **Isotonic solution.** The red blood cell will retain its normal shape in this environment as the amount of water entering the cell is the same as the amount leaving the cell.
C. **Hypotonic solution**. The red blood cell in this environment will become visibly swollen and potentially rupture as water rushes into the cell.

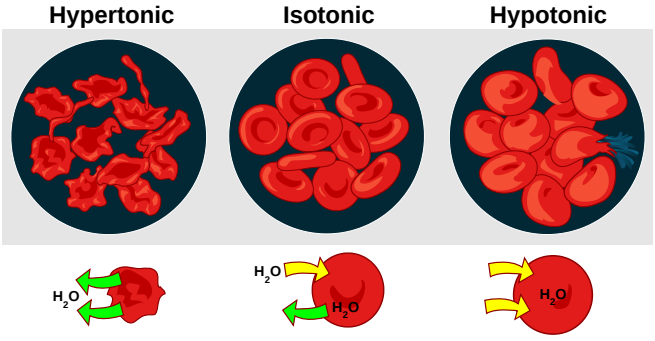


Figure **3.7.5**: Osmosis demonstration with Red Blood cells places in a hypertonic, isotonic, and hypotonic solution.

FACILITATED DIFFUSION

Water and many other substances cannot simply diffuse across a membrane. Hydrophilic molecules, charged ions, and relatively large molecules such as glucose all need help with diffusion. The help comes from special proteins in the membrane known as **transport proteins**. Diffusion with the help of transport proteins is called **facilitated diffusion**. There are several types of transport proteins, including channel proteins and carrier proteins (Figure **3.7.6**)

- Channel proteins form pores, or tiny holes, in the membrane. This allows water molecules and small ions to pass through the membrane without coming into contact with the hydrophobic tails of the lipid molecules in the interior of the membrane.
- Carrier proteins bind with specific ions or molecules, and in doing so, they change shape. As carrier proteins change shape, they carry the ions or molecules across the membrane.

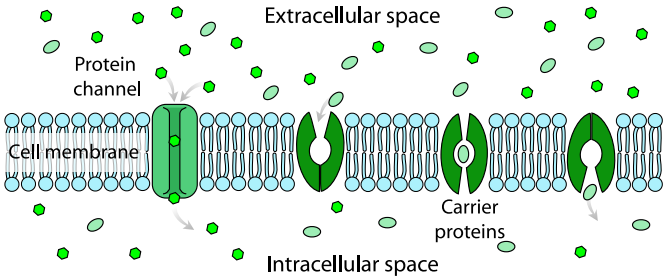


Figure **3.7.6**: Facilitated Diffusion Across a Cell Membrane. Channel proteins and carrier proteins help substances diffuse across a cell membrane. In this diagram, the channel and carrier proteins are helping substances move into the cell (from the extracellular space to the intracellular space). The channel protein has an opening that allows the substances to cross. In a carrier protein, the substance binds to the protein, which then causes the protein to changes shape, thereby releasing the substance into the cell.

REVIEW

1. What is the main difference between passive and active transport?
2. Summarize three different ways that passive transport can occur, and give an example of a substance that is transported in each way.
3. Explain how transport across the plasma membrane is related to the homeostasis of the cell.
4. Why can generally only very small, hydrophobic molecules across the cell membrane by simple diffusion?
5. Explain how facilitated diffusion assists in osmosis in cells. Be sure to define osmosis and facilitated diffusion in your answer.
6. Imagine a hypothetical cell with a higher concentration of glucose inside the cell than outside. Answer the following questions about this cell, assuming all transport across the membrane is passive, not active.
   A. Can the glucose simply diffuse across the cell membrane? Why or why not?
   B. Assuming that there are glucose transport proteins in the cell membrane, which way would glucose flow – into or out of the cell? Explain your answer.
   C. If the concentration of glucose was equal inside and outside of the cell, do you think there would be a net flow of glucose across the cell membrane in one direction or the other? Explain your answer.
7. What are the similarities and differences between channel proteins and carrier proteins?
8. *True or False.* Only active transport, not passive transport, involves transport proteins.
9. *True or False.* Oxygen and carbon dioxide can squeeze between the lipid molecules in the plasma membrane.
10. *True or False.* Ions easily diffuse across the cell membrane by simple diffusion.
11. Controlling what enters and leaves the cell is an important function of the:
    A. nucleus
    B. vesicle
    C. plasma membrane
    D. Golgi apparatus

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3.8: ACTIVE TRANSPORT AND HOMEOSTASIS

LIKE PUSHING A HUMVEE UPHILL

You can tell by their faces that these airmen are expending a lot of energy trying to push this Humvee up a slope. The men are participating in a competition that tests their brute strength against that of other teams. The Humvee weighs about 13,000 pounds, so it takes every ounce of energy they can muster to move it uphill against the force of gravity. Transport of some substances across a plasma membrane is a little like pushing a Humvee uphill — it can't be done without adding energy.



Figure **3.8.1**: Pushing a machine up a hill.

WHAT IS ACTIVE TRANSPORT?

Some substances can pass into or out of a cell across the plasma membrane without any energy required because they are moving from an area of higher concentration to an area of lower concentration. This type of transport is called passive transport as you learned in the last section. Other substances require energy to cross a plasma membrane often because they are moving from an area of lower concentration to an area of higher concentration. This type of transport is called **active transport**. The energy for active transport comes from the energy-carrying molecule called ATP (adenosine triphosphate). Active transport may also require transport proteins, such as carrier proteins, which are embedded in the plasma membrane. Two types of active transport are pump and vesicle transport.

PUMP

Two pump mechanisms (primary and secondary active transports) exist for the transport of small-molecular weight material and macromolecules. The **primary active transport** moves ions across a membrane and creates a difference in charge across that membrane. The primary active transport system uses ATP to move a substance, such as an ion, into the cell, and often at the same time, a second substance is moved out of the cell. The **sodium-potassium pump** is a mechanism of active transport that moves sodium ions out of the cell and potassium ions into the cells — in all the trillions of cells in the body! Both ions are moved from areas of lower to higher concentration, so energy is needed for this "uphill" process. The energy is provided by ATP. The sodium-potassium pump also requires carrier proteins. Carrier proteins bind with specific ions or molecules, and in doing so, they change shape. As carrier proteins change shape, they carry the ions or molecules across the membrane. Figure **3.8.2** shows in greater detail how the sodium-potassium pump works and the specific roles played by carrier proteins in this process.

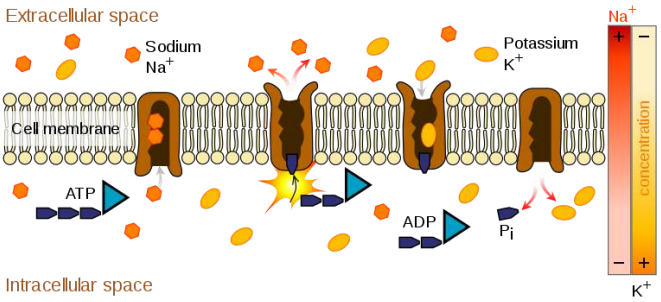


Figure **3.8.2**: The sodium-potassium pump. The sodium-potassium pump moves sodium ions (Na^+) out of the cell and potassium ions (K^+) into the cell. First, three sodium ions bind with a carrier protein in the cell membrane. Then, the carrier protein receives a phosphate group from ATP. When ATP loses a phosphate group, energy is released. The carrier protein changes shape, and as it does, it pumps the three sodium ions out of the cell. At that point, two potassium ions bind to the carrier protein. The process is reversed, and the potassium ions are pumped into the cell.

To appreciate the importance of the sodium-potassium pump, you need to know more about the roles of sodium and potassium in the body. Both are essential dietary minerals, meaning you have to obtain them in the foods you eat. Both sodium and potassium are also electrolytes, meaning that they dissociate into ions (charged particles) in solution, which allows them to conduct electricity. Normal body functions require a very narrow range of concentrations of sodium and potassium ions in body fluids, both inside and outside of cells.

- Sodium is the principal ion in the fluid outside of cells. Normal sodium concentrations are about 10 times higher outside than inside of cells.
- Potassium is the principal ion in the fluid inside of cells. Normal potassium concentrations are about 30 times higher inside than outside of cells.

These differences in concentration create an electrical gradient across the cell membrane, called the membrane potential. the **secondary active transport** describes the movement of material using the energy of the electrochemical gradient established by the primary active transport. Using the energy of the electrochemical gradient created by the primary active transport system, other substances such as amino acids and glucose can be brought into the cell through membrane channels. ATP itself is formed through secondary active transport using a hydrogen ion gradient in the mitochondrion. Tightly controlling the membrane potential is critical for vital body functions, including the transmission of nerve impulses and the contraction of muscles. A large percentage of the

body's energy goes to maintaining this potential across the membranes of its trillions of cells with the sodium-potassium pump.

VESICLE TRANSPORT

Some molecules, such as proteins, are too large to pass through the plasma membrane, regardless of their concentration inside and outside the cell. Very large molecules cross the plasma membrane with a different sort of help, called **vesicle transport**. Vesicle transport requires energy, so it is also a form of active transport. There are two types of vesicle transport: endocytosis and exocytosis.

ENDOCYTOSIS

Endocytosis is a type of vesicle transport that moves a substance into the cell. The plasma membrane completely engulfs the substance, a vesicle pinches off from the membrane, and the vesicle carries the substance into the cell. It is used by all cells of the body because most substances important to them are polar and consist of big molecules, and thus cannot pass through the hydrophobic plasma membrane. When an entire cell or other solid particle is engulfed, the process is called **phagocytosis**. When fluid is engulfed, the process is called **pinocytosis**. When the content is taken in specifically with the help of receptors on the plasma membrane, it is called **receptor-mediated endocytosis**.

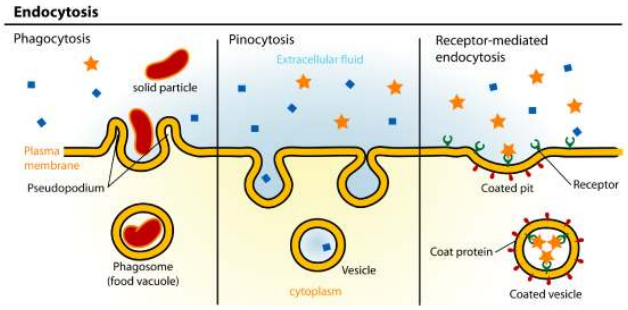


Figure **3.8.3**: (On the right) Phagocytosis is when the plasma membrane wraps around a solid particle outside the cell using projections called pseudopodia. The membrane then pinches off to form a phagosome (food vacuole). (Middle)Pinocytosis is when the membrane folds to form a vesicle that carries substances dissolved in the extracellular fluid. (On the left) Receptor-mediated endocytosis occurs when the receptors on the plasma membrane bind to specific particles. The coated pit region of the membrane forms a coated vesicle containing the receptors with their bound particles.

A targeted variation of endocytosis employs binding proteins in the plasma membrane that are specific for certain substances. The particles bind to the proteins and the plasma membrane invaginates, bringing the substance and the proteins into the cell. If passage across the membrane of the target of **receptor-mediated endocytosis** is ineffective, it will not be removed from the tissue fluids or blood. Instead, it will stay in those fluids and increase in concentration. Some human diseases are caused by a failure of receptor-mediated endocytosis. For example, the form of cholesterol termed low-density lipoprotein or LDL (also referred to as “bad” cholesterol) is removed from the blood by receptor-mediated endocytosis. In the human genetic disease familial hypercholesterolemia, the LDL receptors are defective or missing entirely. People with this condition have life-threatening levels of cholesterol in their blood because their cells cannot clear the chemical from their blood.

EXOCYTOSIS

Exocytosis is a type of vesicle transport that moves a substance out of the cell. A vesicle containing the substance moves through the cytoplasm to the cell membrane. Then, the vesicle membrane fuses with the cell membrane, and the substance is released outside the cell.

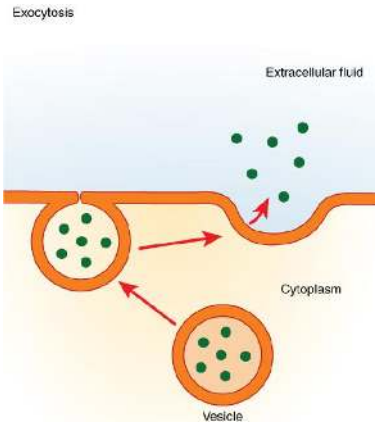


Figure **3.8.4**: Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

HOMEOSTASIS AND CELL FUNCTION

For a cell to function normally, a stable state must be maintained inside the cell. For example, the concentration of salts, nutrients, and other substances must be kept within a certain range. The process of maintaining stable conditions inside a cell (or an entire organism) is homeostasis. Homeostasis requires constant adjustments because conditions are always changing both inside and outside the cell. The processes described in this and previous lessons play important roles in homeostasis. By moving substances into and out of cells, they keep conditions within normal ranges inside the cells and the organism as a whole.

FEATURE:FEATURE: MY HUMAN BODY

Maintaining the proper balance of sodium and potassium in body fluids by active transport is necessary for life itself, so it's no surprise that getting the right balance of sodium and potassium in the diet is important for good health. Imbalances may increase the risk of high blood pressure, heart disease, diabetes, and other disorders.

If you are like the majority of Americans, sodium and potassium are out of balance in your diet. You are likely to consume too much sodium and too little potassium. Follow these guidelines to help ensure that these minerals are in balance in the foods you eat:

- Total sodium intake should be less than 2300 mg/day. Most salt in the diet is found in processed foods or added with a salt shaker. Stop adding salt and start checking food labels for sodium content. Foods considered low in sodium have less than 140 mg/serving (or 5% daily value).
- Total potassium intake should be 4700 mg/day. It's easy to add potassium to the diet by choosing the right foods, and there are plenty of choices. Most fruits and vegetables are high in potassium, but especially potatoes, bananas, oranges, apricots, plums, leafy greens, tomatoes, lima beans, and avocado. Other foods with substantial amounts of potassium are fish, meat, poultry, and whole grains.

REVIEW

1. Define active transport.
2. What is the sodium-potassium pump? Why is it so important?
3. Name two types of vesicle transport. Which type moves substances out of the cell?
4. What are the similarities and differences between phagocytosis and pinocytosis?
5. The sodium-potassium pump is a:
   A. Phospholipid
   B. Protein
   C. Carbohydrate
   D. Ion
6. What is the functional significance of the shape change of the carrier protein in the sodium-potassium pump after the sodium ions bind?
7. A potentially deadly poison derived from plants called ouabain blocks the sodium-potassium pump and prevents it from working. What do you think this does to the sodium and potassium balance in cells? Explain your answer.
8. True or False. The sodium-potassium pump uses one protein to pump both sodium and potassium.
9. True or False. Vesicles are made of the nuclear membrane.
10. What is an electrical gradient across the cell membrane called?
11. Chemical signaling molecules called neurotransmitters are released from nerve cells (neurons) through vesicles. This is an example of:
    A. Pinocytosis
    B. Phagocytosis
    C. Endocytosis
    D. Exocytosis
12. The energy for active transport comes from
    A. ATP
    B. RNA
    C. Carrier proteins
    D. Sodium ions
13. Transport proteins that move substances into and out of a cell are located in which structure?

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3.9: CELLULAR RESPIRATION

BRING ON THE S'MORES!

This inviting campfire can be used for both heat and light. Heat and light are two forms of energy that are released when a fuel like wood is burned. The cells of living things also get energy by "burning." They "burn" glucose in the process called cellular respiration.



Figure **3.9.1**: Burning logs that convert carbon in wood into carbon dioxide and a significant amount of thermal energy.

Inside every cell of all living things, energy is needed to carry out life processes. Energy is required to break down and build up molecules and to transport many molecules across plasma membranes. All of life's work needs energy. A lot of energy is also simply lost to the environment as heat. The story of life is a story of energy flow — its capture, its change of form, its use for work, and its loss as heat. Energy, unlike matter, cannot be recycled, so organisms require a constant input of energy. Life runs on chemical energy. Where do living organisms get this chemical energy?

WHERE DO ORGANISMS GET ENERGY FROM?

The chemical energy that organisms need comes from food. Food consists of organic molecules that store energy in their chemical bonds. Glucose is a simple carbohydrate with the chemical formula $C_6H_{12}O_6$. It stores chemical energy in a concentrated, stable form. In your body, glucose is the form of energy that is carried in your blood and taken up by each of your trillions of cells. Cells do cellular respiration to extract energy from the bonds of glucose and other food molecules. Cells can store the extracted energy in the form of ATP (adenosine triphosphate).

WHAT IS ATP?

Let's take a closer look at a molecule of ATP, shown in the figure **3.9.2**. Although it carries less energy than glucose, its structure is more complex. "A" in ATP refers to the majority of the molecule – adenosine – a combination of a nitrogenous base and a five-carbon sugar. "T" and "P" indicate the three phosphates, linked by bonds that hold the energy actually used by cells. Usually, only the outermost bond breaks to release or spend energy for cellular work.

An ATP molecule is like a rechargeable battery: its energy can be used by the cell when it breaks apart into ADP (adenosine diphosphate) and phosphate, and then the "worn-out battery" ADP can be recharged using new energy to attach a new phosphate and rebuild ATP. The materials are recyclable, but recall that energy is not! ADP can be further reduced to AMP (adenosine monophosphate and phosphate, releasing additional energy. As with ADP "recharged" to ATP, AMP can be recharged to ADP.

How much energy does it cost to do your body's work? A single cell uses about 10 million ATP molecules per second and recycles all of its ATP molecules about every 20-30 seconds.

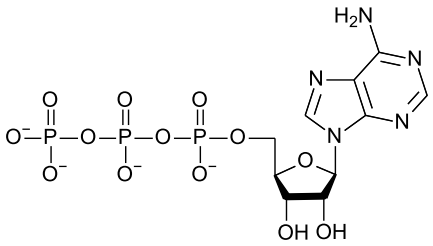


Figure **3.9.2**: Chemical structure of ATP consists of a 5-carbon sugar (ribose) attached to a nitrogenous base (adenine) and three phosphates. When the covalent bond between the terminal phosphate group and the middle phosphate group breaks, energy is released which is used by the cells to do work.

WHAT IS CELLULAR RESPIRATION?

Some organisms can make their own food, whereas others cannot. An **autotroph** is an organism that can produce its own food. The Greek roots of the word *autotroph* mean "self" (*auto*) "feeder" (*troph*). Plants are the best-known autotrophs, but others exist, including certain types of bacteria and algae. Oceanic algae contribute enormous quantities of food and oxygen to global food chains. Plants are also **photoautotrophs**, a type of autotroph that uses sunlight and carbon from carbon dioxide to synthesize chemical energy in the form of carbohydrates. **Heterotrophs** are organisms incapable of photosynthesis that must therefore obtain energy and carbon from food by consuming other organisms. The Greek roots of the word *heterotroph* mean "other" (*hetero*) "feeder" (*troph*), meaning that their food comes from other organisms. Even if the food organism is another animal, this food traces its origins back to autotrophs and the process of photosynthesis. Humans are heterotrophs, as are all animals. Heterotrophs depend on autotrophs, either directly or indirectly.

Cellular respiration is the process by which individual cells break down food molecules, such as glucose and release energy. The process is similar to burning, although it doesn't produce light or intense heat as a campfire does. This is because cellular respiration releases the energy in glucose slowly, in many small steps. It uses the energy that is released to form molecules of ATP, the energy-carrying molecules that cells use to power biochemical processes. Cellular respiration involves many chemical reactions, but they can all be summed up with this chemical equation:

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + \text{Energy}$$

where the energy that is released is in chemical energy in ATP (vs. thermal energy as heat). The equation above shows that glucose ($C_6H_{12}O_6$) and oxygen (O_2) react to form carbon dioxide (CO_2) and water H_2O, releasing energy in the process. Because oxygen is required for cellular respiration, it is an **aerobic** process.

Cellular respiration occurs in the cells of all living things, both autotrophs and heterotrophs. All of them catabolize glucose to form ATP. The reactions of cellular respiration can be grouped into three main stages and an intermediate stage: **glycolysis**, **Transformation of pyruvate**, the **Krebs cycle** (also called the citric acid cycle), and **Oxidative Phosphorylation**. Figure 3.9.3 gives an overview of these three stages, which are also described in detail below.

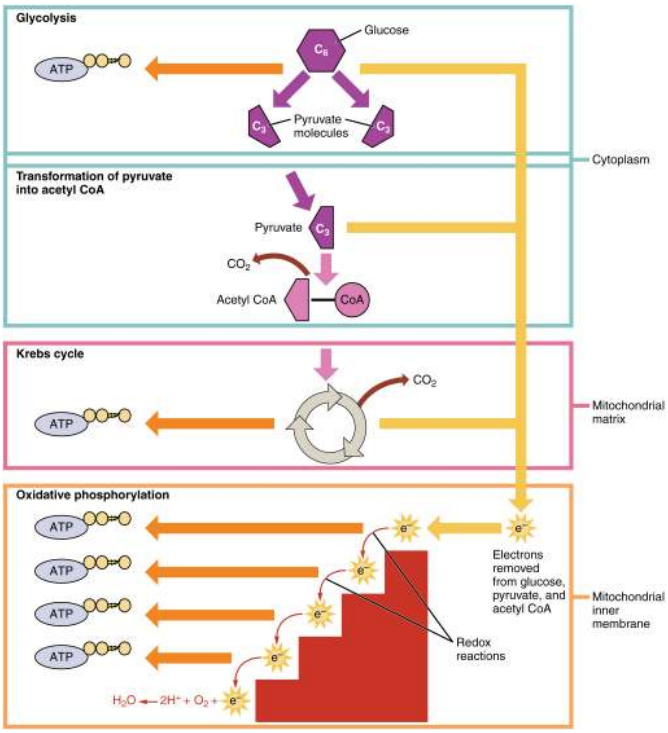


Figure 3.9.3: Cellular respiration takes place in the stages shown here. The process begins with Glycolysis. In this first step, a molecule of glucose, which has six carbon atoms, is split into two three-carbon molecules. The three-carbon molecule is called pyruvate. Pyruvate is oxidized and converted into Acetyl CoA. These two steps occur in the cytoplasm of the cell. Acetyl CoA enters into the matrix of mitochondria, where it is fully oxidized into Carbon Dioxide via the Krebs cycle. Finally, During the process of oxidative phosphorylation, the electrons extracted from food move down the electron transport chain in the inner membrane of the mitochondrion. As the electrons move down the ETC and finally to oxygen, they lose energy. This energy is used to phosphorylate AMP to make ATP.

GLYCOLYSIS

The first stage of cellular respiration is **glycolysis**. This process is shown in the top box in Figure 3.9.3 showing a 6-carbon molecule being broken down into two 3-carbon pyruvate molecules. ATP is produced in this process which takes place in the cytosol of the cytoplasm.

SPLITTING GLUCOSE

The word *glycolysis* means "glucose splitting," which is exactly what happens in this stage. Enzymes split a molecule of glucose into two molecules of pyruvate (also known as pyruvic acid). This occurs in several steps, as shown in figure 3.9.4. Glucose is first split into glyceraldehyde 3-phosphate (a molecule containing 3 carbons and a phosphate group). This process uses 2 ATP. Next, each glyceraldehyde 3-phosphate is converted into pyruvate (a 3-carbon molecule). this produces two 4 ATP and 2 NADH.

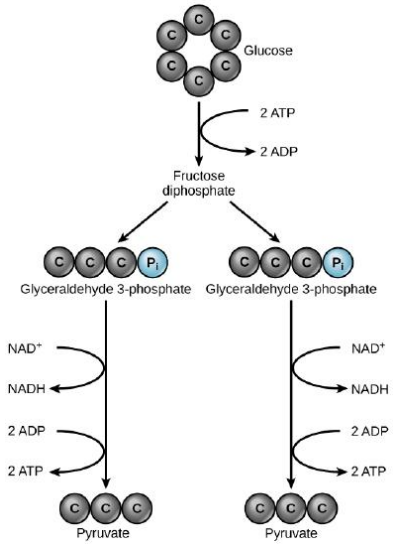


Figure 3.9.4: In glycolysis, a glucose molecule is converted into two pyruvate molecules.

RESULTS OF GLYCOLYSIS

Energy is needed at the start of glycolysis to split the glucose molecule into two pyruvate molecules. These two molecules go on to stage II of cellular respiration. The energy to split glucose is provided by two molecules of ATP. As glycolysis proceeds, energy is released, and the energy is used to make four molecules of ATP. As a result, there is a **net gain of two ATP molecules** during glycolysis. high-energy electrons are also transferred to energy-carrying molecules called electron carriers through the process
known as reduction. The electron carrier of glycolysis is **NAD+ (nicotinamide adenine diphosphate)**. Electrons are transferred to 2 NAD+ to produce two molecules of NADH. The energy stored in NADH is used in stage III of cellular respiration to make more ATP. At the end of glycolysis, the following has been produced:

- 2 molecules of NADH
- 2 net molecules of ATP

TRANSFORMATION OF PYRUVATE INTO ACETYL-COA

In eukaryotic cells, the pyruvate molecules produced at the end of glycolysis are transported into mitochondria, which are sites of cellular respiration. If oxygen is available, aerobic respiration will go forward. In mitochondria, pyruvate will be transformed into a two-carbon acetyl group (by removing a molecule of carbon dioxide) that will be picked up by a carrier compound called

coenzyme A (CoA), which is made from vitamin B_5. The resulting compound is called acetyl CoA and its production is frequently called the oxidation or the Transformation of Pyruvate (see Figure **3.9.5**. Acetyl CoA can be used in a variety of ways by the cell, but its major function is to deliver the acetyl group derived from pyruvate to the next pathway step, the Citric Acid Cycle.

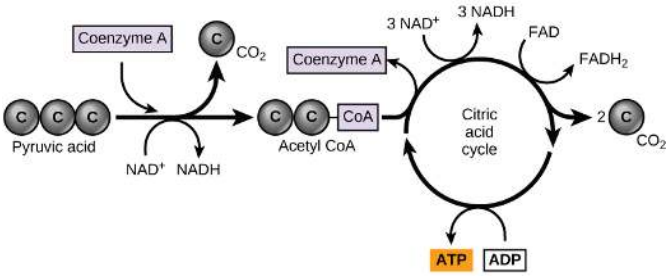


Figure **3.9.5**: Pyruvate is converted into acetyl-CoA before entering the Citric Acid Cycle (Krebs cycle)

CITRIC ACID CYCLE

Before you read about the last two stages of cellular respiration, you need to review the structure of the mitochondrion, where these two stages take place. As you can see from Figure **3.9.6**, a mitochondrion has an inner and outer membrane. The space between the inner and outer membrane is called the intermembrane space. The space enclosed by the inner membrane is called the matrix. The second stage of cellular respiration, the Krebs cycle, takes place in the matrix. The third stage, electron transport, takes place on the inner membrane.

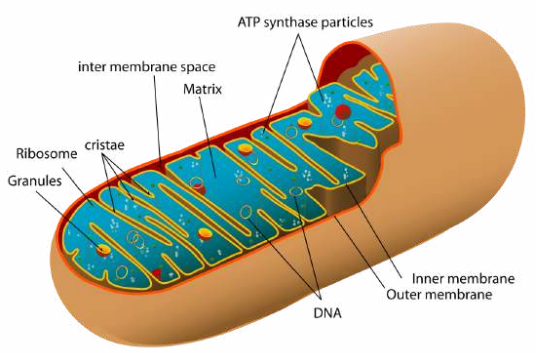


Figure **3.9.6**: The structure of a mitochondrion is defined by an inner and outer membrane. The space inside the inner membrane is full of fluid, enzymes, ribosomes, and mitochondrial DNA. This space is called a matrix. The inner membrane has a larger surface area as compared to the outer membrane. Therefore, it creases. The extensions of the creases are called cristae. The space between the outer and inner membrane is called intermembrane space.

Recall that glycolysis produces two molecules of pyruvate (pyruvic acid). Pyruvate, which has three carbon atoms, is split apart and combined with CoA, which stands for coenzyme A. The product of this reaction is acetyl-CoA. These molecules enter the matrix of a mitochondrion, where they start the Citric Acid Cycle. The third carbon from pyruvate combines with oxygen to form carbon dioxide, which is released as a waste product. High-energy electrons are also released and captured in NADH. The reactions that occur next are shown in Figure **3.9.7**.

STEPS OF THE CITRIC ACID (KREBS) CYCLE

The Citric Acid Cycle begins when acetyl-CoA combines with a four-carbon molecule called OAA (oxaloacetate; see the lower panel of Figure **3.9.7**). This produces citric acid, which has six carbon atoms. This is why the Krebs cycle is also called the citric acid cycle. After citric acid forms, it goes through a series of reactions that release energy. This energy is captured in molecules of ATP and electron carriers. The Krebs cycle has two types of energy-carrying electron carriers: NAD+ and FAD. The transfer of electrons to FAD during the Kreb's Cycle produces a molecule of $FADH_2$. Carbon dioxide is also released as a waste product of these reactions. The final step of the Krebs cycle regenerates OAA, the molecule that began the Krebs cycle. This molecule is needed for the next turn through the cycle. Two turns are needed because glycolysis produces two pyruvate molecules when it splits glucose.

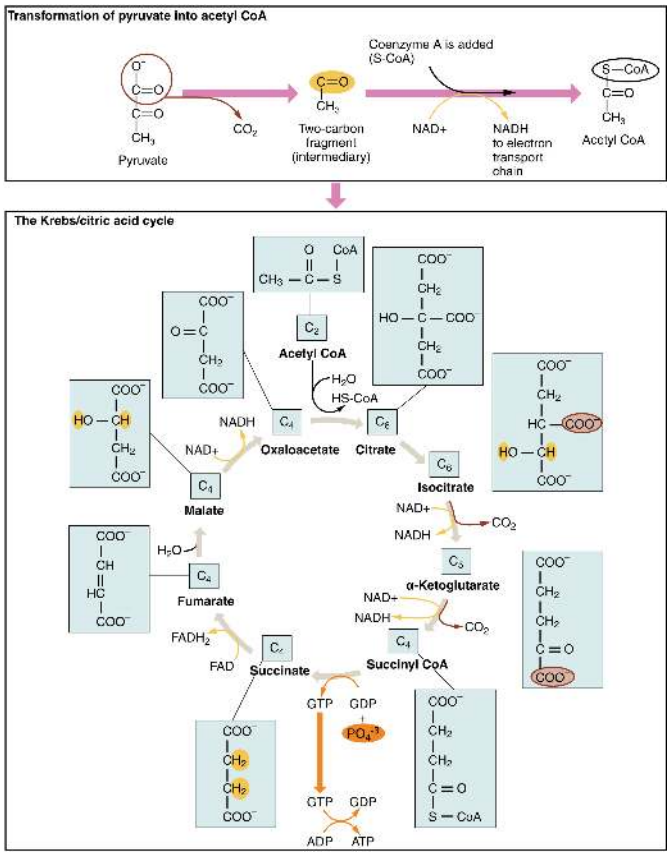


Figure **3.9.7**: In the Citric Acid Cycle, the acetyl group from acetyl CoA is attached to a four-carbon oxaloacetate molecule to form a six-carbon citrate molecule. Through a series of steps, citrate is oxidized, releasing two carbon dioxide molecules for each acetyl group fed into the cycle. In the process, three NAD^+ molecules are reduced to NADH, one FAD molecule is reduced to $FADH_2$, and one ATP or GTP (depending on the cell type) is produced (by substrate-level phosphorylation). Because the final product of the citric acid cycle is also the first reactant, the cycle runs continuously in the presence of sufficient reactants.

RESULTS OF THE CITRIC ACID CYCLE

After the second turn through the Citric Acid Cycle, the original glucose molecule has been broken down completely. All six of its carbon atoms have combined with oxygen to form carbon dioxide. The energy from its chemical bonds has been stored in a total of 16 energy-carrier molecules. These molecules are:

- 2 ATP
- 8 NADH
- 2 $FADH_2$
- 6 CO_2: 2 CO_2 from Transformation of Acetyl CoA and 4 CO_2 from Citric Acid Cycle.

OXIDATIVE PHOSPHORYLATION

Oxidative phosphorylation is the final stage of aerobic cellular respiration. There are two substages of oxidative phosphorylation, Electron transport chain and Chemiosmosis. In these stages, energy from NADH and $FADH_2$, which result from the previous stages of cellular respiration, is used to create ATP.

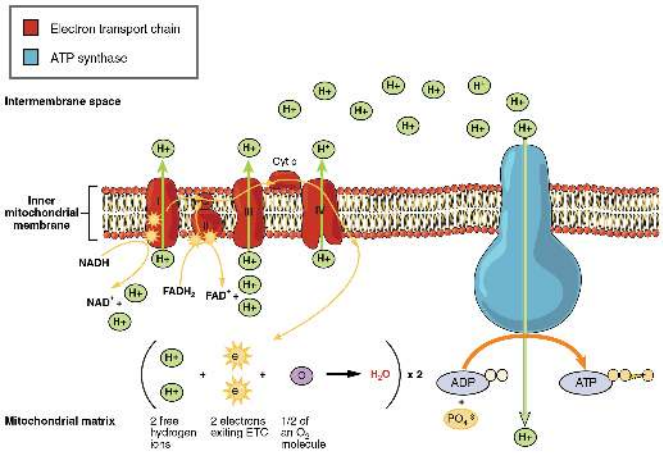


Figure **3.9.8**: Oxidative Phosphorylation: Electron Transport chain and Chemiosmosis.

ELECTRON TRANSPORT CHAIN (ETC)

During this stage, high-energy electrons are released from NADH and $FADH_2$, and they move along electron-transport chains found in the inner membrane of the mitochondrion. An electron-transport chain is a series of molecules that transfer electrons from molecule to molecule by chemical reactions. These molecules are found making up the three complexes of the electron transport chain (red structures in the inner membrane in Figure **3.9.8**). As electrons flow through these molecules, some of the energy from the electrons is used to pump hydrogen ions (H+) across the inner membrane, from the matrix into the intermembrane space. This ion transfer creates an electrochemical gradient that drives the synthesis of ATP. The electrons from the final protein of the ETC are gained by the oxygen molecule, and it is reduced to water in the matrix of the mitochondrion.

CHEMIOSMOSIS

The pumping of hydrogen ions across the inner membrane creates a greater concentration of these ions in the intermembrane space than in the matrix – producing an electrochemical gradient. This gradient causes the ions to flow back across the membrane into the matrix, where their concentration is lower. The flow of these ions occurs through a protein complex, known as the ATP synthase complex (see blue structure in the inner membrane in Figure **3.9.8**. The ATP synthase acts as a channel protein, helping the hydrogen ions across the membrane. The flow of protons through ATP synthase is considered chemiosmosis. ATP synthase also acts as an enzyme, forming ATP from ADP and inorganic phosphate. It is the flow of hydrogen ions through ATP synthase that gives the energy for ATP synthesis. After passing through the electron-transport chain, the low-energy electrons combine with oxygen to form water.

HOW MUCH ATP?

You have seen how the three stages of aerobic respiration use the energy in glucose to make ATP. How much ATP is produced in all three stages combined? Glycolysis produces 2 ATP molecules, and the Krebs cycle produces 2 more. Electron transport from the molecules of NADH and $FADH_2$ made from glycolysis, the transformation of pyruvate, and the Krebs cycle creates as many as 32 more ATP molecules. Therefore, a total of up to 36 molecules of ATP can be made from just one molecule of glucose in the process of cellular respiration.

REVIEW

1. What is the purpose of cellular respiration? Provide a concise summary of the process.
2. Draw and explain the structure of ATP (Adenosine Tri-Phosphate).
3. State what happens during glycolysis.
4. Describe the structure of a mitochondrion.
5. Outline the steps of the Krebs cycle.
6. What happens during the electron transport stage of cellular respiration?
7. How many molecules of ATP can be produced from one molecule of glucose during all three stages of cellular respiration combined?
8. Do plants undergo cellular respiration? Why or why not?
9. Explain why the process of cellular respiration described in this section is considered aerobic.
10. Name three energy-carrying molecules involved in cellular respiration.
11. Energy is stored within chemical _____ within a glucose molecule.
12. *True or False*. During cellular respiration, NADH and ATP are used to make glucose.
13. *True or False*. ATP synthase acts as both an enzyme and a channel protein.
14. *True or False*. The carbons from glucose end up in ATP molecules at the end of cellular respiration.
15. Which stage of aerobic cellular respiration produces the most ATP?

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3.10: FERMENTATION

FAST AND FURIOUS

The muscles of this sprinter will need a lot of energy to complete their short race because they will be running at top speed. The action won't last long, but it will be very intense. The energy the sprinter needs can't be provided quickly enough by aerobic cellular respiration. Instead, a different process must be used by their muscle cells to power their activity.



Figure **3.10.1**: Sprinter on the field

MAKING ATP WITHOUT OXYGEN

The cells of living things power their activities with the energy-carrying molecule ATP (adenosine triphosphate). The cells of most living things make ATP from glucose in the process of cellular respiration. This process occurs in three major stages, and one intermediate stage: glycolysis, oxidation of pyruvate, the Krebs cycle, and electron transport. The latter two stages require oxygen, making cellular respiration an aerobic process. There are also other ways of making ATP from glucose without oxygen, such as **anaerobic respiration** and **fermentation,** of making ATP from glucose without oxygen. Our cells do not perform anaerobic respiration. Therefore, we will only focus on fermentation in this section.

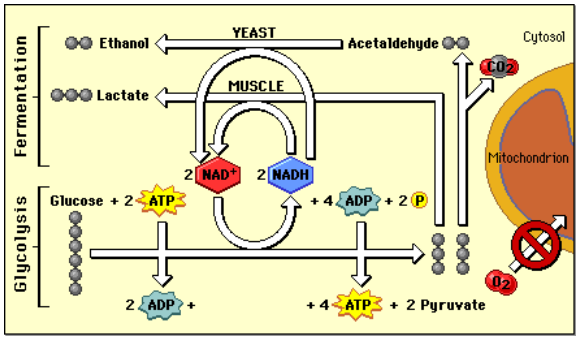


Figure **3.10.2**. The picture shows glycolysis and fermentation. There are two types of fermentation, alcoholic and lactic acid. Fermentation follows glycolysis in the absence of oxygen. Alcoholic fermentation produces ethanol, carbon dioxide, and NAD^+. Lactic acid fermentation produces lactic acid (lactate) and NAD^+. The NAD^+ cycles back to allow glycolysis to continue so more ATP is made. Each black ball in the image represents a carbon atom, and the red balls represent oxygen.

FERMENTATION

Fermentation starts with glycolysis, but it does not involve the latter two stages of aerobic cellular respiration (the Krebs cycle and oxidative phosphorylation). During glycolysis, two NAD+ electron carriers are reduced to two NADH molecules and 2 net ATPs are produced. The NADH must be oxidized back so that glycolysis can continue and cells can continue making 2 ATPs. The cells cannot make more than 2 ATP in fermentation because oxidative phosphorylation does not happen due to a lack of oxygen. There are two types of fermentation, alcoholic fermentation and lactic acid fermentation. Our cells can only perform lactic acid fermentation; however, we make use of both types of fermentation using other organisms.

ALCOHOLIC FERMENTATION

Alcoholic fermentation The process by which this happens is summarized in Figure **3.10.2**. The two pyruvate molecules are shown in this diagram come from the splitting of glucose through glycolysis. This process also produces 2 molecules of ATP. Continued breakdown of pyruvate produces acetaldehyde, carbon dioxide, and eventually ethanol. Alcoholic fermentation requires the electrons from NADH and results in the generation of NAD+.

Yeast in bread dough also uses alcoholic fermentation for energy and produces carbon dioxide gas as a waste product. The carbon dioxide that is released causes bubbles in the dough and explains why the dough rises. Do you see the small holes in the bread in Figure **3.10.3**? The holes were formed by bubbles of carbon dioxide gas.



Figure **3.10.3**: Holes from carbon dioxide gas in bread dough are left behind after the bread bakes.

LACTIC ACID FERMENTATION

Lactic acid fermentation is carried out by certain bacteria, including the bacteria in yogurt. It is also carried out by your muscle cells when you work them hard and fast. This is how the muscles of the sprinter in Figure **3.10.1**get energy for their short-duration but intense activity. The process by which this happens is summarized in Figure **3.10.2**. Again, two pyruvate and two ATP molecules result from glycolysis. Reduction of pyruvate using the electrons carried by NADH produces lactate (i.e. lactic acid). While this is similar to alcoholic fermentation, there is no carbon dioxide produced in this process.

Did you ever run a race, lift heavy weights, or participate in some other intense activity and notice that your muscles start to feel a burning sensation? This may occur when your muscle cells use lactic acid fermentation to provide ATP for energy. The buildup of lactic acid in the muscles causes the feeling of burning. The painful sensation is useful if it gets you to stop overworking your muscles and allow them a recovery period during which cells can eliminate the lactic acid.

PROS AND CONS OF FERMENTATION

With oxygen, organisms can use aerobic cellular respiration to produce up to 36 molecules of ATP from just one molecule of glucose. Without oxygen, some human cells must use fermentation to produce ATP, and this process produces only two molecules of ATP per molecule of glucose. Although fermentation produces less ATP, it has the advantage of doing so very quickly. It allows your muscles, for example, to get the energy they need for short bursts of intense activity. Aerobic cellular respiration, in contrast, produces ATP more slowly.

FEATURE: MYTH VS. REALITY

Myth: lactic acid build-up can cause muscle fatigue and a burning sensation in muscles. The soreness is thought to be due to microscopic damage to the muscle fibers.

Reality: The statement about lactic acid causing the burn in the muscle has no solid experimental proof. Alternate hypotheses suggest that through the production of lactic acid, the internal pH of the muscle decreases, triggering contraction in muscle due to the activation of motor neurons.

REVIEW

1. State the main difference between aerobic cellular respiration and fermentation.
2. What is fermentation?
3. Compare and contrast alcoholic and lactic acid fermentation.
4. Identify the major pro and the major con of fermentation relative to aerobic cellular respiration.
   A. What process is shared between aerobic cellular respiration and fermentation? Describe the process briefly.
   B. Why is this process able to occur in fermentation as well as aerobic respiration?
5. Which type of metabolic process occurs in the human body?
   A. Aerobic cellular respiration
   B. Alcoholic fermentation
   C. Lactic acid fermentation
   D. Both A and C
6. *True or False.* Lactic acid fermentation produces carbon dioxide.
7. *True or False.* Types of bacteria can carry out alcoholic fermentation and lactic acid fermentation.
8. *True or False.* No ATP is produced by fermentation.
9. Both lactic acid fermentation and alcoholic fermentation use which acid molecules to make their final products?
10. Which type of process is used in the making of bread and wine?
    A. Alcoholic fermentation
    B. Lactic acid fermentation
    C. Aerobic cellular respiration
    D. Prokaryotic respiration
11. Is fermentation an aerobic or anaerobic process?
12. What is the reactant, or starting material, shared by aerobic respiration and both types of fermentation?

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3.11: CASE STUDY CONCLUSION- TIRED AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: MORE THAN JUST TIRED

Jasmin discovered that her extreme fatigue, muscle pain, vision problems, and vomiting were due to problems in her mitochondria. Mitochondria are small membrane-bound organelles found in eukaryotic cells that provide energy for the cells of the body. They do this by carrying out the final two steps of aerobic cellular respiration, the Krebs cycle, and electron transport, which is the major way that the human body breaks down the sugar glucose from food into a form of energy cells can use, namely the molecule ATP.

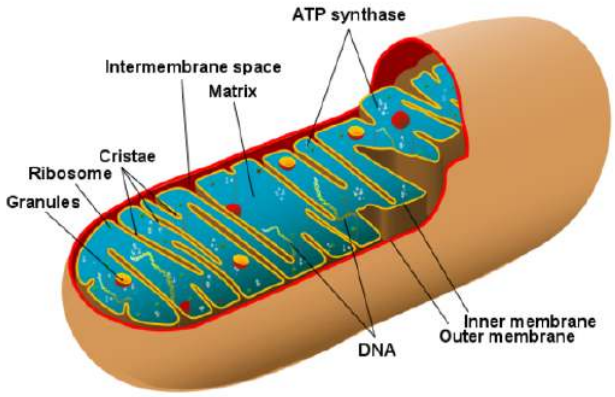


Figure **3.11.1**: Mitochondrial structures. You can see the outer membrane, the inner membrane with cristae, intermembrane space, and matrix with granules, ribosomes, and mitochondrial DNA. ATP synthase is located in the inner membrane.

Because mitochondria provide energy for cells, you can probably easily see why Jasmin was experiencing extreme fatigue, particularly after running. Her damaged mitochondria could not keep up with her need for energy, particularly after intense exercise which requires a lot of additional energy. What is perhaps not so obvious are the reasons for her other symptoms, such as blurry vision, muscle spasms, and vomiting. But all the cells in the body require energy in order to function properly. Mitochondrial diseases can cause problems in mitochondria in any cell of the body, including muscle cells and cells of the nervous system, which includes the brain and nerves. The nervous system and muscles work together to control vision and digestive system functions, such as vomiting, so when they are not functioning properly, a variety of symptoms can emerge. This also explains why Jasmin's niece, who also has mitochondrial disease, has symptoms related to brain function, such as seizures and learning disabilities. Our cells are microscopic and mitochondria are even tinier, but they are essential for the proper functioning of our bodies and when they are damaged, serious health effects can occur.

A seemingly confusing aspect of mitochondrial diseases is that the type of symptoms, severity of symptoms, and age of onset can vary wildly between people — even within the same family! In Jasmin's case, she did not notice symptoms until adulthood, while her niece had more severe symptoms starting at a much younger age. However, this makes sense when you know more about how mitochondrial diseases work.

Inherited mitochondrial diseases can be due to damage in either the DNA in the nucleus of cells or the DNA in the mitochondria themselves. Recall that mitochondria are thought to have evolved from prokaryotic organisms that were once free-living, but then infected or were engulfed by larger cells. One of the pieces of evidence that supports this endosymbiotic theory is that mitochondria have their own, separate DNA. When the mitochondrial DNA is damaged or mutated, it can result in some types of mitochondrial diseases. However, these mutations do not typically affect *all of* the mitochondria in a cell. During cell division, organelles such as mitochondria are replicated and passed down to the new daughter cells. If some of the mitochondria are damaged, and others are not, the daughter cells can have different amounts of damaged mitochondria. This helps explain the wide range of symptoms in people with mitochondrial diseases, even ones in the same family because different cells in their bodies are affected to different extents. Jasmin's niece was affected strongly and her symptoms were noticed early, while Jasmin's symptoms were milder and did not become apparent until adulthood.

There is still much more that needs to be discovered about the different types of mitochondrial diseases. But by learning about cells, their organelles, how they obtain energy, and how they divide, you should now have a better understanding of the biology behind these diseases. Apply your understanding of cells to your own life — can you think of other diseases that affect cellular structures or functions, maybe that even affect people you know? Since your entire body is made of cells, when they are damaged or not functioning properly it can cause a wide variety of health problems.

CHAPTER SUMMARY

In this chapter, you learned many facts about cells. Specifically, you learned that:

- Cells are the basic units of structure and function of living things.
- The first cells, from cork, were observed by Hooke in the 1600s. Soon after, van Leeuwenhoek observed other living cells.
- In the early 1800s, Schwann and Schleiden theorized that cells are the basic building blocks of all living things. Around 1850, Virchow saw cells dividing and added that living cells arise only from other living cells. These ideas led to cell theory, which states that all organisms are made of cells, all life functions occur in cells, and all cells come from other cells.
- The invention of the electron microscope in the 1950s allowed scientists to see organelles and other structures inside cells for the first time.

- There is variation in cells, but all cells have a plasma membrane, cytoplasm, ribosomes, and DNA.
  - The plasma membrane is composed mainly of a bilayer of phospholipid molecules and forms a barrier between the cytoplasm inside the cell and the environment outside the cell. It allows only certain substances to pass in or out of the cell. Some cells have extensions of their plasma membrane with other functions, such as flagella or cilia.
  - The cytoplasm is a thick solution that fills a cell and is enclosed by the cell membrane. It helps give the cell shape, holds organelles, and provides a site for many of the biochemical reactions inside the cell. The liquid part of the cytoplasm is called cytosol.
  - Ribosomes are small structures where proteins are made.
- Cells are usually very small so they have a large enough surface-area-to-volume ratio to maintain normal cell processes. Cells with different functions often have different shapes.
- Prokaryotic cells do not have a nucleus. Eukaryotic cells have a nucleus as well as other organelles. An organelle is a structure within the cytoplasm of a cell that is enclosed within a membrane and performs a specific job.
- The cytoskeleton is a highly organized framework of protein filaments and tubules that criss-cross the cytoplasm of a cell. It gives the cell structure and helps to hold cell structures such as organelles in place.
- The nucleus is the largest organelle in a eukaryotic cell and is considered to be the cell's control center. It contains DNA and controls gene expression, including which proteins the cell makes.
- The mitochondrion is an organelle that makes energy available to cells. According to the widely accepted endosymbiotic theory, mitochondria evolved from prokaryotic cells that were once free-living organisms that infected or were engulfed by larger prokaryotic cells.
- The endoplasmic reticulum (ER) is an organelle that helps make and transport proteins and lipids. Rough endoplasmic reticulum (RER) is studded with ribosomes. Smooth endoplasmic reticulum (SER) has no ribosomes.
- The Golgi apparatus is a large organelle that processes proteins and prepares them for use both inside and outside the cell. It is also involved in the transport of lipids around the cell.
- Vesicles and vacuoles are sac-like organelles that may be used to store and transport materials in the cell or as chambers for biochemical reactions. Lysosomes and peroxisomes are vesicles that break down foreign matter, dead cells, or poisons.
- Centrioles are organelles located near the nucleus that help organize the chromosomes before cell division so each daughter cell receives the correct number of chromosomes.
- There are two basic ways that substances can cross the cell's plasma membrane: passive transport, which requires no energy; and active transport, which requires energy.
- No energy is needed for passive transport because it occurs when substances move naturally from an area of higher concentration to an area of lower concentration. Types of passive transport in cells include:
  - Simple diffusion, which is the movement of a substance due to differences in concentration without any help from other molecules. This is how very small, hydrophobic molecules, such as oxygen and carbon dioxide, enter and leave the cell.
  - Osmosis, which is the diffusion of water molecules across the membrane.
  - Facilitated diffusion, which is the movement of a substance across a membrane due to differences in concentration but only with the help of transport proteins in the membrane, such as channel proteins or carrier proteins. This is how large or hydrophilic molecules and charged ions enter and leave the cell.
- Active transport requires energy to move substances across the plasma membrane, often because the substances are moving from an area of lower concentration to an area of higher concentration or because of their large size. Two examples of active transport are the sodium-potassium pump and vesicle transport.
  - The sodium-potassium pump moves sodium ions out of the cell and potassium ions into the cell, both against a concentration gradient, in order to maintain the proper concentrations of both ions inside and outside the cell and to thereby control membrane potential.
  - Vesicle transport uses vesicles to move large molecules into or out of cells.
- Energy is the ability to do work and is needed by every living cell to carry out life processes.
- The form of energy that living things need is chemical energy, and it comes from food. Food consists of organic molecules that store energy in their chemical bonds.
- Organisms mainly use glucose and ATP for energy. Glucose is the compact, stable form of energy that is carried in the blood and taken up by cells. ATP contains less energy and is used to power cellular processes.
- Cellular respiration is the aerobic process by which living cells break down glucose molecules, release energy, and form molecules of ATP. This process involves Glycolysis, Transformation of Pyruvate, Krebs Cycle, and Oxidative phosphorylation. Overall, in this process, glucose and oxygen react to form carbon dioxide and water.
  - The first stage of cellular respiration, called glycolysis, takes place in the cytoplasm. In this step, enzymes split a molecule of glucose into two molecules of pyruvate, which releases energy that is transferred to ATP.
  - Pyruvate is transformed to Acetyl CoA in the intermediate stage
  - The second major stage of cellular respiration, called the Krebs cycle, takes place in the matrix of a mitochondrion. During this stage, two turns through the cycle result in all of the carbon atoms from the two pyruvate molecules forming

carbon dioxide and the energy from their chemical bonds being stored in a total of 16 energy-carrying molecules (including 4 from glycolysis).
    - The third stage of cellular respiration, Oxidative Phosphorylation, takes place on the inner membrane of the mitochondrion. Electrons are transported from molecule to molecule down an electron-transport chain. Some of the energy from the electrons is used to pump hydrogen ions across the membrane, creating an electrochemical gradient that drives the synthesis of many more molecules of ATP.
    - In all three stages of aerobic cellular respiration combined, as many as 36 molecules of ATP are produced from just one molecule of glucose.
- Some organisms can produce ATP from glucose by anaerobic respiration, which does not require oxygen. Many human cells perform fermentation that also does not require oxygen. It is performed to recycle NADH back into NAD+. There are two types: alcoholic fermentation and lactic acid fermentation. Both start with glycolysis.
    - Alcoholic fermentation is carried out by single-celled organisms including yeasts and some bacteria. We use alcoholic fermentation in these organisms to make biofuels, bread, and wine.
    - Lactic acid fermentation is undertaken by certain bacteria, including the bacteria in yogurt, and also by our muscle cells when they are worked hard and fast.
    - Anaerobic respiration produces far less ATP than does aerobic cellular respiration, but it has the advantage of being much faster.

CHAPTER SUMMARY REVIEW

1. For the following questions, choose whether the description applies to eukaryotic cells, prokaryotic cells, or both.
    A. Has a nuclear membrane
    B. Has a plasma membrane made of a phospholipid bilayer
    C. Can be in a multicellular organism
    D. Has ribosomes
    E. Has an endoplasmic reticulum
    F. Its DNA replicates before cell division
    G. Has a single circular chromosome
    H. Has cytoplasm that splits into two daughter cells during cell division
    I. Has a cell cycle that includes interphase and mitosis
    J. The type of cell that most likely evolved to become mitochondria
2. Name one example of a prokaryotic organism and one example of a eukaryotic organism.
3. Neurons are cells in the nervous system that transmit messages. They use energy to maintain the balance of sodium and potassium ions inside and outside of them, which is critical for their ability to send messages.
    A. What kind of transport is this maintenance of sodium and potassium ion concentrations – active or passive? Explain your reasoning.
    B. What creates the barrier between the inside and the outside of these cells?
    C. What molecule uses energy to maintain the balance of sodium and potassium ions inside and outside of neurons? Describe two reasons why such a molecule is required.
    D. What form of energy is used in this process?
    E. Briefly explain how the energy in the food you eat gets there and provides energy for your neurons in the form necessary to power this process.
4. Explain why the inside of the plasma membrane, the side that faces the cytoplasm of the cell, must be hydrophilic.
5. *True or False*. Anaerobic and aerobic cellular respiration both produce ATP.
6. *True or False*. The cell membrane can also be called the plasma membrane.
7. *True or False*. Each phospholipid molecule in the cell membrane has two heads and a tail.
8. *True or False*. For cells, a smaller size is generally more efficient.
9. *True or False*. DNA is located in the nucleus of prokaryotic cells.
10. *True or False*. Cilia and flagella stick out of the cell membrane but are not made of cell membrane themselves.
11. Which statement about the cell membrane is false?
    A. It encloses the cytoplasm
    B. It protects and supports the cell
    C. It keeps all external substances out of the cell
    D. None of the above
12. During diffusion, substances move from an area of **X?** concentration to an area of **Y?** concentration.
    A. higher, lower
    B. lower, higher
    C. higher, equal
    D. lower, equal
13. Which type of respiration involves electron transport?
    A. Where does this electron transport occur within the cell?
    B. Energy from electron transport is used to pump hydrogen ions across a membrane. Is this active or passive transport of hydrogen ions? Explain your answer.
    C. After the process described in part B, hydrogen ions then flow from a region of higher concentration to a region of lower concentration. Is this active or passive transport of hydrogen ions? Explain your answer.

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CHAPTER OVERVIEW

4: BIOLOGICAL EVOLUTION

This chapter outlines how Darwin developed his theory of evolution by natural selection, Wallace's contribution to the theory, and evidence for evolution. The chapter also describes tools for studying evolution, processes of microevolution and macroevolution, and how Earth formed and life first evolved.

4.1: Case Study- Everyday Evolution

4.2: Darwin, Wallace, and the Theory of Evolution by Natural Selection

4.3: Evidence for Evolution

4.4: Microevolution

4.5: Macroevolution

4.6: Tools for Studying Evolution

4.7: Adaptation in Humans

4.8: Case Study Conclusion- Flu and Chapter Summary

Thumbnail: A silhouette of human evolution. (CC BY SA 3.0 Unported; Tkgd2007).

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4.1: CASE STUDY- EVERYDAY EVOLUTION

CASE STUDY: FLU, FROM PIGS TO YOU

One night in April 2009, Mateo woke up soaked in sweat. He had a fever of 102.4 °F, chills, an intense headache, and body aches. He soon develops a sore throat and a bad cough. The next day he felt so sick and exhausted that he could hardly get out of bed, and his fever and other symptoms lasted for days. Clearly, this was not just a mild cold virus — Mateo most likely had influenza, commonly known as the flu.



Figure **4.1.1**: Sow and five piglets

While watching TV as he recovered in bed, Mateo saw a news report about a new "swine flu" strain of the influenza virus that was spreading in people throughout North America, particularly in Mexico. It was called the swine flu because scientists thought it most likely originated in pigs, based on similarities in its genetic sequence with viruses that infect pigs. However, contact with pigs was not necessary for people to catch swine flu. This version seemed to spread directly between people, similar to the typical seasonal flu virus.

Mateo's symptoms were similar to those described in the news report on swine flu. Although he was beginning to recover, he saw that others were not so lucky. Many people with swine flu developed severe pneumonia, and some even died. Because this was a new strain of flu virus that was significantly different than the previous seasonal flu viruses, the existing flu vaccine was largely ineffective against swine flu. Therefore, the only way to try to prevent infection by the swine flu virus was to limit exposure to it, including avoiding contact with people with the flu and using good hand washing practices. The news report showed people in Mexico wearing masks as they went about their daily lives, to try to prevent exposure to the virus.

By June 2009, Mateo was back to normal, but many other people worldwide were not. Within just a few months, the swine flu had spread from North America to over 70 countries and territories throughout the world. The World Health Organization declared the spread of swine flu to be a pandemic, meaning that a significant portion of the world's population was infected. In September 2009, over 99% of the influenza viruses circulating in the U.S. were the swine flu strain, which is also known as the 2009 H1N1 virus. If you had the flu in the U.S. during this time period, chances are high that it was the swine flu.



Figure **4.1.2**: Train passengers in Mexico City in April 2009, wearing masks to protect against the swine flu epidemic.

How could a new viral strain like this emerge so suddenly? And how could it change from infecting pigs to infecting humans? This is an example of evolution in action. You may think of evolution as something that occurred in the distant past, for instance, how humans evolved from earlier primates. But evolution is occurring all the time. As you will learn in this chapter, evolution is the process by which characteristics of biological entities, such as living organisms or viruses, change over time. Evolution can occur very slowly or more quickly, but it is particularly rapid in viruses and bacteria. In the *Case Study Conclusion* for this chapter, you will learn specifically about how the 2009 H1N1 virus evolved from a virus that infects pigs to one that infects humans.

CHAPTER OVERVIEW: BIOLOGICAL EVOLUTION

In this chapter, you will learn about the theory of evolution, evidence for **evolution,** how evolution works, and the evolution of living organisms on Earth. Specifically, you will learn about:

- Darwin's theory of evolution by natural selection and how he developed this theory.
- Evidence for the theory of evolution from fossils, DNA, and observations of living organisms.
- Microevolution, which is an evolution that occurs over a relatively short period of time within a population.
- How allele frequencies in a population change due to the forces of evolution, which include mutation, gene flow, genetic drift, and natural selection.
- Macroevolution, which is an evolution that occurs at or above the species level. This includes the generation of new species and coevolution between species.
- Influences on the timing of macroevolution.
- The tools used by scientists to study evolution including the fossil record, methods of establishing the age of fossils, and molecular clocks based on DNA or amino acid sequences.

As you read this chapter and learn more about evolution, think about the following questions about the swine flu virus.

1. Viruses can replicate quickly. Why does this contribute to their rapid rate of evolution?

2. Mutation plays an important role in the evolution of viruses. How does mutation relate to evolution?
3. One of the reasons why the 2009 H1N1 swine flu virus evolved is that different types of influenza viruses can exchange genetic material with each other if they infect the same host, in a process called reassortment. Why might this lead to a new strain of influenza virus with different characteristics? How is this similar to the genetic variation produced by sexual reproduction?
4. It is thought that contact between North American and Eurasian pigs, possibly through international trade, may have contributed to the evolution of the swine flu virus. What are some other examples in which the movement of organisms or contact between organisms has contributed to evolutionary changes?

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4.2: DARWIN, WALLACE, AND THE THEORY OF EVOLUTION BY NATURAL SELECTION

STEPPING BACK IN TIME

The Grand Canyon, shown in Figure **4.2.1**, is an American icon and one of the wonders of the natural world. It is also a record of the past. Look at the rock layers in the picture. If you were to walk down a trail to the bottom of the canyon, with each step-down, you would be taking a step back in time. That's because lower layers of rock represent the more distant past. The rock layers and the fossils they contain show the prehistory of the region and its organisms over a 2-billion-year time span. Although Charles Darwin never visited the Grand Canyon, he saw rock layers and fossils in other parts of the world. They were one inspiration for his theory of evolution. Darwin's theory rocked the scientific world. In this concept, you will read why.

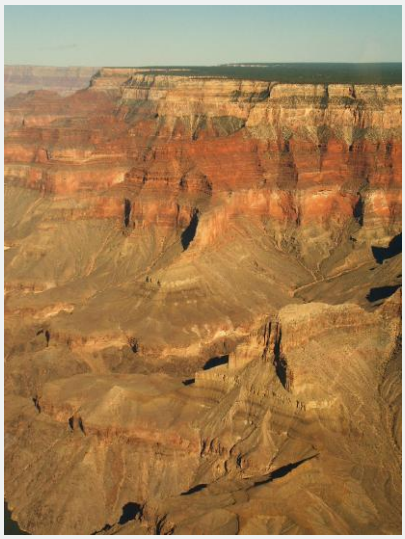


Figure **4.2.1**: Grand Canyon

WHAT IS THE THEORY OF EVOLUTION BY NATURAL SELECTION?

Eighteenth-century Englishman Charles Darwin is one of the most famous scientists who ever lived. His place in the history of science is well deserved. Darwin's theory of evolution by natural selection represents a giant leap in human understanding. It explains and unifies all of biology. Darwin's theory actually contains two major ideas:

1. One idea is that evolution occurs. In other words, organisms change over time. Life on Earth has changed as descendants diverged from common ancestors in the past.
2. The other idea is that evolution occurs by natural selection. Natural selection is the process in which living things with beneficial traits produce more offspring than others do. This results in changes in the traits of living things over time.

In Darwin's day, most people believed that all species were created at the same time and remained unchanged thereafter. They also believed that Earth was only 6,000 years old. Therefore, Darwin's ideas revolutionized biology. How did Darwin come up with these important ideas? It all started when he went on a voyage.

VOYAGE OF THE BEAGLE

In 1831, when Darwin was just 22 years old, he set sail on a scientific expedition on a ship called the *HMS Beagle*. Darwin was the naturalist on the voyage. As a naturalist, it was his job to observe and collect specimens of plants, animals, rocks, and fossils wherever the expedition went ashore. The route the ship took and the stops they made are shown on the map below. Darwin was fascinated by nature, so he loved his job on the *Beagle*. He spent more than three years of the five-year trip exploring nature on distant continents and islands. While he was away, a former teacher published Darwin's accounts of his observations. By the time Darwin finally returned to England, he had become famous as a naturalist.

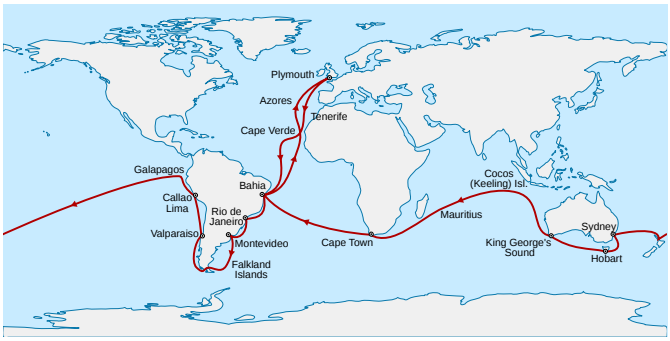


Figure **4.2.2**: Voyage of the Beagle. This map shows the route of Darwin's 5-year voyage on the HMS Beagle. Each stop along the way is labeled. The route starts with Sydney. Along the way they stopped at Hobart, King George's Sound, Cocos island, Mauritius, Cape town, Bahia, Azores, Plymouth, Tenerife, Bhaia again, Rio de Janeiro, Montevideo Islands, Valparaiso, Callao Lima, Galapagos, and then back to Sydney. Darwin and the others on board eventually circled the globe.

DARWIN'S OBSERVATIONS

During the long voyage, Darwin made many observations that helped him form his theory of evolution. For example:

- He visited tropical rainforests and other new habitats where he saw many plants and animals he had never seen before, such as the giant iguana and booby bird pictured below. These observations impressed him with the great diversity of life.
- He experienced an earthquake that lifted the ocean floor 2.7 meters (9 feet) above sea level. He also found rocks containing fossil seashells in mountains high above sea level. These observations suggested that continents and oceans had changed dramatically over time and continue to change in dramatic ways.
- He visited rock ledges that had clearly once were beaches that had gradually built up over time. This suggested that slow, steady

processes also change Earth's surface.

- He dug up fossils of gigantic extinct mammals, such as the ground sloth, fossils of which are also pictured below. This was hard evidence that organisms looked very different in the past. It suggested that living things — like the Earth's surface — change over time.



Figure **4.2.3**: On his voyage, Darwin saw giant marine iguanas and blue-footed boobies. He also dug up the fossil skeleton of a giant ground sloth-like the one shown here. From left: Giant Marine Iguana, Blue-Footed Boobies, and Fossil Skeleton of a Giant Ground Sloth in a museum.

THE GALÁPAGOS ISLANDS

Darwin's most important observations were made on the **Galápagos Islands** (shown on the map above of the *Beagle* voyage). The Galápagos Islands are a group of 16 small volcanic islands that are 966 kilometers (600 miles) off the west coast of South America. Individual Galápagos islands differ from one another in important ways. Some are rocky and dry; others have better soil and more rainfall. Darwin noticed that the plants and animals on the different islands also differed. For example, the giant tortoises on one island had saddle-shaped shells, whereas those on another island had dome-shaped shells, as you can see in the photos below. People who lived on the islands could even tell which island a tortoise came from by its shell. This started Darwin thinking about the origin of species. He wondered how each island came to have its own type of tortoise.

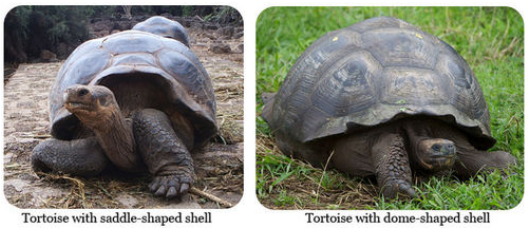


Figure **4.2.4**: Galápagos tortoises have differently shaped shells depending on which island they inhabit. Tortoises with saddle-shaped shells can reach up to eat plant leaves above their head. Tortoises with dome-shaped shells cannot reach up in this way. These two types of tortoises live on islands with different environments and food sources. How might this explain the differences in their shells?

OTHER INFLUENCES ON DARWIN

Science, like evolution, always builds on the past. Darwin didn't develop his theory completely on his own. He was influenced by the ideas of earlier thinkers.

WRITINGS OF EARLIER SCIENTISTS

Three scientists whose writings influenced Darwin were Lamarck, Lyell, and Malthus.

1. Jean Baptiste Lamarck (1744–1829) was an important French naturalist. He was one of the first scientists to propose that species change over time. However, Lamarck was wrong about how species change. His idea of the **inheritance of acquired characteristics** is incorrect. Traits an organism develops during its own life cannot be passed on to offspring, as Lamarck believed.
2. Charles Lyell (1797–1875) was a well-known English geologist. Darwin took his book, *Principles of Geology*, with him on the *Beagle*. In the book, Lyell argued that gradual geological processes have slowly shaped Earth's surface over very long periods of time. From this, Lyell inferred that Earth must be far older than most people believed.
3. Thomas Malthus (1766–1834) was an English economist. He wrote an essay titled *On Population*. In the essay, Malthus argued that human populations grow faster than the resources they depend on. When populations become too large, famine and disease break out. In the end, this keeps populations in check by killing off the weakest members.

KNOWLEDGE OF ARTIFICIAL SELECTION

These weren't the only influences on Darwin. He was also aware that humans could breed plants and animals to have useful traits. By selecting which plants or animals were allowed to reproduce, they could change an organism's traits over time. The pigeons in the figure below are good examples. Darwin called this type of change in organisms **artificial selection**. He used the word *artificial* to distinguish it from natural selection.



Figure **4.2.5**: Artificial Selection in Pigeons. Pigeon hobbyists breed pigeons to have certain characteristics. Artificial selection in pigeons. The two fancy-looking pigeons on the right were both bred from the common rock-pigeon on the far left.

DARWIN DEVELOPS HIS THEORY

Darwin spent many years thinking about the work of Lamarck, Lyell, and Malthus; what he had seen on his voyage; and what he knew about artificial selection. What did all this mean? How did it all fit together? Eventually, it all came together in his theory of evolution by natural selection. It's easy to see how these influences helped shape Darwin's ideas, although it actually took Darwin years to formulate his theory. His reasoning went like this:

1. Like Lamarck, Darwin assumed that species can change over time. The fossils he found helped convince him of that.
2. From Lyell, Darwin saw that Earth and its life were very old. Thus, there had been enough time for evolution to produce the great diversity of life that Darwin had observed.

3. From Malthus, Darwin knew that populations could grow faster than their resources. This “overproduction of offspring” led to a “struggle for existence,” in Darwin’s words.
4. From artificial selection, Darwin knew that some offspring have chance variations that can be inherited. In nature, offspring with certain variations might be more likely to survive the “struggle for existence” and reproduce. If so, they would pass their favorable variations to their offspring.
5. Darwin coined the term **fitness** to refer to an organism’s relative ability to survive and produce fertile offspring. Nature selects the variations that are most useful. Therefore, he called this type of selection natural selection.
6. Darwin knew artificial selection could change domestic species over time. He inferred that natural selection could also change wild species over time. In fact, he thought that if a species changed enough, it might evolve into a new species.

IT'S WALLACE’S THEORY TOO

Did you ever hear the saying that “great minds think alike?” It certainly applies to Charles Darwin and another English naturalist named Alfred Russel Wallace. Wallace lived at about the same time as Darwin and also traveled to distant places to study nature. Wallace wasn’t as famous as Darwin, but he developed basically the same theory of evolution. While working in what is now Malaysia, Wallace sent Darwin a paper he had written explaining his evolutionary theory. Wallace's ideas served to confirm what Darwin already thought. It also pushed Darwin to finish and publish his book, *On the Origin of Species.* Published in 1859, the book changed science forever. It clearly spelled out Darwin’s theory of evolution by natural selection and provided convincing arguments and evidence to support it.

APPLYING DARWIN'S AND WALLACE’S THEORY

The following example applies Darwin’s and Wallace's theory of evolution by natural selection. It explains how giraffes came to have such long necks, like those shown in the photo below.

- In the past, giraffes had short necks. But there was a chance variation in neck length. Some giraffes had necks a little longer than the average.
- Then, as now, giraffes fed on tree leaves. Perhaps the climate became drier, and leaves became scarcer. There would be more giraffes than the trees could support. Thus, there would be a “struggle for existence.”
- Giraffes with longer necks had an advantage. They could reach leaves other giraffes could not. Therefore, long-necked giraffes were more likely to survive and reproduce. In other words, they had greater fitness.
- These giraffes passed the long-neck trait to their offspring. With each successive generation, the population contained giraffes with longer necks. Eventually, all the giraffes had very long necks.

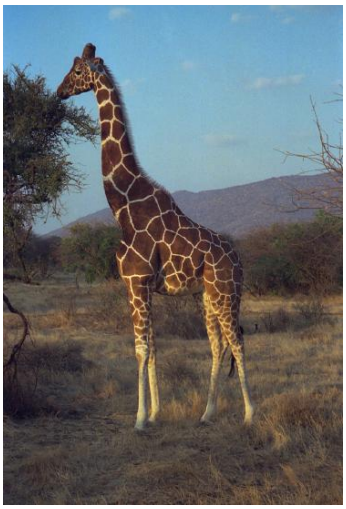


Figure **4.2.6**. African Giraffes. Giraffes feed on leaves high in trees. Their long necks allow them to reach leaves that other ground animals cannot. As this example shows, chance variations may help a species survive if the environment changes. Variation among species helps ensure that at least one species will be able to survive environmental change.

FEATURE: RELIABLE SOURCES

In the first chapter of his book *On the Origin of Species*, Charles Darwin discussed how artificial selection, also called selective breeding, had been successful in changing the traits of animals, including pigeons, cats, cattle, and dogs. He used this discussion as a springboard to introduce his idea of natural selection as well as to provide support for it.

The use of selective breeding to change the traits of other species has a very long history. In fact, archaeological evidence indicates that selective breeding of both plants and animals began as early as 10,000 years ago in the Middle East when previous hunter-gatherers began to domesticate animals and cultivate cereal plants. Around this time, changes in climate led to increasing drought, which forced people to concentrate around permanent water sources. These population concentrations could not be supported by wild animals and plants in the vicinity, providing a stimulus for the invention of agriculture and the use of selective breeding to increase the amount of available food. For thousands of years, species of plants such as wheat and rice and of animals such as goats and sheep were selectively bred and changed from their wild ancestors.

In the New World, the wild grain called teosinte, pictured on the left in Figure **4.2.7**, was selectively bred by Native Americans to produce larger and more numerous edible kernels. The result was modern maize (commonly called corn), shown on the right in the same picture. Teosinte was very small with fewer grains on it. The modern corn is bulky and with a lot more grain on it. After maize was created, it spread across the Americas and was introduced to Europe by European explorers and traders. Today,

maize is still a dietary staple and the most widely grown grain crop in the Americas.



Figure **4.2.7**: Selective breeding changed teosinte (left) to modern maize (right). The middle ear is a hybrid produced by breeding teosinte with maize.

The wild ancestors of domesticated wheat and rice were easy to identify because the modern species resemble their wild counterparts. However, that wasn't the case with maize, which looks very different from teosinte. Maize also appeared quite suddenly in the archaeological record, so its origin has been of special interest.

Go online to learn more about the selective breeding of teosinte to maize. Use only reliable sources such as university websites to find answers to the following questions:

1. Where and when was teosinte selectively bred to produce maize?
2. How did the change from wild teosinte to modern maize occur so rapidly?
3. What is the genetic basis of this change?

REVIEW

1. State Darwin's theory of evolution by natural selection.
2. Describe two observations Darwin made on his voyage on the *Beagle* that helped him develop his theory of evolution.
3. What is the inheritance of acquired characteristics? Which scientist developed this mistaken idea?
4. What is artificial selection? How does it work?
5. How did Alfred Russel Wallace contribute to the theory of evolution by natural selection?
6. Apply Darwin's theory of evolution by natural selection to a specific case. For example, explain how Galápagos tortoises could have evolved saddle-shaped shells.
7. Why did Darwin's observations of Galápagos tortoises cause him to wonder how species originate?
8. Explain how the writings of Charles Lyell and Thomas Malthus helped Darwin develop his theory of evolution by natural selection.
9. If a person builds big muscles due to a special diet and a lot of weightlifting, are big muscles a trait that will be automatically passed down to their children? Why or why not?
10. If a hypothetical ecosystem had unlimited resources available for all the organisms living in it, how do you think this would affect evolution?
11. What is the best definition of "fitness" in terms of evolution?
    A. The amount of lean muscle mass in an organism
    B. The ability of an organism to exercise for a long period of time
    C. An organism's ability to survive to an old age
    D. An organism's ability to survive and produce fertile offspring
12. In natural selection, organisms are selected by _____ ; in artificial selection, organisms are selected by _____ .
13. Explain why naturally occurring variations between individuals are important for evolution.
14. *True or False.* Modern maize evolved from teosinte through natural selection.
15. *True or False.* The theory of evolution states that living organisms on earth all evolved at once and then stopped changing.
16. *True or False.* Fossils of extinct animals are one type of evidence that supports Darwin's theory of evolution.

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4.3: EVIDENCE FOR EVOLUTION

A HORSE IS A HORSE, OF COURSE, OF COURSE

This drawing was created in 1848, but it's likely that you recognize the animal it depicts as a horse. Although horses haven't changed that much since this drawing was made, they have a long evolutionary history during which they changed significantly. How do we know? The answer lies in the fossil record.



Figure **4.3.1**: Horse

EVIDENCE FROM FOSSILS

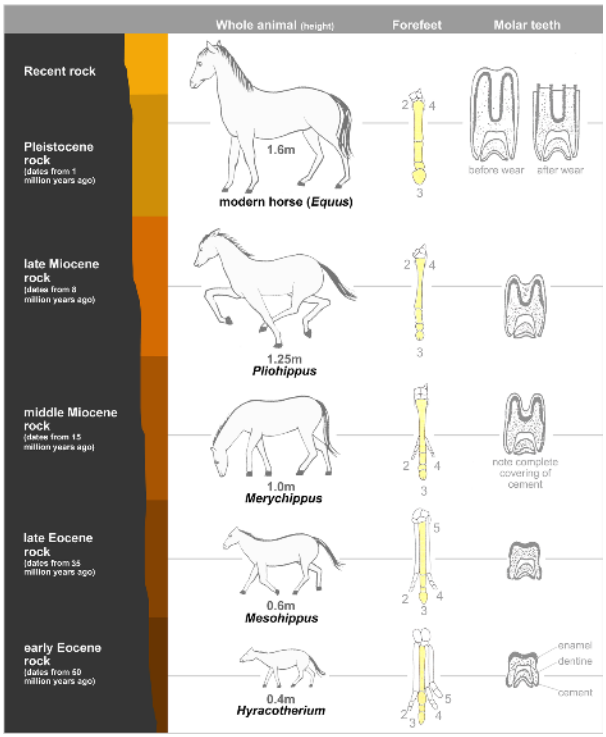


Figure **4.3.2**: Evolution of the Horse. The fossil record reveals how horses evolved. The lineage that led to modern horses (Equus) grew taller over time (from the 0.4 m Hyracotherium in early Eocene to the 1.6 m Equus). This lineage also developed longer molar teeth and the degeneration of the outer phalanges on the feet.

Fossils are a window into the past. They provide clear evidence that evolution has occurred. Scientists who find and study fossils are called *paleontologists*. How do they use fossils to understand the past? Consider the example of the horse, outlined in figure **4.3.2**. Fossils spanning a period of more than 50 million years show how the horse evolved.

The oldest horse fossils show what the earliest horses were like. They were only 0.4 m tall, or about the size of a fox, and they had four long toes. Other evidence shows they lived in wooded marshlands, where they probably ate soft leaves. Over time, the climate became drier, and grasslands slowly replaced the marshes. Later fossils show that horses changed as well.

- They became taller, which would help them see predators while they fed in tall grasses. Eventually, they reached a height of about 1.6 m.
- They evolved a single large toe that eventually became a hoof. This would help them run swiftly and escape predators.
- Their molars (back teeth) became longer and covered with hard cement. This would allow them to grind tough grasses and grass seeds without wearing out their teeth.

EVIDENCE FROM LIVING SPECIES

Scientists can learn a great deal about evolution by studying living species. They can compare the anatomy, embryos, and DNA of modern organisms to help understand how they evolved.

COMPARATIVE ANATOMY

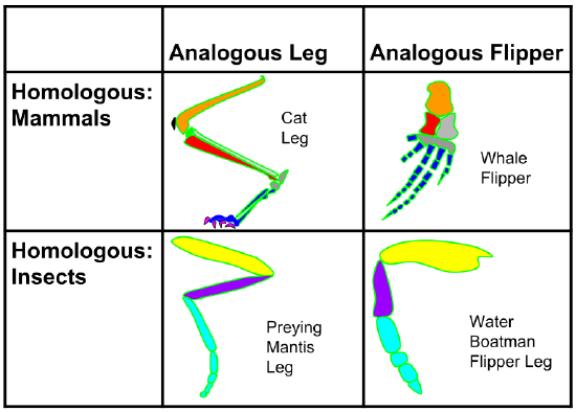


Figure **4.3.3**: Mammals (such as cats and whales) have homologous limb structures - with a different overall look but the same bones. Insects (such as praying mantis and water boatman) also have homologous limbs. Cat legs and praying mantis legs are analogous - looking similar but from different evolutionary lineages.

Comparative anatomy is the study of the similarities and differences in the structures of different species. Similar body parts may be homologous structures or analogous structures. Both provide evidence for evolution.

Homologous structures are structures that are similar in related organisms because they were inherited from a common ancestor. These structures may or may not have the same function in the descendants. Figure **4.3.3** shows the upper appendages of several

different mammals. They all have the same basic pattern of bones, although they now have different functions. All of these mammals inherited this basic bone pattern from a common ancestor.

Analogous structures are structures that are similar in unrelated organisms. The structures are similar because they evolved to do the same job, not because they were inherited from a common ancestor. For example, the wings of bats and birds, shown in the figure that follows, look similar on the outside and have the same function. However, wings evolved independently in the two groups of animals. This is apparent when you compare the pattern of bones inside the wings.

COMPARATIVE EMBRYOLOGY

Comparative embryology is the study of the similarities and differences in the embryos of different species. Similarities in embryos are likely to be evidence of common ancestry. All vertebrate embryos, for example, have gill slits and tails. All of the embryos in Figure **4.3.4**, except for fish, lose their gill slits by adulthood, and some of them also lose their tail. In humans, the tail is reduced to the tail bone. Thus, similarities organisms share as embryos may no longer be present by adulthood. This is why it is valuable to compare organisms in the embryonic stage.

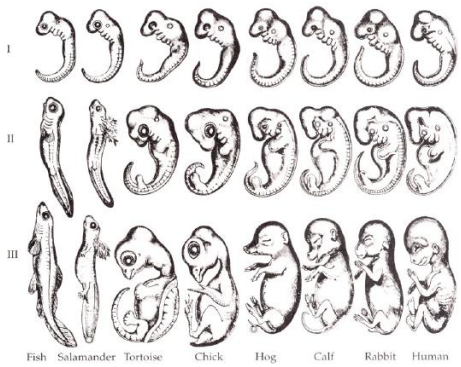


Figure **4.3.4**: Embryos of different vertebrates look much more similar than the animals do at later stages of life. Rows I, II, and III illustrate the development of the embryos of fish on the far left, salamander, tortoise, chick, hog, calf, rabbit, and human on the far right, from the earliest to the latest stages.

VESTIGIAL STRUCTURES

Structures like the human tail bone are called **vestigial structures**. Evolution has reduced their size because the structures are no longer used. The human appendix is another example of a vestigial structure. It is a tiny remnant of a once-larger organ. In a distant ancestor, it was needed to digest food, but it serves no purpose in the human body today. Why do you think structures that are no longer used shrink in size? Why might a full-sized, unused structure reduce an organism's fitness?

COMPARING DNA

Darwin could compare only the anatomy and embryos of living things. Today, scientists can compare their DNA. Similar DNA sequences are the strongest evidence for evolution from a common ancestor. Look at the diagram in Figure **4.3.5**. The diagram is a **cladogram,** a branching diagram showing related organisms. Each branch represents the emergence of new traits that separate one group of organisms from the rest. The cladogram in the figure shows how humans and apes are related based on their DNA sequences.

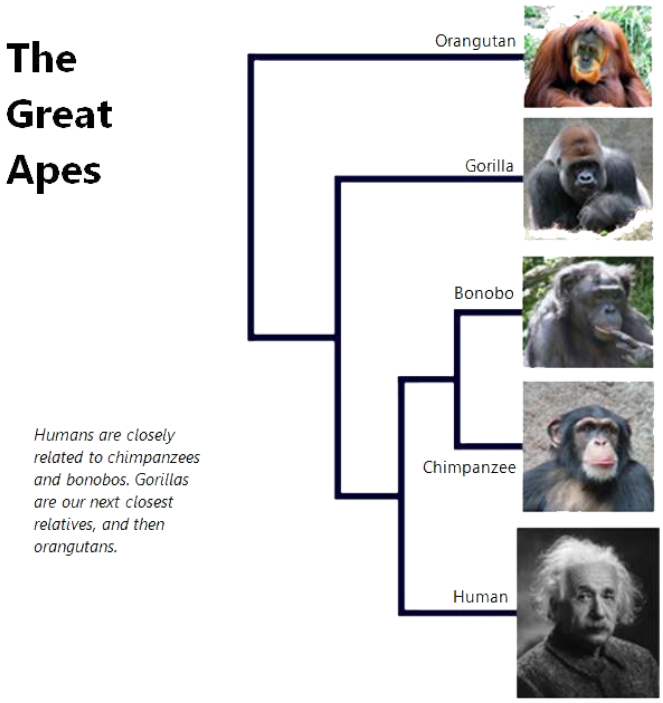


Figure **4.3.1**: Figure **4.3.5**: Cladogram of Humans and Apes. This cladogram is based on DNA comparisons. It shows how humans are related to apes by descent from common ancestors. Humans are most closely related to chimpanzees and Bonobo (our common ancestor existed most recently). We are less closely related to gorillas, and even less closely related to Orangutan.

EVIDENCE FROM BIOGEOGRAPHY

Biogeography is the study of how and why organisms live where they do. It provides more evidence for evolution. Let's consider the camel family as an example.

BIOGEOGRAPHY OF CAMELS: AN EXAMPLE

Today, the camel family includes different types of camels (Figure **4.3.6**). All of today's camels are descended from the same camel ancestors. These ancestors lived in North America about a million years ago.

Early North American camels migrated to other places. Some went to East Asia via a land bridge during the last ice age. A few of them made it all the way to Africa. Others went to South America by crossing the Isthmus of Panama. Once camels reached these different places, they evolved independently. They evolved adaptations that suited them for the particular environment where they lived. Through natural selection, descendants of the original camel ancestors evolved the diversity they have today.

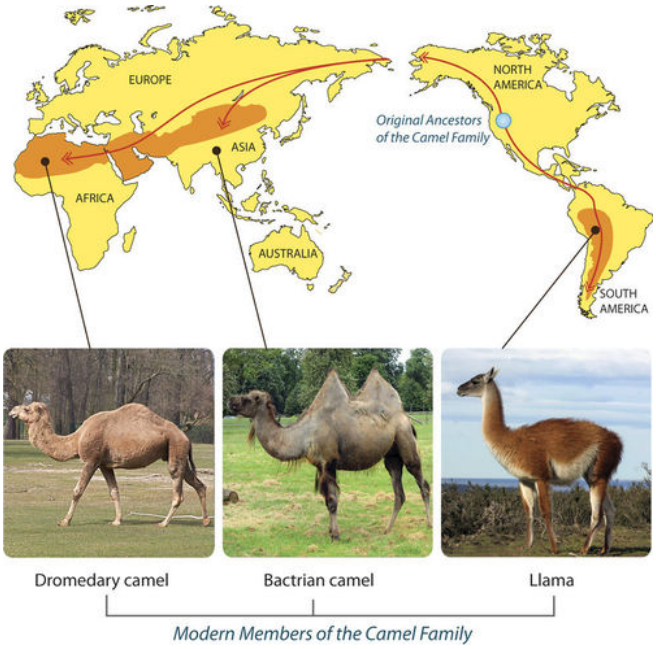


Figure **4.3.6**. Camel Migrations and Present-Day Variation. Members of the camel family now live in different parts of the world. Dromedary camels are found in Africa, Bactrian camels in Asia, and Llamas in South America. They differ from one another in a number of traits. However, they share basic similarities. This is because they all evolved from a common ancestor. What differences and similarities do you see?

ISLAND BIOGEOGRAPHY

The biogeography of islands yields some of the best evidence for evolution. Consider the birds called finches that Darwin studied on the Galápagos Islands (Figure **4.3.7**)). All of the finches probably descended from one bird that arrived on the islands from South America. Until the first bird arrived, there had never been birds on the islands. The first bird was a seed eater. It evolved into many finch species, each adapted for a different type of food. This is an example of **adaptive radiation**. This is the process by which a single species evolves into many new species to fill available ecological niches.

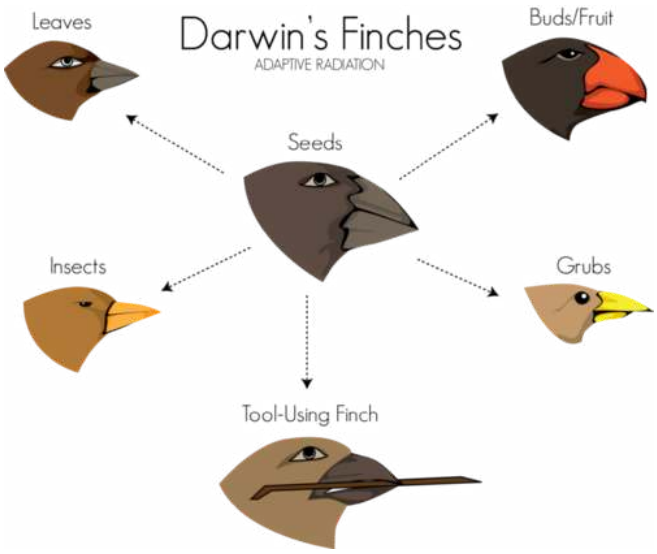


Figure **4.3.7**: Galápagos finches differ in beak size and shape, depending on the type of food they eat. Those eating buds and fruits have the largest beaks. Insect and grub eaters have narrower beaks

EYEWITNESSES TO EVOLUTION

In the 1970s, biologists Peter and Rosemary Grant went to the Galápagos Islands to re-study Darwin's finches. They spent more than 30 years on the project, but their efforts paid off. They were able to observe evolution by natural selection actually taking place.

While the Grants were on the Galápagos, a drought occurred, so fewer seeds were available for finches to eat. Birds with smaller beaks could crack open and eat only the smaller seeds. Birds with bigger beaks could crack open and eat seeds of all sizes. As a result, many of the smaller-beaked birds died in the drought, whereas birds with bigger beaks survived and reproduced. As shown in Figure **4.3.8**, within 2 years, the average beak size in the finch population increased. In other words, evolution by natural selection had occurred.

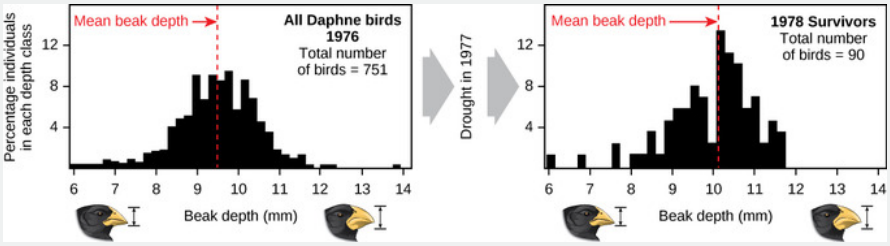


Figure **4.3.8**. Evolution of Beak Size in Galápagos Finches. The left graph shows the beak sizes of the entire finch population studied by the Grants in 1976. The right graph shows the beak sizes of the survivors in 1978. In just 2 years, the mean beak size increased from about 9 mm to just above 10 mm.

REVIEW

1. How do paleontologists learn about evolution?
2. Describe what fossils reveal about the evolution of the horse.
3. What are vestigial structures? Give an example.
4. Define biogeography.
5. Describe an example of island biogeography that provides evidence of evolution.
6. Humans and apes have five fingers they can use to grasp objects. Are these analogous or homologous structures? Explain.
7. Compare and contrast homologous and analogous structures. What do they reveal about evolution?
8. Why does comparative embryology show similarities between organisms that do not appear to be similar as adults?
9. What does a cladogram show?
10. Explain how DNA is useful in the study of evolution.
11. A bat wing is more similar in anatomical structure to a cat forelimb than to a bird wing. Answer the following questions about these structures.
    A. Which pairs are homologous structures?
    B. Which pairs are analogous structures?
    C. Based on this, do you think a bat is more closely related to a cat or to a bird? Explain your answer.
    D. If you wanted to test the answer you gave to part c, what is a different type of evidence you could obtain that might help answer the question?
12. *True or False*. Fossils are the only type of evidence that supports the theory of evolution.
13. *True or False*. Adaptive radiation is a type of evolution that produces new species.

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4.4: MICROEVOLUTION

SCHOOL DAYS

Except for their plastic lunch coolers, you might think that this picture of children on their way to school came from the 1800s. In fact, the picture is a photograph that was taken in 2006. The children are part of a religious community called the Amish, whose founders first came to the U.S. in the 1700s. Amish people shun modern conveniences such as electricity and automobiles. Their lives are more similar to the lives of their founders than to those of most other people in the U.S. today. As you will learn when you read this concept, the Amish are an example of one way in which populations may evolve.



Figure **4.4.1**: Amish On the way to school

GENES IN POPULATIONS

Individuals do not evolve because their genes do not change over time. Instead, evolution occurs at the level of the population. A **population** consists of organisms of the same species that live in the same area. In terms of evolution, the population is assumed to be a relatively closed group. This means that most mating takes place within the population. Evolutionary change that occurs over relatively short periods of time within populations is called **microevolution**. The science that focuses on evolution within populations is **population genetics**. It is a combination of evolutionary theory and Mendelian genetics.

THE GENE POOL

The genetic makeup of an individual is the individual's genotype. A population consists of many individuals and therefore many genotypes. All the genotypes together make up the population's gene pool. The **gene pool** consists of all the genes of all the members of the population. For each gene, the gene pool includes all the different **alleles** of the gene that exist in the population. An allele is referred to as a version of a gene. For a given gene, the population is characterized by the frequency of the different alleles in the gene pool. **Allele frequency** is how often an allele occurs in a gene pool relative to the other alleles for the same gene.

FORCES OF EVOLUTION

The factors that cause allele frequencies to change are called the **forces of evolution.** There are four such forces: mutation, gene flow, genetic drift, and natural selection.

GENETIC DRIFT

Genetic drift is a random change in allele frequencies that occurs in a small population. When a small number of parents produce just a few offspring, allele frequencies in the offspring may differ, just by chance, from allele frequencies in the parents. This is like tossing a coin. If you toss a coin just a few times, you may, by chance, get more or less than the expected 50 percent heads and 50 percent tails. Due to such chance variations in small populations, allele frequencies drift over time.

There are two special conditions under which genetic drift occurs. They are called the bottleneck effect and founder effect.

1. The bottleneck effect occurs when a population suddenly gets much smaller. This might happen because of a natural disaster such as a forest fire or disease epidemic. By chance, allele frequencies of the survivors may be different from those of the original population.
2. The founder effect occurs when a few individuals start or found a new population. By chance, allele frequencies of the founders may be different from allele frequencies of the population they left. An example of the founder effect occurred in the Amish, as described in figure **4.4.2**.



Figure **4.4.2**: Founder Effect in the Amish Population. The Amish population in the U.S. and Canada had approximately 200 founders who immigrated in the 1700s. The population has grown to almost 250,000 individuals who rarely interact with people outside the Amish community. One of the founders carried a recessive allele for a rare condition called Ellis-van Creveld syndrome - a type of dwarfism that results in extra fingers and short limbs as seen in this image. Today the Amish population has far more cases of this syndrome than any other population in the world.

MUTATION

Mutation creates new genetic variation in a gene pool. It is how all new alleles first arise. In sexually reproducing species, the mutations that matter for evolution are those that occur in gametes. Only these mutations can be passed to offspring. For any given gene, the chance of a mutation occurring in a given gamete is very low. Thus, mutations alone do not have much effect on allele frequencies. However, mutations provide the genetic variation needed for other forces of evolution to act.

GENE FLOW

Gene flow occurs when individuals move into or out of a population. If the rate of migration is high, this can have a significant effect on allele frequencies. Allele frequencies may change in the population the migrants leave as well as in the population the migrants enter. An

example of gene flow occurred during the Vietnam War in the 1960s and 1970s. Many young American servicemen had children with Vietnamese women. Most of the servicemen returned to the United States after the war. However, they left copies of their genes behind in their offspring. In this way, they changed the allele frequencies in the Vietnamese gene pool. Do you think the gene pool of the U.S. was also affected? Why or why not?

NATURAL SELECTION

Natural selection occurs when there are differences in fitness among members of a population. As a result, some individuals pass more genes to the next generation than do other members of the population. This causes allele frequencies to change over time. The example of sickle cell anemia, which is shown in the following table and described below, shows how natural selection can keep even a harmful allele in a gene pool.

Table **4.4.1**: Sickle Cell Anemia and Natural Selection

Genotype	Phenotype	Fitness
AA	100% normal hemoglobin	Somewhat reduced fitness because of no resistance to malaria
AS	Enough normal hemoglobin to prevent sickle-cell anemia	Highest fitness because of resistance to malaria
SS	100% abnormal hemoglobin, causing sickle-cell anemia	Greatly reduced fitness because of sickle-cell anemia

The allele (*S*) for sickle cell anemia is a harmful, autosomal recessive allele. It is caused by a mutation in the normal allele (*A*) for hemoglobin (the oxygen-carrying protein on red blood cells). Malaria is a deadly tropical disease that is common in many African populations. Heterozygotes (*AS*) with the sickle cell allele are resistant to malaria. Therefore, they are more likely to survive and reproduce. This keeps the *S* allele in the gene pool.

The sickle cell example shows that fitness depends on phenotypes and also on the environment. What do you think might happen if malaria were to be eliminated in an African population with a relatively high frequency of the *S* allele? How might the fitness of the different genotypes change? How might this affect the frequency of the *S* allele?

The sickle cell trait is controlled by a single gene. Natural selection for polygenic traits, which are controlled by multiple genes, is more complex, although it is less complicated if you consider just phenotypes for polygenic traits rather than genotypes. There are three major ways that natural selection can affect the distribution of phenotypes for a polygenic trait. The three ways are shown in the graphs in Figure **4.4.3**.

1. **Disruptive selection** occurs when phenotypes in the middle of the range are selected against. This results in two overlapping phenotypes, one at each end of the distribution. An example is a **sexual dimorphism**. This refers to differences between the phenotypes of males and females of the same species. In humans, for example, males and females have different average heights and body shapes.
2. **Stabilizing selection** occurs when phenotypes at both extremes of the phenotypic distribution are selected against. This narrows the range of variation. An example is human birth weight. Babies that are very large or very small at birth are less likely to survive, and this keeps birth weight within a relatively narrow range.
3. **Directional selection** occurs when one of two extreme phenotypes is selected for. This shifts the distribution toward that extreme. This is the type of natural selection that the Grants observed in the beak size of Galápagos finches. Larger beaks were selected for during drought, so beak size increased over time.

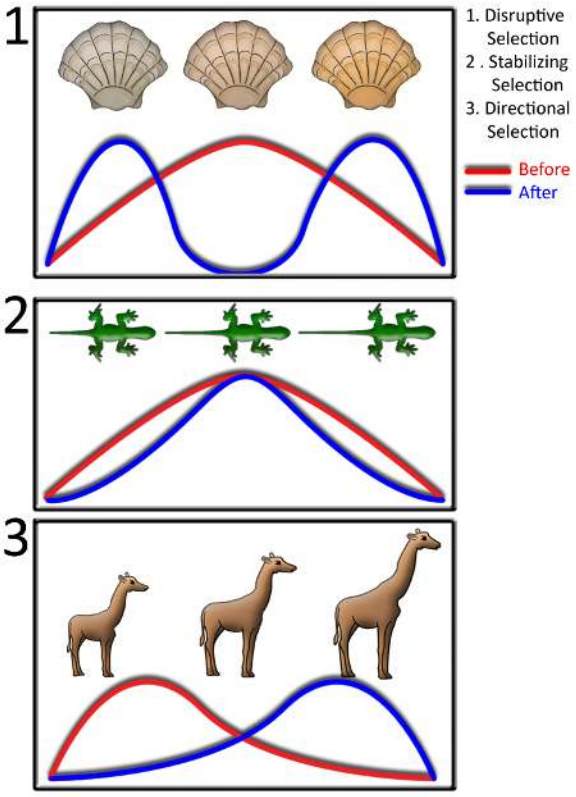


Figure **4.4.3**: Natural Selection for a Polygenic Trait. Natural selection may affect the distribution of a polygenic trait. The top panel shows the disruptive selection in the oyster shell shades. The lightest and darkest shades are more prevalent. The middle panel shows the stabilizing selection. Most lizards have median-sized tails. The bottom bottom panel shows the directional selection of the giraffe's neck size.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Recently reported research may help solve one of the most important and long-lasting mysteries of human biology. The mystery is why people with the *AS* genotype for sickle cell hemoglobin are protected from malaria. As you read above, their sickle cell hemoglobin gives them higher fitness in malaria areas than normal homozygotes (AA) who have only normal hemoglobin.

The malaria parasite and its mosquito vector were discovered in the late 1800s. The genetic basis of sickle cell hemoglobin

anemia and the resistance to malaria it confers were discovered around 1950. Since then, scientists have assumed, and some evidence has suggested, that the few sickle-shaped red blood cells of heterozygotes make them less hospitable hosts for the malaria parasite than the completely normal red blood cells of *AA* homozygotes. This seems like a reasonable hypothesis, but is it the correct one? The new research suggests a different hypothesis.

Working with genetically engineered mice as model organisms, researchers in Portugal discovered that an enzyme that produces the gas carbon monoxide is expressed at much higher levels in the presence of sickle cell hemoglobin than normal hemoglobin. Furthermore, the gas seems to protect the infected host from developing the lesions and symptoms of malaria, even though it does not seem to interfere with the life cycle of the malaria parasite in red blood cells. These findings may lead to new therapies for treating malaria, which is still one of the most serious public health problems in the world. The findings may also shed light on other abnormal hemoglobin variants that are known to protect against malaria.

REVIEW

1. Why are populations, rather than individuals, the units of evolution?
2. What is a gene pool?
3. List and define the four forces of evolution.
4. Why is mutation needed for evolution to occur, even though it usually has little effect on allele frequencies?
5. What is the founder effect? Give an example.
6. Identify three types of natural selection for polygenic traits.
7. Explain why genetic drift is most likely to occur in a very small population.
8. In some species, females prefer to mate with males that have certain genetically determined characteristics, such as bright coloration or a large, showy tail. How will this alter allele frequency in a population?
9. Which of the following may cause genetic drift?
   A. A natural disaster
   B. A large population where members mate with each other and also with new migrants that come into the population.
   C. An island with no birds that becomes populated by a small number of a species of bird.
   D. Both A and C
10. *True or False*. Allele frequencies can change within an organism.
11. *True or False*. Most populations on Earth are in Hardy-Weinberg equilibrium.
12. *True or False*. Genotype frequency can change if there is migration into or out of the population.

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4.5: MACROEVOLUTION

AN EVOLUTIONARY "ARMS" RACE

The garter snake in Figure **4.5.1** preys on a variety of small animals, including small amphibians called rough-skinned newts. The newts produce a powerful toxin that is concentrated in their skin. Garter snakes have evolved resistance to this toxin through a series of lucky genetic mutations, allowing them to safely prey upon the newts. The predator-prey relationship between these animals has created an evolutionary "arms" race. It has resulted in extremely high toxin levels in the newts and ever greater resistance to the toxin in the snakes. This is an example of the **coevolution** of two species. Coevolution is a type of macroevolution.



Figure **4.5.1**: Coast Garter Snake with red, white, and black pattern.

WHAT IS MACROEVOLUTION?

Macroevolution is an evolution that occurs at or above the level of the species. It is the result of microevolution taking place over many generations. Macroevolution may involve evolutionary changes in two interacting species, as in coevolution, or it may involve the emergence of one or more brand new species.

ORIGIN OF SPECIES

One of the main topics in macroevolution is how new species arise. The process by which a new species evolves is called **speciation**. How does speciation occur? How does one species evolve into two or more new species? To understand how a new species forms, it is important to review what a **species** is. A species is a group of organisms that can breed and produce fertile offspring together in nature. For a new species to arise, some members of a species must become reproductively isolated from the rest of the species. This means they can no longer interbreed with other members of the species. How does this happen? Usually, they become geographically isolated first.

ALLOPATRIC SPECIATION

Assume that some members of a species become geographically separated from the rest of the species. If they remain separated long enough, they may evolve genetic differences. If the differences prevent them from interbreeding with members of the original species, they have evolved into a new species. Speciation that occurs in this way is called **allopatric speciation**. An example of allopatric speciation involves Kaibab squirrels that live on the rim of the Grand Canyon, as shown in figure **4.5.2**.

Notes about these two groups of squirrels:

- Kaibab squirrels are found only on the north rim of the Grand Canyon, on the Kaibab Plateau. Abert's squirrels occupy a larger area on the south rim of the Grand Canyon.
- Kaibab squirrels became geographically isolated from Abert's squirrels, which are found on the south rim of the canyon.
- In isolation, Kaibab squirrel« evolved distinct characteristics, such as a complete whitetail.
- Abert's squirrels are the original species from which Kaibab squirrels diverged. Kaibab squirrels are currently classified as a subspecies of Abert's squirrels.
- Kaibab squirrels may eventually become different enough to be classified as a separate species.

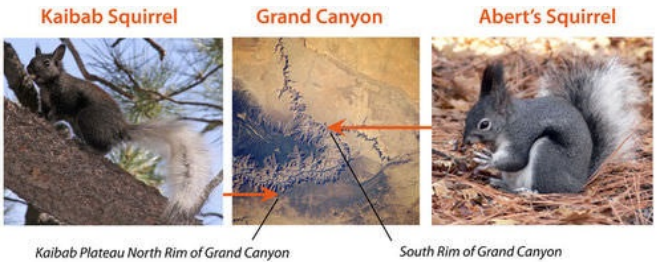


Figure **4.5.2**: Allopatric Speciation in the Kaibab Squirrel. The Kaibab squirrel is in the process of becoming a new species.

SYMPATRIC SPECIATION

Less often, a new species arises without geographic separation. This is called **sympatric speciation**.

1. Hawthorn flies lay eggs in hawthorn trees. The eggs hatch into larvae that feed on hawthorn fruits. Both the flies and trees are native to the U.S.
2. Apple trees were introduced to the U.S. by European settlers in the 1600s. Now, apple trees often grow near hawthorn trees. Some hawthorn flies started to lay eggs in nearby apple trees. When the eggs hatched, the larvae fed on apples.
3. Over time, the two fly populations — those that feed on hawthorn fruits and those that feed on apples — evolved reproductive isolation because they breed at different times. Their breeding season matches the season when apples or hawthorn fruits mature.
4. Because they rarely interbreed, the two populations of flies are evolving other genetic differences. They appear to be in the process of becoming separate species. As this example shows, behaviors, as well as physical traits, may evolve and lead to speciation.



Figure 4.5.3: Sympatric Speciation in Hawthorn Flies (far left panel). Hawthorn flies are diverging from one species into two due to two different habitats, Hawthorne tree (middle panel) and apple tree (right panel).

COEVOLUTION

Evolution generally occurs in response to changes in the environment. Environmental change often involves other species of organisms. In fact, many species evolve along with other species with which they interact. This is called **coevolution**. As one species changes, the other species must also change in order to adapt. The coevolution of rough-skinned newts and garter snakes is described above. Many other cases of coevolution occur in flowering plants and the species that pollinate them. The flowering plant and hummingbird in Figure 4.5.4 are an example. They have evolved matching structures. The tubular flowers of the plant are matched by the long, narrow beak of the hummingbird.



Figure 4.5.4: Results of Coevolution in a Flower and Its Pollinator. The very long mouth part of this hummingbird has coevolved with the tubular flower it pollinates. Only this species of bird can reach the nectar deep in the narrow flower.

TIMING OF MACROEVOLUTION

Is evolution slow and steady? Or does it occur in fits and starts? It may depend on what else is going on, such as changes in climate or geologic conditions.

- When climate and geologic conditions are stable, evolution may occur steadily and gradually. This is how Darwin thought evolution occurred. This model of the timing of evolution is called **gradualism**.
- When climate or geologic conditions are changing, evolution may occur more quickly. Long periods of little change may be interrupted by bursts of relatively rapid change. This model of the timing of evolution is called **punctuated equilibrium**. It is generally better supported by the fossil record than is gradualism.

REVIEW

1. Define speciation.
2. Describe how allopatric speciation occurs.
3. What is gradualism? When is it most likely to apply?
4. Describe the timing of evolutionary change according to the punctuated equilibrium model.
5. Why is sympatric speciation less likely to occur than allopatric speciation?
6. Why would macroevolution occur more quickly when there are major changes in the environment, such as changing the climate or geologic conditions, than when the environment is stable?
7. What is reproductive isolation? Why is it necessary for speciation to occur?
8. Kaibab squirrels are an example of what kind of speciation?
9. Imagine there is a large lake that dries up in certain regions, creating several smaller, separate lakes. The original lake had a particular species of fish and some fish got trapped in each of the smaller lakes as the large lake dried up.
    A. Is there a greater chance of speciation in the fish in the smaller, separate lakes or in the original large lake? Explain your answer.
    B. If new fish species evolve from the original species in the small, separate lakes, would this be sympatric or allopatric speciation? Explain your answer.
    C. If speciation occurred in the small lakes as described in part b, and then flooding occurred and the small lakes joined to become one large lake again, do you think the fish are likely to become one species again? Why or why not?
10. *True or False.* Speciation due to two populations breeding at different times in the same area is an example of sympatric speciation.
11. *True or False.* Coevolution always occurs between individuals of the same species.
12. Explain what the “punctuated” and “equilibrium” periods are in “punctuated equilibrium”.

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4.6: TOOLS FOR STUDYING EVOLUTION

MYTHS ABOUT EARTH

This interesting image is a 19th-century representation of Earth that is based on an ancient Hindu myth. According to the myth, Earth rests on the backs of elephants, which in turn stand on the back of a giant turtle. Virtually all human cultures and religions have developed myths about Earth and its origins. For example, until fairly recently, many Westerners thought that Earth was created in a day and that this occurred just a few thousand years ago. However, a diversity of evidence has since convinced the scientific community that Earth actually formed by natural processes from stardust a mind-boggling 4.5 to 4.6 billion years ago. Evidence also suggests that life first appeared on Earth up to 4 billion years ago and has been evolving ever since.

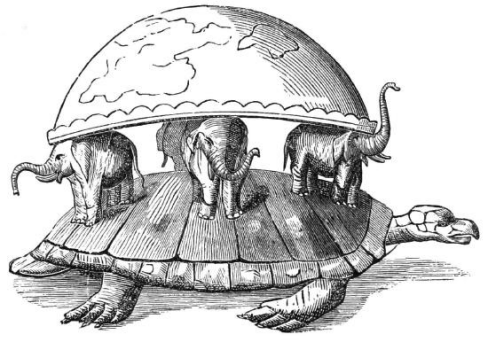


Figure **4.6.1**: The Hindu Earth

EARTH IN A DAY

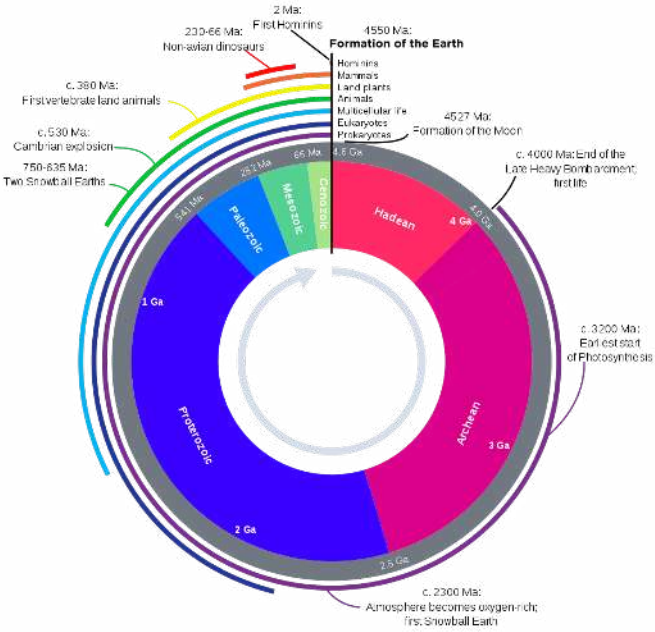


Figure **4.6.2**: The geological clock: a projection of Earth's 4.6 Ga history on a clock ("Ma" = a million years (Megayear) ago; "Ga" = a billion years (Gigayear) ago).

It can be difficult to wrap your mind around such vast amounts of time as the age of Earth and its early life forms. A useful way for envisioning the relative amounts of time that passed between Earth's origin and important events in biological evolution is to condense the total period of time to a 24-hour day, as shown in Figure **4.6.2**. On this scale, Earth would have formed at midnight, and the first life would have appeared at about 3:00 a.m. Humans would have appeared only during the last minute of the day. If we are such newcomers on planet Earth, how do we know about the vast period of time that went before us? How have we learned about the distant past?

THE FOSSIL RECORD

Much of what we know about the history of life on Earth is based on the fossil record, so this is an extremely important tool in the study of evolution. The **fossil record** is the record of life that unfolded over four billion years on Earth as reconstructed from the discovery and analysis of fossils. **Fossils** are the preserved remains or traces of organisms that lived in the past. The soft parts of organisms almost always decompose quickly after death. On occasion, the hard parts — mainly bones, teeth, or shells — remain long enough to mineralize and form fossils. An example of a complete fossil skeleton is pictured inFigure **4.6.3**.



Figure **4.6.3**: Extinct Lion Fossil. This fossilized skeleton represents an extinct lion species. It is rare for fossils to be so complete and well preserved as this one.

To be preserved as fossils, remains must be covered quickly by sediments or preserved in some other way. For example, they may be frozen in glaciers or trapped in tree resin or rock, like the frog shown in Figure **4.6.4**. Sometimes traces of organisms — such as footprints or burrows — are preserved. The conditions required for fossils to form rarely occur. Therefore, the chance of any given organism being preserved as a fossil is extremely low.



Figure **4.6.4**: The photo shows an ancient frog fossilized in rock.

In order for fossils to “tell” us the story of life, their chronology must be established. This means that fossils must be dated. Only then can they help scientists reconstruct how life changed over time. Fossils can be dated in two different ways, called relative dating and absolute dating.

- **Relative dating** determines which of two fossils is older or younger than the other, but not their age in years. Relative dating is based on the positions of fossils in rock layers. Lower layers were laid down earlier, so they are assumed to contain older fossils. This is illustrated in the figure below.
- **Absolute dating** determines how long ago a fossil organism lived, giving the fossil age in years. Absolute dating may be based on the amount of carbon-14 or other radioactive elements that remains in a fossil.

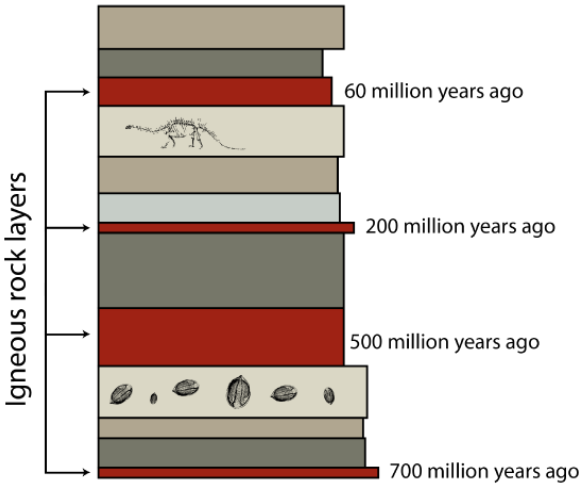


Figure **4.6.5**: Relative Dating Using Rock Layers. Relative dating establishes which of two fossils is older than the other. It is based on the rock layers in which the fossils formed. The fossils which are deeper are older than the fossils which are more superficial.

MOLECULAR CLOCKS

Molecular clocks are also valuable tools for studying evolution. A **molecular clock** uses DNA sequences (or the amino acid sequence of proteins that DNA encodes) to estimate how long it has been since related species diverged from a common ancestor. Molecular clocks are based on the assumption that mutations accumulate through time at a steady average rate for a given region of DNA. Species that have accumulated greater differences in their DNA sequences are assumed to have diverged from their common ancestor in the more distant past. Molecular clocks based on different regions of DNA may be used together for more accuracy. Look at the comparisons of DNA in the table below. Based on these data, which organism do you think shared the most recent common ancestor with humans?

Table **4.6.1**: DNA similarities of chimpanzee, mouse, chicken, and fruit fly species is to human DNA.

Organism	Similarity with Human DNA (percent)
Chimpanzee	98
Mouse	85
Chicken	60
Fruit Fly	44

FEATURE: MYTH VS. REALITY

Myth: Gaps in the fossil record disprove evolution.

Reality: Gaps in the fossil record, where transitional fossils between ancestral and descendant groups have not been found, are to be expected. The chances of organisms being fossilized are low. Some organisms do not preserve well, and conditions needed for fossilization are only rarely present. If evolution is occurring rapidly, the chances of transitional fossils forming are even lower. Even if fossils of transitional organisms do form, they must be discovered by researchers to be added to the fossil record. The vast majority of fossils have not been found. Researchers are studying the fossilization process to shed light on how much of the fossil record has not yet been discovered.

Fortunately, like fingerprints at a murder scene, the fossil record is just one type of evidence for evolution. In addition to fossils, molecular sequences and other types of evidence are all used together to reveal how life on Earth evolved.

REVIEW

1. Based on a 24-hour day, at what time did mammals evolve? How much of Earth's past had already taken place by that time? When did the first living things evolve?
2. What is the fossil record?
3. Why is the fossil record incomplete?
4. Compare and contrast relative and absolute dating of fossils.
5. Explain what molecular clocks can reveal about the evolution of life.
6. Why is it important for the study of evolution to know a fossil’s relative age compared to another fossil?
7. If fossil A is located above fossil B and fossil B is located above fossil C in different rock layers, arrange the three fossils in order of their likely age, from oldest to youngest.
8. Which tool could you use to study the evolutionary relationships between species that are still alive?

   A. Carbon-14 dating
   B. Molecular clocks

C. Relative position in the fossil record
D. None of the above

9. Use the *History of Earth in a Day* model above to answer the following questions.
   A. Which came first, free oxygen on Earth or the evolution of animals?
   B. During which geologic period did multicellular life evolve?
   C. About how much of Earth's history had elapsed before eukaryotes evolved?
   D. What is the name of our current era?
10. *True or False*. Fossils are always composed of actual tissue from extinct organisms.
11. *True or False*. Absolute dating of fossils is usually done using a molecular clock.

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4.7: ADAPTATION IN HUMANS

GOT LACTASE?

Do you remember this “got milk?” slogan from the 1990s? It was used in ads for milk in which celebrities were pictured wearing milk “mustaches.” While the purpose of the “got milk?” ads was to sell more milk, there is no denying that drinking milk can be good for one’s health. Milk is naturally high in protein and minerals. It can also be low in fat or even fat-free if treated to remove the lipids that naturally occur in milk. However, before you reach for a tall, cold glass of milk, you might want to ask yourself another question: “got lactase?”



Figure **4.7.1**: got milk slogan

ADAPTATION TO LACTOSE

Do you drink milk? Or do you avoid drinking milk and consuming milk products because they cause you discomfort? If the latter is the case, then you may have trouble digesting milk.

MILK, LACTOSE, AND LACTASE

Milk naturally contains not only proteins and lipids; it also contains carbohydrates. Specifically, milk contains the sugar **lactose.** Lactose is a disaccharide (two-sugar) compound that consists of one molecule each of galactose and glucose, as shown in the structural formula below. Lactose makes up between 2 and 8 percent of milk by weight. The exact amount varies both within and between species.

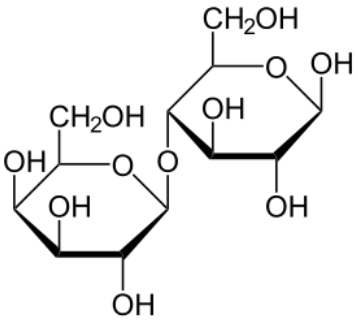


Figure **4.7.2**: Chemical structure of lactose which is consists of one molecule of galactose (left) and one molecule of glucose (right)

Lactose in milk must be broken down into its two component sugars to be absorbed by the small intestine. The enzyme **lactase** is needed for this process, as shown in the diagram below. Human infants are almost always born with the ability to synthesize lactase. This allows them to readily digest the lactose in their mother’s milk (or in infant formula). However, in the majority of infants, lactase synthesis begins to decline at about 2 years of age, and less and less lactase is produced throughout childhood.

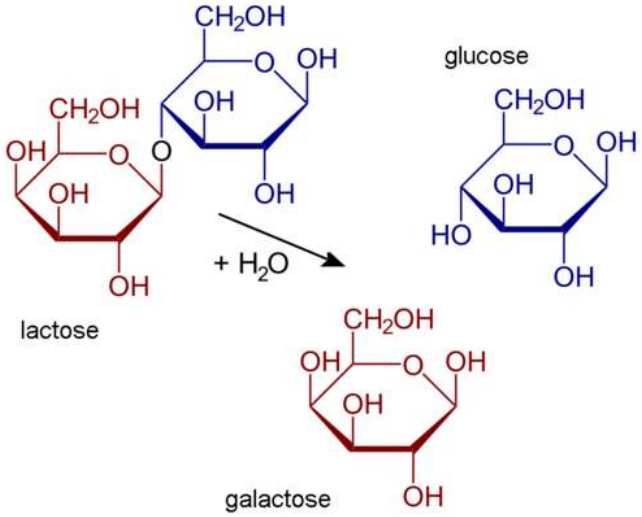


Figure **4.7.3**: The enzyme lactase is needed to break down the milk sugar lactose into its galactose and glucose components.

Lactose intolerance is the inability of older children and adults to digest lactose in milk. People who are lactose intolerant may be able to drink small quantities of milk without any problems, but if they try to consume larger amounts, they are likely to suffer adverse effects. For example, they may have abdominal bloating and cramping, flatulence (gas), diarrhea, nausea, and vomiting. The symptoms may occur from one-half to two hours after milk is consumed and are generally worse when the quantity of milk consumed is greater. The symptoms result from the inability of the small intestine to digest and absorb lactose, so the lactose is passed on to the large intestine, where normal intestinal bacteria start breaking it down through the process of fermentation. This process releases gas and causes other symptoms of lactose intolerance.

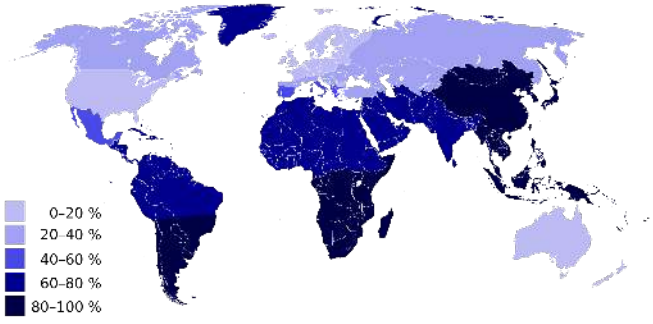


Figure **4.7.4**: Worldwide distribution of lactose intolerance in human populations. This map is a broad general indicator; more specific data can be found in this Lancet article from 2017.

Lactose intolerance is actually the original and normal condition of the human species, as it is of all other mammalian species. Early humans were hunter-gatherers that subsisted on wild plant and animal foods. The animal foods may have included meat and eggs but did not include milk because animals had not been domesticated. Therefore, beyond the weaning period, milk was not available for people to drink in early human populations. It makes good biological

sense to stop synthesizing an enzyme that the body does not need. After a young child is weaned, it is a waste of materials and energy to keep producing lactase when milk is no longer likely to be consumed.

Overall, an estimated 60 percent of the world's adult human population is thought to be lactose intolerant today. You can see the geographic distribution of modern human lactose intolerance on the map in Figure **4.7.4**. Lactose intolerance (dark blue) approaches 100 percent in populations throughout southern South America, southern Africa, and East and Southeast Asia.

Lactose intolerance is not considered to be a medical problem because its symptoms can be avoided by not consuming milk or milk products. Dietary control of lactose intolerance may be a matter of trial and error, however, because different people may be able to consume different quantities of milk before symptoms occur. If you are lactose intolerant, be aware that low-fat and fat-free milk may contain somewhat more lactose than full-fat milk because the former often have added milk solids that are relatively high in lactose.

LACTASE PERSISTENCE



Figure **4.7.5**: Sami (or Laplander) people in northern Scandinavia are traditional reindeer herders, and they are nearly 100 percent lactase persistent. This photo of a Sami man and his daughter on a reindeer was taken in 1900. Few Sami still herd reindeer today, but their lactase persistence has persisted.

Lactase persistence is the opposite of lactose intolerance. People who are lactase persistent continue to produce the enzyme lactase beyond infancy and generally throughout life. As a consequence, they are able to digest lactose and drink milk at older ages without adverse effects. The map above can also be read to show where lactase persistence occurs today. Populations with a low percentage of lactose intolerance (including North Americans of European descent) have high percentages of lactase-persistent people.

Lactase persistence is a uniquely human trait that is not found in any other mammalian species. Why did lactase persistence evolve in humans? When some human populations began domesticating and keeping herds of animals, animal milk became a potential source of food. Animals such as cows, sheep, goats, camels, and even reindeer (Figure **4.7.5**) can be kept for their milk. These kinds of animal milk also contain lactose, so natural selection would be strong for any individuals who kept producing lactase beyond infancy and could make use of this nutritious food. Eventually, the trait of lactase persistence would increase in frequency and come to be the predominant trait in dairying populations.

It is likely that lactase persistence occurs as a result of both genes and the environment. Some people inherit genes that help them keep producing lactase after infancy. Geneticists think that several different mutations for lactase persistence arose independently in different populations within the last 10,000 years. Part of lactase persistence may be due to continued exposure to milk in the diet in childhood and adulthood. In other words, a person may be genetically predisposed to synthesize lactase at older ages because of a mutation but may need the continued stimulation of milk drinking to keep producing lactase.

THRIFTY GENE OR DRIFTY GENE?

Besides variation in lactase persistence, human populations may vary in how efficiently they use calories in the foods they consume. People in some populations seem to be able to get by on quantities of food that would be inadequate for others, so they tend to gain weight easily. What explains these differences in people?

THRIFTY GENE HYPOTHESIS

In 1962, human geneticist James Neel proposed the **thrifty gene hypothesis**. According to this hypothesis, so-called "thrifty genes" evolved in some human populations because they allowed people to get by on fewer calories and store the rest as body fat when food was plentiful. According to Neel's hypothesis, thrifty genes would have increased in frequency through natural selection because they would help people survive during times of famine. People with the genes would be fatter and able to rely on their stored body fat for calories when food was scarce.

Such thrifty genes would have been advantageous in early human populations of hunter-gathers if food scarcity was recurrent stress. However, in modern times, when most people have access to enough food year-round, thrifty genes would no longer be advantageous. In fact, under conditions of plentiful food, having thrifty genes would predispose people to gain weight and develop obesity. They would also tend to develop a chronic disease associated with obesity, particularly type II diabetes. **Diabetes mellitus** is a disease that occurs when there are problems with the pancreatic hormone **insulin,** which normally helps cells take up glucose from the blood and controls blood glucose levels. In type II diabetes, body cells become relatively resistant to insulin, leading to high blood glucose. This causes symptoms including excessive thirst and urination. Without treatment, diabetes can lead to serious consequences, such as blindness and kidney failure.

Neel proposed his thrifty gene hypothesis not on the basis of genetic evidence for thrifty genes but as a possible answer to the mystery of why genes that seem to promote diabetes have not been naturally selected out of some populations. The mystery arose from observations that certain populations — such as South Pacific

Islanders, sub-Saharan Africans, and southwestern Native Americans — developed high levels of obesity and diabetes after they abandoned traditional diets and adopted Western diets. This is reflected in figure **4.7.6** which shows the 2017-2018 rates of diabetes in the US. Prevalence of diagnosed diabetes was highest among American Indians/Alaska Natives (14.7%), people of Hispanic origin (12.5%), and non-Hispanic blacks (11.7%), followed by non-Hispanic Asians (9.2%) and non-Hispanic whites (7.5%). An important note for studies based on race: any two humans have 99.9% similar DNA. The 0.1% difference causes variation in physical traits that humans have used to construct races. Biologically, all humans belong to just one race. Different traits are selected in different environments due to natural selection and genetic drift.

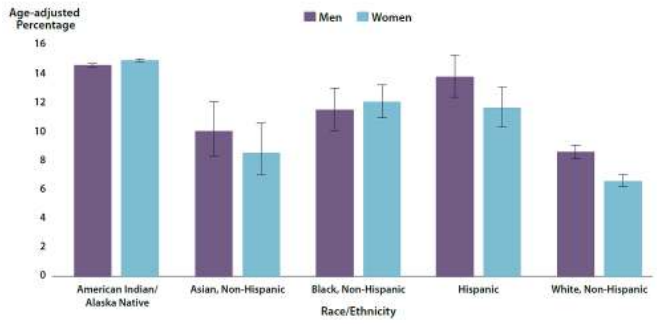


Figure **4.7.6**: Age-adjusted estimated prevalence of diagnosed diabetes by race/ethnicity group and sex for adults aged 18 years or older, United States, 2017–2018

ASSESSING THE THRIFTY GENE HYPOTHESIS

One of the assumptions underlying the thrifty gene hypothesis is that human populations that recently developed high rates of obesity and diabetes after Western contact had a long history of recurrent famine. Anthropological evidence contradicts this assumption for at least some of the populations in question. For example, South Pacific Islanders have long lived in a "land of plenty," with lush tropical forests year-round on islands surrounded by warm waters full of fish. Another assumption underlying the thrifty gene hypothesis is that hunter-gatherer people became significantly fatter during periods of plenty. Again, there is little or no evidence that hunter-gatherers traditionally deposited large fat stores when food was readily available.

Some geneticists have searched directly for so-called thrifty genes. Studies have revealed many genes with small effects associated with obesity or diabetes. However, these genes can explain only a few percentage points of the total population variation in obesity or diabetes.

THE DRIFTY GENE AND OTHER HYPOTHESES

Given the lack of evidence for the thrifty gene hypothesis, several researchers have suggested alternative hypotheses to explain population variation in obesity and diabetes. One hypothesis posits that susceptibility to obesity and diabetes may be a side effect of heat adaptation. According to this idea, some populations evolved lower metabolic rates as an adaptation to heat stress, because lower metabolic rates reduced the amount of heat that the body produced. The lower metabolic rates also predisposed people to gain excess weight and develop obesity and diabetes.

A thrifty phenotype hypothesis has also been proposed. This hypothesis suggests that individuals who have inadequate nutrition during fetal development might develop an insulin-resistant phenotype. The insulin-resistant phenotype would supposedly prepare these individuals for a life of famine, based on the environment within the womb. In a famine-free environment, however, the thrifty phenotype would lead to the development of diabetes.

The most recent alternative to the thrifty gene hypothesis is the drifty gene hypothesis proposed by biologist John Speakman. He argues that genes protecting humans from obesity were under strong natural selection pressure for a very long period of time while human ancestors were subject to the risk of predation. According to this view, being able to outrun predators would have been an important factor in selecting against fatness. When the risk of predation was lessened, perhaps as early as 2 million years ago, genes keeping fatness in check would no longer be selected for. Without selective pressure for these genes, their frequencies could change randomly due to genetic drift. In some populations, by chance, frequencies of the genes could decrease to relatively low levels, whereas in other populations the frequencies could be much higher.

FEATURE: MYTH VS. REALITY

Myth: Lactose intolerance is an allergy to milk.

Reality: Lactose intolerance is not an allergy because it is not an immune system response. Rather, it is a sensitivity to milk that is caused by lactase deficiency so the sugar in milk cannot be digested. Milk allergy does exist, but it is a different condition that occurs in only about 4 percent of people. It results when milk proteins (not milk sugar) trigger an immune reaction. How can you determine whether you have lactose intolerance or a milk allergy? If you can drink lactose-free milk without symptoms, it is likely that you are lactose intolerant and not allergic to milk. However, if lactose-free milk also produces symptoms, it is likely that you have a milk allergy. Note that it is possible to have both conditions.

Myth: If you are lactose intolerant, you will never be able to drink milk or consume other dairy products without suffering adverse physical symptoms.

Reality: Lactose intolerance does not mean that consuming milk and other dairy products is out of the question. Besides lactose-free milk, which is widely available, many dairy products have relatively low levels of lactose, so you may be able to consume at least small amounts of them without discomfort. For example, you may be able to consume milk in the form of yogurt without any problems because the bacteria in

yogurt produce lactase that breaks down the lactose. Greek yogurt may be your best bet because it is lower in lactose, to begin with. Aged cheeses also tend to have relatively low levels of lactose because of the cheese-making process. Finally, by gradually adding milk or milk products to your diet, you may be able to increase your tolerance to lactose.

REVIEW

1. Distinguish between the terms lactose and lactase.
2. What is lactose intolerance, and what percentage of all people have it?
3. Where and why did lactase persistence evolve?
4. What is the thrifty gene hypothesis?
5. How well is the thrifty gene hypothesis supported by evidence?
6. Describe an alternative hypothesis to the thrifty gene hypothesis.
7. Do you think that a lack of exposure to dairy products might affect a person's lactase level? Why or why not?
8. Describe an experiment you would want to do or data you would want to analyze that would help to test the thrifty phenotype hypothesis. Remember, you are studying people, so be sure it is ethical! Discuss possible confounding factors that you should control for in this study, or that might affect the interpretation of your results.
9. Explain the relationship between insulin, blood glucose, and type II diabetes.
10. *True or False.* Lactose persistence evolved more recently than lactose intolerance.
11. *True or False.* The drifty gene hypothesis is dependent on the assumption that fatter people cannot run as effectively as thinner people.
12. What two ethnic groups in the U.S. have a particularly high rate of death from diabetes? What other types of data would you want to observe to determine whether certain ethnic groups are more susceptible to diabetes? Explain why this additional data would be helpful.

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4.8: CASE STUDY CONCLUSION- FLU AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: FLU, FROM PIGS TO YOU

In April 2009, the world was hit with a swine flu pandemic. The Centers for Disease Control estimates that within that first year, 43 to 89 million people worldwide contracted the swine flu and that it contributed to 8,870 to 18,300 deaths. Some people with swine flu were spared serious complications, such as Mateo, who you read about it at the beginning of this chapter. At the time, the swine flu spread rapidly because as a newly evolved viral strain, most people had no natural immunity against it, and the existing flu vaccine could not prevent it. But by November 2009, a swine flu vaccine was developed, and now it is included in the annual flu vaccine in the U.S. By August 2010, the World Health Organization declared the H1N1 swine flu pandemic to be over. The virus is still around, but because of the vaccine and the natural immunity of those who had the virus previously, its infection rate is no longer of pandemic proportions.

The swine flu virus appears to have originated in pigs and later evolved the ability to infect humans. How could this happen? Scientists think that a process called reassortment played a critical role. In reassortment, influenza viruses can exchange genetic material with each other if they have infected the same cells. This creates new combinations of genes, somewhat similar to the genetic mixing that occurs in sexual reproduction when two parents with different genes reproduce with each other. As you know, genes help dictate the characteristics of an organism, or in this case, a virus. Therefore, the production of novel combinations of genes due to viral reassortment can lead to the evolution of new viral characteristics.

In addition to reassortment, influenza viruses have other characteristics that cause them to evolve quickly. In contrast to sexual reproduction, the replication of viruses to produce new "offspring" particles is much more rapid. As you have learned in this chapter, evolution is typically a slow process that takes place over many generations. But if these generations are produced rapidly, as in the case of viruses and bacteria, it speeds the rate of evolution. Additionally, RNA viruses have a very high rate of genetic mutation. The rapid evolution of the influenza virus is one of the reasons why the annual seasonal flu vaccine is not always effective against every strain.

But why did this flu pandemic come from pigs? Pigs are actually an ideal "mixing bowl" for the evolution of influenza viruses because pigs can become infected with influenza viruses from other species, including birds and humans. Therefore, genetic reassortment can occur in pigs between viral strains that normally infect different species. This is what scientists think occurred to produce the 2009 H1N1 swine flu virus. The 2009 H1N1 has gene segments from the birds, humans, and two different pig influenza viruses, and is therefore called a "quadruple reassortant" virus. In the case of the 2009 H1N1, this resulted in a new influenza strain that could infect humans, and be passed directly from person to person.

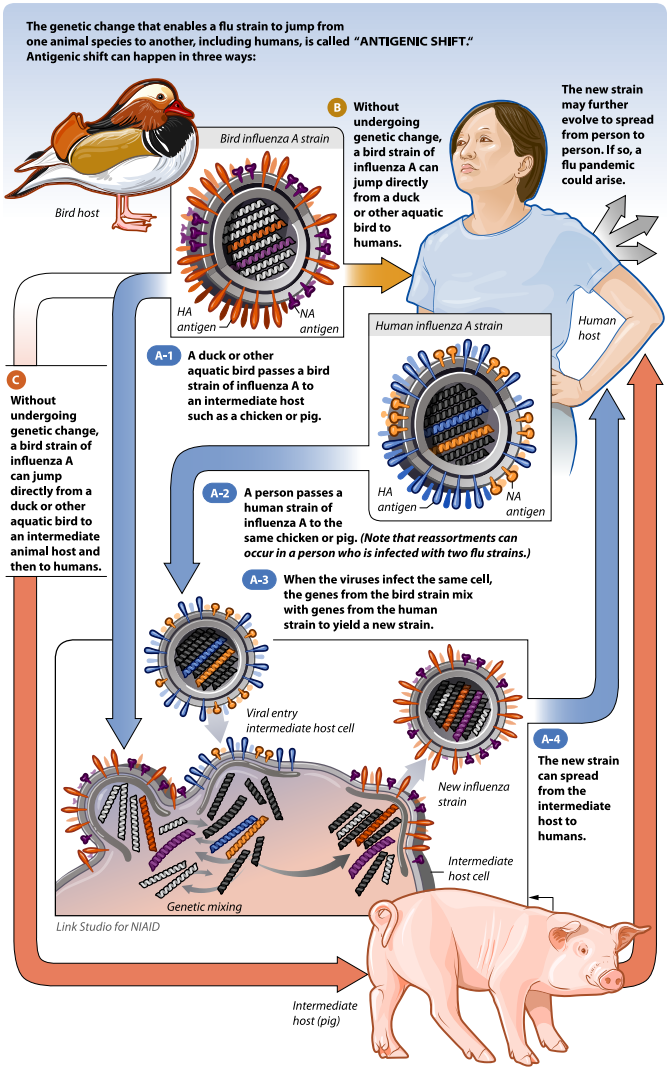


Figure **4.8.1**: Different viruses that infect pig may combine the pieces of their genetic material to make a new virus

Scientists do not know exactly when and where the 2009 H1N1 evolved, but they think that the reassortment event may have occurred several years prior to the 2009 pandemic. This is based on evidence gathered from "molecular evolution" techniques, which are similar to the molecular clock technique described in this chapter. Influenza viruses are known to mutate at a relatively steady rate. The genetic sequences of the new 2009 H1N1 strain were compared to the sequences in related, older influenza viruses to count the number of new mutations, in order to give an estimate of when the new viral strain evolved.

Probably one of the final events that resulted in the generation of the 2009 H1N1 virus was contact between North American and Eurasian pigs. This is because prior to 2009, there were "triple reassortant" variants of H1N1 with gene segments from a bird, human, and North American pig influenza already in existence. The 2009 H1N1 strain

additionally contained gene segments from influenza from Eurasian pigs, resulting in the “quadruple reassortant” virus. Scientists think that contact between pigs from these different regions, through international trade or other methods of contact, could have created this new strain. As you have learned in this chapter, the migration of organisms to new locations as well as contact between different organisms can influence evolution in many ways. Some examples are the migration of ancestral camels throughout the world, the coevolution of flowers and their pollinators, and the “founder effect” of small populations that move to new locations, such as the Amish.

Along with fossils, comparative anatomy and embryology, DNA analysis, and biogeography, evidence for evolution includes direct observation of it occurring. Peter and Rosemary Grant observed evolution occurring in the change in beak size of Galápagos finches. The evolution of the swine flu virus is another example of evolution in action. Evolution is not just a thing of the past — it is an ongoing and important process that affects our ecosystem, species, and even our health. Like viruses, bacteria also evolve rapidly, and the evolution of antibiotic resistance in bacteria is a growing public health concern. You can see that evolution is very relevant to our lives today.

CHAPTER SUMMARY

In this chapter, you learned about the theory of evolution, evidence for evolution, how evolution works, and the evolution of living organisms on Earth. Specifically, you learned:

- Darwin’s theory of evolution by natural selection states that living things with beneficial traits produce more offspring than others do. This leads to changes in the traits of living things over time.
  - During his voyage on the *Beagle*, Darwin made many observations that helped him develop his theory of evolution, particularly on the Galápagos Islands.
  - Darwin was influenced by other early thinkers, including Lamarck, Lyell, and Malthus. He was also influenced by his knowledge of artificial selection.
  - Wallace’s paper on evolution confirmed Darwin’s ideas. It also pushed him to publish his book, *On the Origin of Species*. The book clearly spells out his theory and provides extensive evidence and well-reasoned arguments to support it.
- Fossils provide a window into the past and are evidence for evolution. Scientists who find and study fossils are called paleontologists.
- Scientists compare the anatomy, embryos, and DNA of living things to understand how they evolved. Evidence for evolution is provided by homologous and analogous structures.
- Biogeography is the study of how and why plants and animals live where they do, which provides additional evidence for evolution. On island chains, such as the Galápagos, one species may evolve into many new species to fill available niches. This is called adaptive radiation.
- Peter and Rosemary Grant re-studied Galápagos finches. During a drought in the 1970s, they were able to directly observe evolution occurring.
- Microevolution refers to evolution that occurs over a relatively short period of time within a population. Macroevolution refers to evolution that occurs at or above the level of species as the result of microevolution taking place over many generations.
- The population is the unit of evolution, and population genetics is the science that studies evolution at the population level. A population’s gene pool consists of all the genes of all the members of the population. For a given gene, the population is characterized by the frequency of different alleles in the gene pool.
- There are four forces of evolution: mutation, which creates new alleles; gene flow, in which migration changes allele frequencies; genetic drift, which is a random change in allele frequencies that may occur in a small population; and natural selection, in which allele frequencies change because of differences in fitness among individuals.
- New species arise in the process of speciation. Allopatric speciation occurs when some members of a species become geographically isolated and evolve genetic differences. If the differences prevent them from interbreeding with the original species, a new species has evolved. Sympatric speciation occurs without geographic isolation first occurring.
- Coevolution occurs when interacting species evolve together. An example is flowering plants and their pollinators.
- Darwin thought that evolution occurs steadily and gradually. This model of evolution is called gradualism. The fossil record better supports the model of punctuated equilibrium. In this model, long periods of little change are interrupted by bursts of relatively rapid change.
- The fossil record is the record of life on Earth as reconstructed from the discovery and analysis of fossils. It is one of the most important tools in the study of evolution, but it is incomplete because fossilization is rare. To be added to the fossil record, fossils must be dated using relative or absolute dating methods.
- Molecular clocks are additional tools for reconstructing how life on Earth evolved. Molecular clocks use DNA or protein sequences to estimate how much time has passed since related species diverged from a common ancestor.
- The geologic time scale is a timeline of Earth's history. It divides Earth's chronology into smaller units of time such as eons and eras that are based on major changes in geology, climate, and living things.
- Milk contains the sugar lactose, a disaccharide. Lactose must be broken down into its two component sugars to be absorbed by the small intestine, and the enzyme lactase is needed for this process.
- In about 60 percent of people worldwide, the ability to synthesize lactase and digest lactose declines after the first two years of life. These people become lactose intolerant and cannot

consume much milk without suffering symptoms such as bloating, cramps, and diarrhea.

- In populations that herded milking animals for thousands of years, lactase persistence evolved. People who were able to synthesize lactase and digest lactose throughout life were strongly favored by natural selection. People who descended from these early herders generally still have lactase persistence. That includes many Europeans and European-Americans.
- Human populations may vary in how efficiently they use calories in food. Some people (especially South Pacific Islanders, Native Americans, and sub-Saharan Africans) seem to be able to get by on fewer calories than would be adequate for others, so they tend to easily gain weight, become obese, and develop diseases such as diabetes.
- The thrifty gene hypothesis answers the question of how genes for this ability could have evolved. It proposes that "thrifty genes" were selected for because they allowed people to use calories efficiently and store body fat when food was plentiful so they had a reserve to use when food was scarce. Thrifty genes become detrimental and lead to obesity and diabetes when food is plentiful all of the time.
- Several assumptions underlying the thrifty gene hypothesis have been called into question, and genetic research has been unable to actually identify thrifty genes. Alternate hypotheses to the thrifty gene hypothesis have been proposed, including the drifty gene hypothesis. The latter hypothesis explains variation in the tendency to become obese by genetic drift on neutral genes.

CHAPTER SUMMARY REVIEW

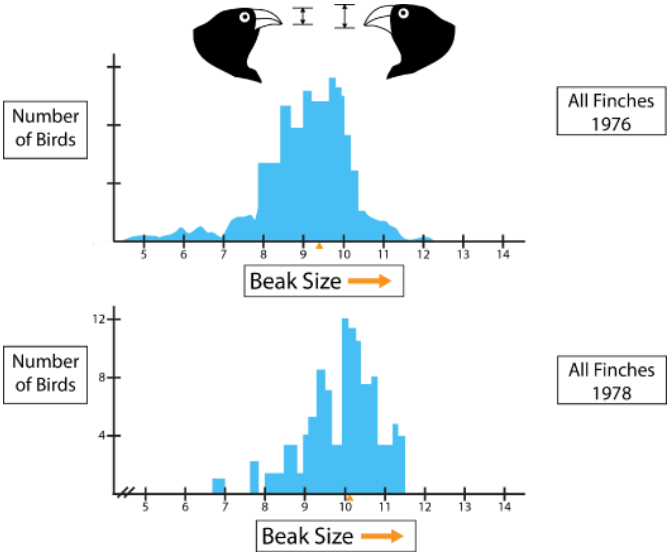


Figure **4.8.2**: Evolution of Beak Size in Galápagos Finches

1. Data from Peter and Rosemary Grant's study on the evolution of beak size in Galápagos finches is shown above. The top graph (1976) shows the distribution of beak size in the population before a drought, and the bottom graph (1978) shows beak size after the drought. The drought reduced seed availability. Finches with big beaks can crack open and eat seeds of all sizes, while finches with small beaks can only crack open and eat small seeds. Answer the following questions about this data.
   A. How was the average beak size affected by the drought? Although scientists would calculate this mathematically, you may answer just based on your observation of the graphs.
   B. Explain how natural selection and the "struggle for existence" likely changed the beak size in this population.
   C. Is this an example of microevolution or macroevolution? Explain your answer.
   D. Explain why variation is important for evolution by natural selection, using the data above as a specific example.
   E. What do you notice about the distribution of beak sizes in the 1978 graph — are all the beaks one size? If not, why not?
   F. Is the change in beak size shown here an example of stabilizing selection, disruptive selection, or directional selection?
2. Which of the following is an example of macroevolution?
   A. Speciation
   B. Coevolution
   C. Structures that become larger in a population
   D. A and B
3. Speciation is:
   A. The movement of a species to a new niche
   B. An evolution that occurs within a species
   C. The evolution of a new species from an existing species
   D. The development of analogous structures
4. *True or False*. An individual's genotype is known as their gene pool.
5. *True or False*. New species can evolve without geographic separation.
6. *True or False*. In punctuated equilibrium, the periods of relatively little evolutionary change are shorter than the periods of dramatic change.
7. Describe one example of a major environmental change that influenced the evolution of life on Earth. This change could include climate change, geologic change, change in existing species, change in the atmosphere, etc.
8. Explain why mass extinction events often cause rapid evolutionary changes afterward.
9. *Choose one*. Species with homologous structures are (more/less) likely to be closely related than species with analogous structures.
10. Explain why the fossils of extinct animals provide evidence for evolution.
11. Which of the following is an example of evolution by natural selection?
    A. Humans breeding dogs for certain characteristics
    B. Bats developing wings as an adaptation for flight
    C. A and B
    D. None of the above
12. Compare and contrast Darwin's theory of evolution by natural selection and Lamarck's idea of inheritance of acquired

characteristics.

13. Explain how microevolution and macroevolution relate to each other.
14. The fact that embryonic humans have gill slits is evidence for:
    A. Coevolution
    B. Evolution of analogous structures
    C. Common ancestry of vertebrates
    D. Gene flow
15. The study of allele frequencies in a group of the same species in the same time and place is known as _____ genetics.
16. Explain how biogeography can be used to study adaptive radiation.

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CHAPTER OVERVIEW

5: INTRODUCTION TO THE HUMAN BODY

This chapter outlines the organization of the human body and describes human cells, tissues, organs, organ systems, and body cavities. It also explains how organ systems interact and how feedback mechanisms maintain homeostasis in the body.

5.1: Case Study- Getting to Know Your Body
5.2: Organization of the Body
5.3: Human Cells and Tissues
5.4: Human Organs and Organ Systems
5.5: Human Body Cavities
5.6: Interaction of Organ Systems
5.7: Homeostasis and Feedback
5.8: Case Study Conclusion- Pressure and Chapter Summary

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5.1: CASE STUDY- GETTING TO KNOW YOUR BODY

CASE STUDY: UNDER PRESSURE

Looking at the photo of a football game in Figure 5.1.1, you can see why it is so important that the players wear helmets because players may fall on their heads or on top of each other's heads. Football often involves forceful impact to the head as players tackle each other. This can cause damage to the brain — either temporarily as in the case of a concussion, or long-term and more severe types of damage. Helmets are critical to reducing the incidence of traumatic brain injuries (TBIs), but they do not fully prevent them.



Figure 5.1.1:Football players

Take the example of 43-year-old Dayo. As a former professional football player who also played in college and high school, Dayo sustained many high-impact head injuries over the course of their football playing years. Dayo uses they/ them pronouns. A few years ago, Dayo began experiencing a variety of troubling symptoms, including the loss of bladder control (i.e. the involuntary leakage of urine), memory loss, and difficulty in walking. Symptoms such as these are often signs of damage to the nervous system, which includes the brain, spinal cord, and nerves, but they can result from many different types of injuries or diseases that affect the nervous system. In order to treat Dayo properly, their doctors needed to do several tests to determine the exact cause of their symptoms. These included a spinal tap to see if they had an infection, and an MRI (magnetic resonance imaging) to see if there were any problems with their brain structure.

The MRI revealed the cause of Dayo's symptoms. There are fluid-filled spaces within the brain called ventricles, and Dayo's ventricles were enlarged compared to normal ventricles. Based on this observation combined with the results of other tests, Dayo's doctor diagnosed them with hydrocephalus, a term that literally means "water head." Hydrocephalus occurs when the fluid that fills the ventricles, called cerebrospinal fluid, builds up excessively. This causes the ventricles to become enlarged and puts pressure on the brain, which can cause a variety of neurological symptoms including the ones Dayo was experiencing. You can see the difference between normal ventricles and ventricles that are enlarged due to hydrocephalus in the illustration below. Notice how the brain becomes "squeezed" due to hydrocephalus in the image on the right.

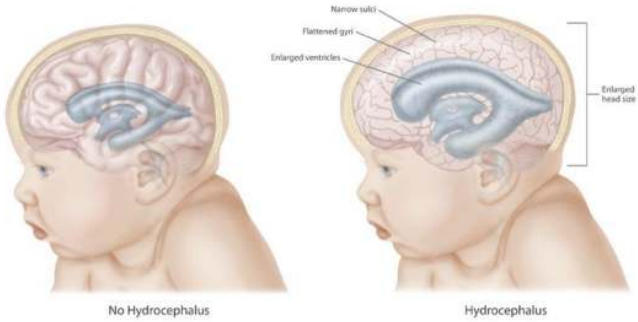


Figure 5.1.2. Comparison of an infant with (on the right) and without hydrocephalus (on the left). The ventricles (shown in blue-gray) are located inside of the brain (shown in pink). Ventricles are enlarged in the infant with hydrocephalus.

Hydrocephalus often occurs at birth, due to genetic factors or events that occurred during fetal development. Because babies are born with skull bones that are not fully fused, the skull of a baby born with hydrocephalus can expand and relieve some of the pressure on the brain, as reflected in the enlarged head size shown above. But adults have fully fused, inflexible skulls, so when hydrocephalus occurs in an adult, the brain experiences all of the increased pressure.

Why did Dayo develop hydrocephalus? There are many possible causes of hydrocephalus in adults, including tumors, infections, hemorrhages, and TBIs. Given their repeated and long history of TBIs due to football, and the absence of any evidence of infection, tumor, or other cause, Dayo's doctor thinks their head injuries were most likely responsible for their hydrocephalus.

Although hydrocephalus is serious, there are treatments. Read the rest of this chapter to learn about the cells, tissues, organs, cavities, and systems of the body, how they are interconnected, and the importance of keeping the body in a state of homeostasis, or balance. The amount of cerebrospinal fluid in the ventricles is normally kept at a relatively steady level, and the potentially devastating symptoms of hydrocephalus are an example of what can happen when a system in the body becomes unbalanced. At the end of the chapter, you will learn about Dayo's treatment and prognosis.

CHAPTER OVERVIEW: INTRODUCTION TO THE HUMAN BODY

In this chapter, you will learn about the general organization and functions of the human body. Specifically, you will learn about:

- The organization of the body from atoms and molecules up through cells, tissues, organs, and organ systems.
- How organ systems work together to carry out the functions of life.
- The variety of different specialized cell types in humans, the four major types of human tissues, and some of their functions.

- What organs are and the 11 major organ systems of the human body.
- Spaces in the body called body cavities, and the organs they hold and protect.
- The tissues and fluid that protect the brain and spinal cord.
- How organ systems communicate and interact in body processes such as cellular respiration, digestion, the fight-or-flight response to stressors, and physical activities such as sports.
- How homeostasis is maintained to keep the body in a relatively steady state, and the problems that can be caused by loss of homeostasis, such as diabetes.

As you read the chapter, think about the following questions:

1. What is the normal function of cerebrospinal fluid?
2. What is a spinal tap and how does it test for infection?
3. In Dayo's case, what organs and organ systems are probably affected by their hydrocephalus? What are some ways in which these organ systems interact?
4. The level of cerebrospinal fluid is normally kept in a state of homeostasis. What are other examples of types of homeostasis that keep your body functioning properly?

ATTRIBUTIONS

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5.2: ORGANIZATION OF THE BODY

A FANTASTIC MACHINE

This six-legged robot in Figure **5.2.1** was created for research, but it looks like it might be fun to play with. It's obviously a complex machine. Think about some other, more familiar machines, such as power drills, washing machines, and lawnmowers. Each machine consists of many parts, and each part does a specific job, yet all the parts work together to perform certain functions. Many people have compared the human body to a machine, albeit an extremely complex one. Like real machines, the human body also consists of many parts that work together to perform certain functions, which in the case of the human body include keeping the organism alive. The human body may be the most fantastic machine on Earth, as you will discover when you learn more about it in this concept.



Figure **5.2.1**: Six-legged walking robot LAURON IV

WHAT THE HUMAN MACHINE CAN DO

Imagine a machine that has all of the following attributes. It can generate a "wind" of 166 km/hr (100 mi/hr), and it can relay messages faster than 400 km/hr (249 mi/hr). It contains a pump that moves about a million barrels of fluid over its lifetime, and it has a control center that contains billions of individual components. The machine in question can even repair itself if necessary and not wear out for up to a century or more. It has all these abilities, and yet it consists mainly of water. What is it? It is the human body.

ORGANIZATION OF THE HUMAN BODY

The human body is a complicated, highly organized structure that consists of trillions of parts that function together to achieve all the functions needed to maintain life. The biology of the human body incorporates the body's structure, the study of which is called anatomy, and the body's functioning, the study of which is called physiology.

The organization of the human body can be seen as a hierarchy of increasing size and complexity, starting at the level of atoms and molecules and ending at the level of the entire organism, which is an individual living thing. You can see the intervening levels of organization in Figure **5.2.2** and read about them in the figure and the sections that follow.

To study the smallest level of organization, scientists consider the simplest building blocks of matter: atoms and molecules. The chemical level of organization considers these two building blocks as atoms bond to form molecules with three-dimensional structures.

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.

The cellular level is considered when a variety of molecules combine to form the fluid and organelles of a body cell. 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, such as a smooth muscle cell, typically consists of flexible membranes that enclose cytoplasm, a water-based cellular fluid together with a variety of tiny functioning units called organelles.

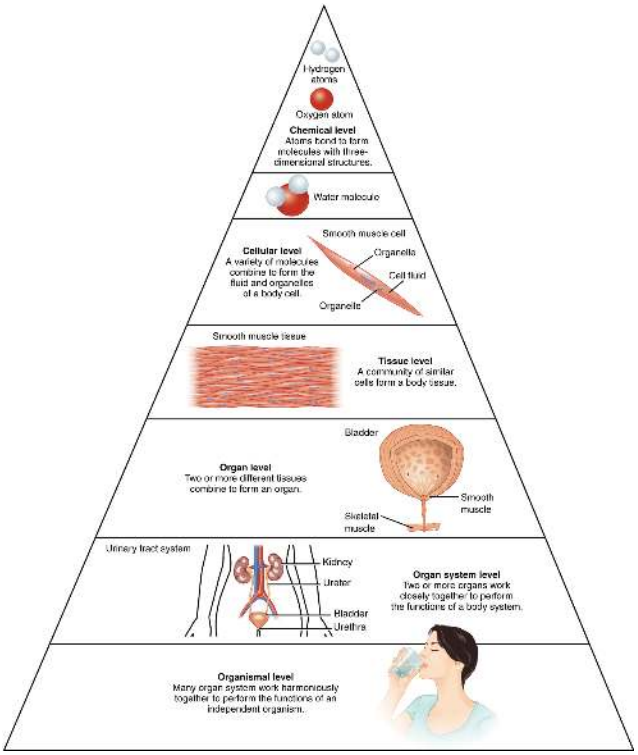


Figure **5.2.2**: This diagram shows the levels of organization of the human body, from atoms to the whole organism.

The tissue level can be studied when a community of similar cells forms a body tissue. 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. For example, when many smooth muscle cells come together both structurally and functionally, these cells collectively form a layer of smooth muscle tissue.

An organ is an anatomically distinct body structure composed of two or more tissue types. Each organ performs one or more specific physiological functions. The human bladder, which is composed of smooth muscle tissue, transitional epithelial tissue, and several types of connective tissue serves the function of storing urine produced by the kidneys.

An organ system level is a group of organs that work together to perform major functions or meet the physiological needs of the body. In the organ example above, both the kidneys and the bladder are organs of the urinary system. The kidneys produce urine, which is moved to the bladder by the ureters. Urine can then leave the bladder, and the body, through the urethra. These four organs work together to rid the body of liquid waste.

CELLS

The basic units of structure and function of the human body, as in all living things, are cells — an amazing 37 trillion of them by the time the average person reaches adulthood! Each cell carries out basic life processes that allow the body to survive. In addition, most human cells are specialized in structure and function to carry out other specific roles. In fact, the human body may consist of as many as 200 different types of cells, each of which has a special job to do. Just a few of these different human cell types are pictured in Figure **5.2.3**. The cells in the figure have obvious differences in structure that reflect their different functions. For example, nerve cells have long projections sticking out from the body of the cell. These projections help them carry electrical messages to other cells.

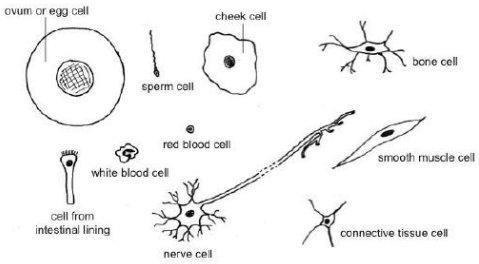


Figure **5.2.3**: A few of the many different types of cells in the human body are illustrated here. Each type of cell is specialized for a particular role in the body.

TISSUES

After the cell, the tissue is the next level of organization in the human body. A **tissue** is a group of connected cells that have a similar function. There are four basic types of human tissues: connective, epithelial, muscle, and nervous tissues. These four tissue types, which are shown in Figure **5.2.4**, make up all the organs of the human body. Connective tissue is composed of cells that are suspended in a matrix. Epithelial tissue is mostly composed of cells that are tightly packed together in sheets. Muscle tissue is also composed of tightly packed cells and some types of muscle, such as the skeletal muscle shown in Figure **5.2.4** contains striation due to the organization of muscle fibers. Nervous tissue is composed of cells with long extensions.

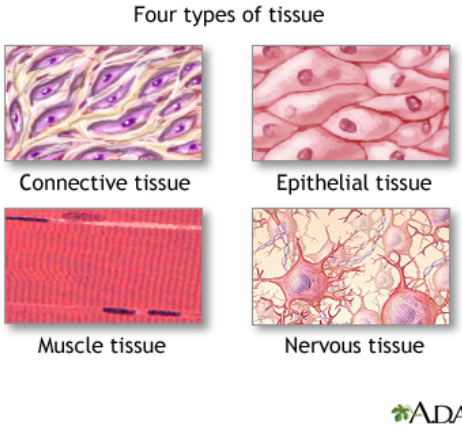


Figure **5.2.4**: Four types of tissues: Connective tissue, Epithelial tissue, Muscle tissue, Nervous tissue

ORGANS AND ORGAN SYSTEMS

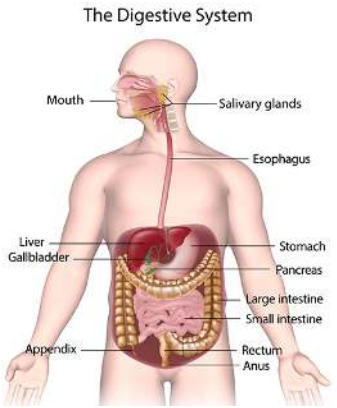


Figure **5.2.5**: A sample organ system (the digestive system) showing the organs within the system (mouth, salivary glands, esophagus, stomach, pancreas, large intestine, small intestine, liver, gallbladder, appendix, rectum, anus).

After tissues, organs are the next level of the organization of the human body. An organ is a structure that consists of two or more types of tissues that work together to do the same job. Examples of human organs include the heart, brain, lungs, skin, and kidneys. Human organs are organized into organ systems; the digestive system is shown in figure Figure **5.2.5**. An organ system is a group of organs that work together to carry out a complex overall function. Each organ of the system does part of the larger job.

A WELL-OILED MACHINE

All of the organs and organ systems of the human body normally work together like a well-oiled machine. This is because they are closely regulated by the nervous and endocrine systems. The nervous system controls virtually all body activities, and the endocrine system secretes hormones that help to regulate these activities. Functioning together, the organ systems supply body cells with all the substances they need and eliminate their wastes. They also keep temperature, pH, and other conditions at just the right levels to support life.

REVIEW

1. How is the human body like a complex machine?
2. Compare and contrast human anatomy and human physiology.
3. Summarize the hierarchical organization of the human body.
4. Relate cell structure to cell function, and give examples of specific cell types in the human body.
5. Define tissue, and identify the four types of tissues that make up the human body.
6. What is an organ? Give three examples of organs in the human body.
7. Define organ system, and name five organ systems in the human body.
8. True or False. How cells use oxygen is an example of physiology.
9. The organ system that secretes hormones is called the _____ system.
10. A neuron is a:
    A. specialized cell
    B. unspecialized cell
    C. an organ
    D. an organ system
11. Which organ system's function is to provide structure to the body and protect internal organs?
12. How is the human body regulated so all of its organs and organ systems work together
13. *True or False.* Organs consist of one or more types of tissue.
14. Give one example of how the respiratory and circulatory systems work together.

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5.3: HUMAN CELLS AND TISSUES

DUST MOP

This photo in Figure **5.3.1** looks like a close-up of an old-fashioned dust mop, and the object it shows has a somewhat similar function. However, the object is greatly enlarged in the photo. Can you guess what it is? The answer may surprise you. It is a scanning electron micrograph of human epithelial cells that line the bronchial passages. The floppy, dust-mop-like extensions are actually microscopic structures called cilia projecting from the outer surface of the epithelial cells. The function of the cilia is to trap dust, pathogens, and other particles in the air before it enters the lungs. The cilia also sway back and forth to sweep the trapped particles upward toward the throat, from which they can be expelled from the body.

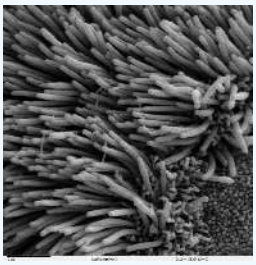


Figure **5.3.1**: Scanning electron microscope image of lung trachea epithelium. There are both ciliated and on-ciliated cells in this epithelium. Note the difference in size between the cilia and the microvilli (on the non-ciliated cell surface)

HUMAN CELLS

Like the ciliated bronchial cells in the micrograph above, many other cells in the human body are very distinctive and well suited for special functions. To perform their special functions, cells may vary in a number of ways.

VARIATION IN HUMAN CELLS

Some cells act as individual cells and are not attached to one another. Red blood cells are a good example. Their main function is to transport oxygen to other cells throughout the body, so they must be able to move freely through the circulatory system. Many other cells, in contrast, act together with other similar cells as part of the same tissue, so they are attached to one another and cannot move freely. For example, epithelial cells lining the respiratory tract are attached to each other to form a continuous surface that protects the respiratory system from particles and other hazards in the air.

Many cells can divide readily and form new cells. Skin cells are constantly dying and being shed from the body and replaced by new skin cells, and bone cells can divide to form new bone for growth or repair. Some other cells, in contrast, such as certain nerve cells, can divide and form new cells only under exceptional circumstances. That's why nervous system injuries such as a severed spinal cord generally cannot heal by the production of new cells, resulting in a permanent loss of function.

Many human cells have the primary job of producing and secreting a particular substance, such as a hormone or an enzyme. For example, special cells in the pancreas produce and secrete the hormone insulin, which regulates the level of glucose in the blood. Some of the epithelial cells that line the bronchial passages produce mucus, a sticky substance that helps trap particles in the air before it passes into the lungs.

DIFFERENT BUT IDENTICAL

All the different cell types within an individual human organism are genetically identical, so no matter how different the cells are, they all have the same genes. How can such different types of cells arise? The answer is the differential regulation of genes. Cells with the same genes can be very different because different genes are expressed depending on the cell type.

EXAMPLES OF HUMAN CELL TYPES

Many common types of human cells — such as bone cells and white blood cells — actually consist of several subtypes of cells. Each subtype, in turn, has a special structure and function. A closer look at these cell types will give you a better appreciation for the diversity of structures and functions of human cells.

BONE CELLS

There are four main subtypes of bone cells, as shown in Figure **5.3.2**. Each type has a different form and function:

1. Osteocytes are star-shaped bone cells that make up the majority of bone tissue. They are the most common cells in mature bone and can live as long as the organism itself. They also control the function of bone cells called osteoblasts and osteoclasts.
2. Osteoblasts are cells with single nuclei that synthesize new bone. They function in organized groups of connected cells called osteons to form the organic and mineral matrix of bone.
3. Osteogenic cells are undifferentiated stem cells that differentiate to form osteoblasts in the tissue that covers the outside of the bone.
4. Osteoclasts are very large, multinucleated cells that are responsible for the breakdown of bones through resorption. The breakdown of bone is very important in bone health because it allows for bone remodeling.

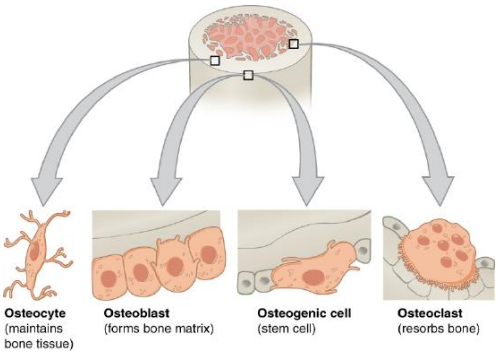


Figure **5.3.2**: Four sub-types of bone cells in the human skeletal system: Osteocytes (maintain bone tissues), Osteoblast (form bone matrix), Osteogenic cells (stem cell), Osteoclasts (reabsorb bone)

WHITE BLOOD CELLS

White blood cells (also called leukocytes) are even more variable than bone cells. Five subtypes of white blood cells are shown in Figure **5.3.3**. All of them are immune system cells involved in defending the body, but each subtype has a different function. They also differ in the normal proportion of all leukocytes they make up.

1. Monocytes make up about 5 percent of leukocytes. They are the biggest cells with extensions and a kidney-shaped nucleus. They engulf and destroy (phagocytize) pathogens in tissues.
2. Eosinophils make up about 2 percent of leukocytes. They have and a bilobed nucleus. They attack larger parasites and set off allergic responses.
3. Basophils make up less than 1 percent of leukocytes. Like eosinophils, these cells also have granules and a bilobed nucleus. They release proteins called histamines that are involved in inflammation.
4. Lymphocytes make up about 30 percent of leukocytes. These are small cells with a large circular nucleus. They include B cells and T cells. B cells produce antibodies against non-self antigens, and T cells destroy virus-infected cells and cancer cells.
5. Neutrophils are the most numerous white blood cells, making up about 62 percent of leukocytes. They have granules and a multilobed nucleus. They phagocytize single-celled bacteria and fungi in the blood.

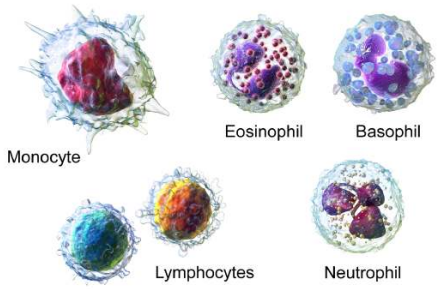


Figure **5.3.3**: Five sub-types of human white blood cells in the human immune system: monocyte, eosinophil, basophil, lymphocyte, neutrophil

TISSUES

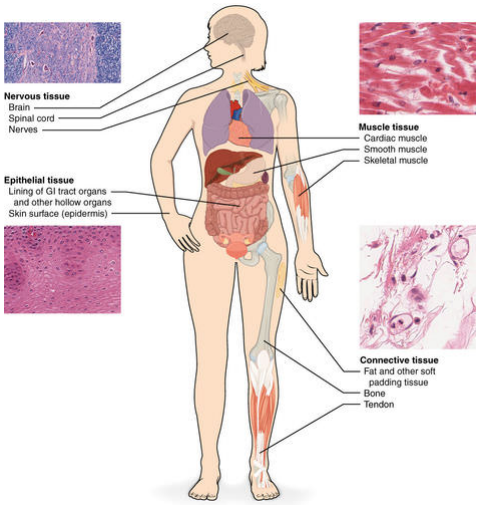


Figure **5.3.4**: There are 4 different types of tissues in our body. Nervous tissue is found in the brain, spinal cord, and nerves. Muscular tissue such as cardiac, smooth, and skeletal muscle. Epithelial tissue lines the GI tract organs and other hollow organs and is found on the skin surface (epidermis). Connective tissue such as fat and other soft padding tissue, bone, and tendon.

Groups of connected cells form tissues. The cells in a tissue may all be the same type or they may be of multiple types. In either case, the cells in the tissue work together to carry out a specific function. There are four main types of human tissues: connective, epithelial, muscle, and nervous tissues.

CONNECTIVE TISSUE

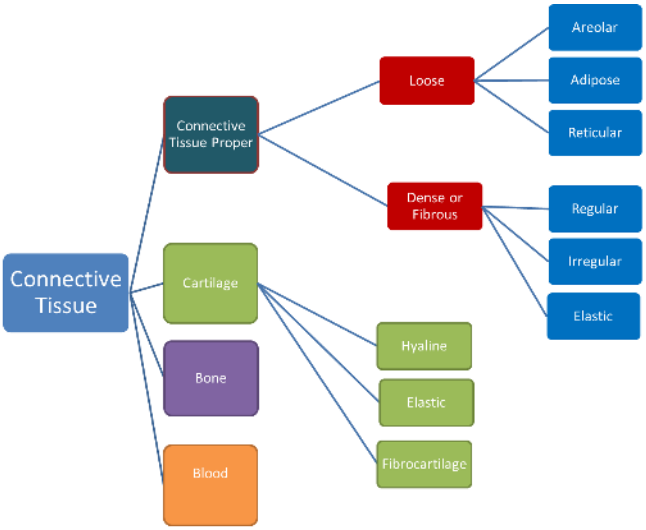


Figure **5.3.5**: The image summarizes the various categories of connective tissues found in the human body. Connective tissue can be classified as connective tissue proper, cartilage, bone, or blood. Cartilage can be classified as hyaline cartilage, elastic cartilage, or fibrocartilage. Connective tissue proper can be classified as loose and dense or fibrous. Loose connective tissue can be classified as areolar, adipose, or reticular. Dense or fibrous connective tissue can be classified as regular, irregular, and elastic.

The most diverse and abundant of all tissues, connective tissue holds cells together and supports the body. Connective tissue is made up of cells suspended in a non-cellular matrix. The matrix (also known as

ground substance) is secreted by the connective tissue cells and determines the characteristics of the connective tissue. It is the consistency of the matrix that determines the function of the connective tissue. The matrix can be liquid, gel-like or solid, all depending on the type of connective tissue. For example, the extracellular matrix of bone is a rigid mineral framework. The extracellular matrix of blood is liquid plasma. Connective tissues such as bone and cartilage generally form the body's structure. There are many sub-types of the four major types of tissues in a human body, see the flow chart in Figure **5.3.5**.

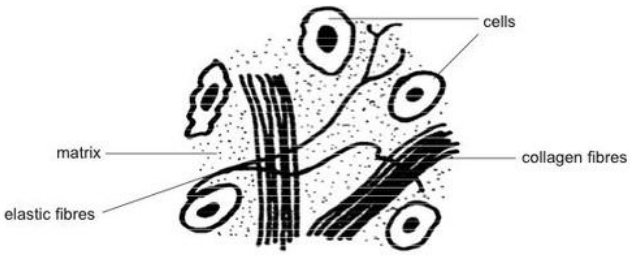


Figure **5.3.6**: General features of connective tissues. The Matrix of most connective tissues is made up of ground substance and protein fibers. There are cells suspended in the matrix.

CONNECTIVE TISSUE PROPER

Fibroblast cells are responsible for synthesizing protein fibers for the matrix. **Collagen fibers** are strong, **elastic fibers** are flexible and **reticular fibers** form a supportive framework for organs and basement membranes. There are two subcategories of connective tissue proper.

LOOSE CONNECTIVE TISSUE

Thin and soft, this tissue contains many collagen and elastic fibers in a jell-like matrix. The cells in loose connective tissue are not close together. This tissue functions in binding the skin to underlying structures. There are three types of loose connective tissue.

1. **Areolar connective tissue** is a common form of loose connective tissue. It is found in the skin and mucous membranes, where it binds the skin or membrane to underlying tissues such as muscles. It is also found around blood vessels and internal organs where it links and supports them.
2. **Adipose connective tissue** is commonly known as fat. This tissue contains fat cells that are specialized for lipid storage. In addition to storing energy, this tissue also cushions and protects the organs.
3. **Reticular connective tissue** is mostly composed of reticular protein fibers which make a skeleton, known as stroma, for the lymphatic and white blood cells. This type of tissue is found in the spleen and other lymphatic system structures.

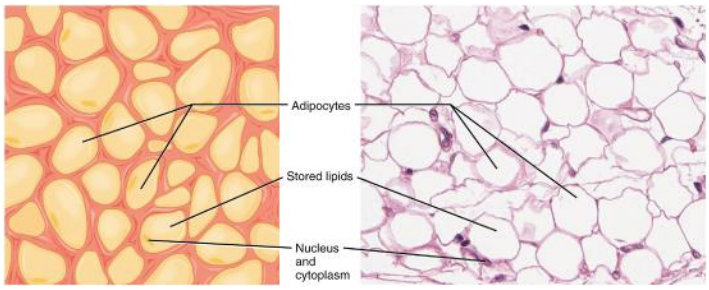


Figure **5.3.7**: Adipose Connective Tissue consists of fat cells (adipocytes with a nucleus and stored lipids in their cytoplasm) with a little extracellular matrix. It stores fat for energy and provides insulation.

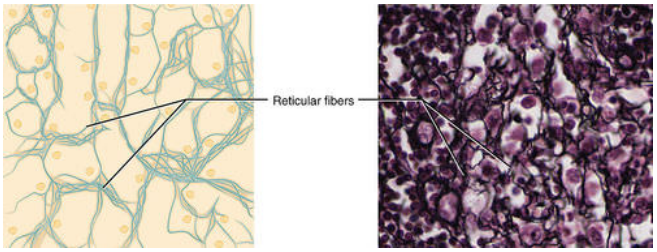


Figure **5.3.8**: Reticular Connective Tissue. This is a loose connective tissue made up of a network of reticular fibers that provides a supportive framework for soft organs

DENSE CONNECTIVE TISSUE PROPER

This tissue consists of three categories, dense regular connective tissue, dense irregular connective tissue, and elastic connective tissue. These tissues differ on the arrangement and composition of the fibrous elements of the extracellular matrix.

1. **Dense regular connective tissue** has extracellular fibers that all run in the same direction and plane. Muscle tendons are a type of dense regular connective tissue.
2. **Dense irregular connective tissue** contains collagen and elastic fibers which are found running in all different directions and planes. The dermis of the skin is composed of dense irregular connective tissue.
3. **Elastic connective tissue**: Made up of freely branching elastic fibers with fibroblasts in the spaces between the fibers, this tissue allows the kind of stretch that is found in the walls of arteries.

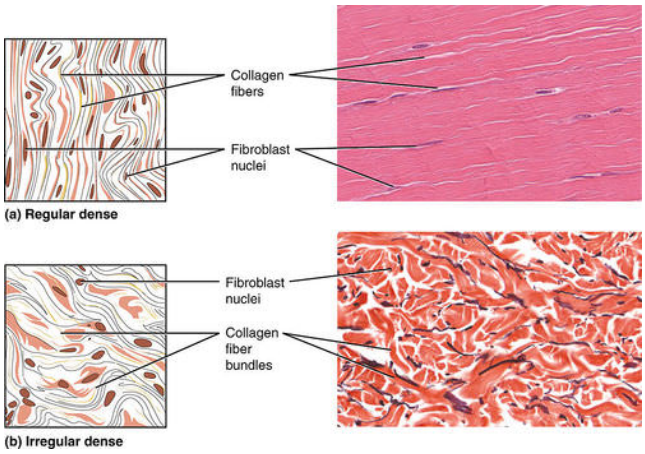


Figure 5.3.9: (a) Dense regular connective tissue consists of collagen fibers packed into parallel bundles. (b) Dense irregular connective tissue consists of collagen fibers interwoven into a mesh-like network..

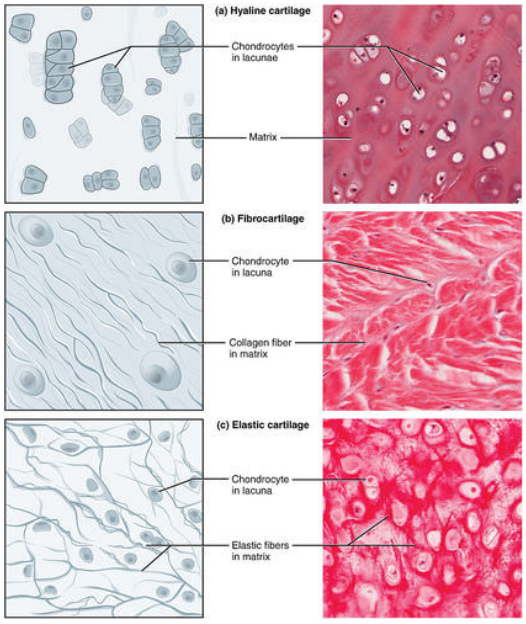


Figure 5.3.10: Cartilage is a connective tissue consisting of collagenous fibers embedded in a firm matrix of chondroitin sulfates. (a) Hyaline cartilage has chondrocytes in lacunae within a matrix. (b) Fibrocartilage has chondrocytes in lacunae within collage fibers in a matrix. (c) Elastic cartilage has chondrocytes in lacunae within elastic fibers in a matrix.

CARTILAGE

This connective tissue is relatively solid and is a non-vascularized tissue (does not have a blood supply). The matrix is produced by cells called chondroblasts. When these cells slow down, they reside is small spaces called lacunae. These mature cells in the lacunae are called chondrocytes. There are three types of cartilage: hyaline cartilage, elastic cartilage, and fibrocartilage.

1. **Hyaline cartilage** is the most common type of cartilage, contains many collagen fibers and is found in many places including the nose, between the ribs and the sternum and in the rings of the trachea.
2. **Elastic cartilage** has many elastic fibers in the matrix and supports the shape of the ears and forms part of the larynx.
3. **Fibrocartilage** is tough and contains many collagen fibers and is responsible for cushioning the knee joint and for forming the disks between the vertebrae.

BONE

Bone is a hard, mineralized tissue found in the skeleton. The bone matrix contains many collagen fibers as well as inorganic mineral salts, calcium carbonate, and calcium phosphate, all features that make it a very rigid structure. Bone cells, called **osteoblasts**, secrete the osteoid substance that eventually hardens around the cells to form an ossified matrix. The **osteon** forms the basic unit of compact bone. Within the

osteon, the osteocytes (mature bone cells) are located in lacunae. Because the bone matrix is very dense, the osteocytes get their nutrition from the central canal via tiny canals called canaliculi.

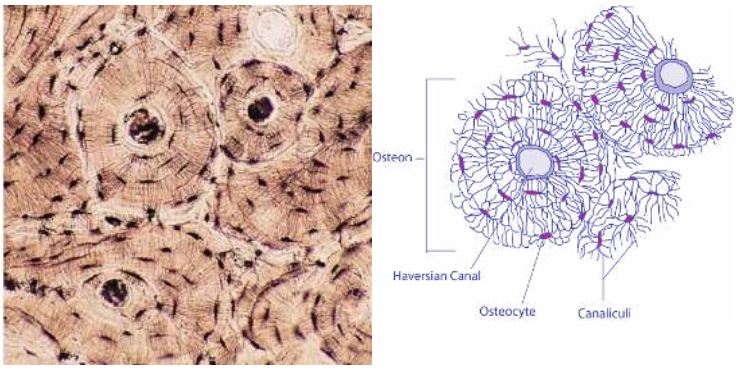


Figure **5.3.11**: The image shows a micrograph as well as an illustration of the cross-section of the compact bone tissue. The osteons are concentric structures that are composed of osteocytes in the lacunae and central (Haversian) canal. The small tunnels, canaliculi, connect osteocytes in the different layers of an osteon.

BLOOD

Blood is considered a type of fluid connective tissue because the matrix of blood is not solid. The fluid matrix is called plasma, and formed elements of this tissue include white blood cells, red blood cells, and platelets. Read more about the composition and function of blood in the cardiovascular system chapter.

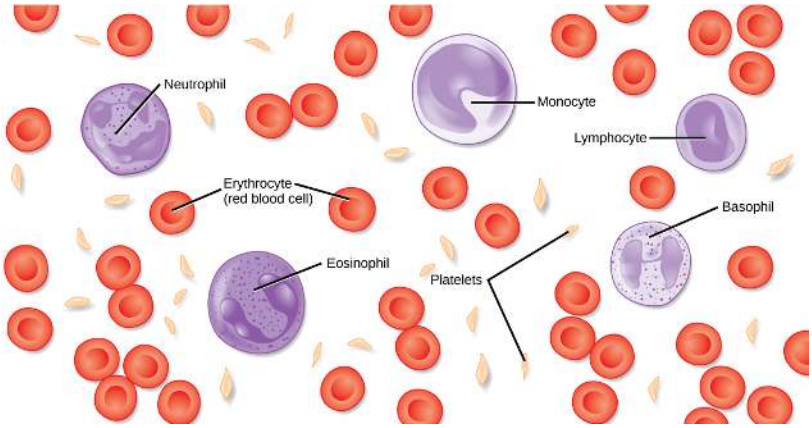


Figure **5.3.12**: The cells and cellular components of human blood are shown. Red blood cells deliver oxygen to the cells and remove carbon dioxide. White blood cells (including neutrophils, monocytes, lymphocytes, eosinophils, and basophils) are involved in the immune response. Platelets form clots that prevent blood loss after injury.

EPITHELIAL TISSUE

Epithelial tissue is made up of cells that line inner and outer body surfaces, such as the skin and the inner surface of the digestive tract. Epithelial tissue that lines inner body surfaces and body openings is called **mucous membrane.** This type of epithelial tissue produces **mucus**, a slimy substance that coats mucous membranes and traps pathogens, particles, and debris. Epithelial tissue protects the body and its internal organs, secretes substances such as hormones in addition to mucus, and absorbs substances such as nutrients.

EPITHELIAL CELL CLASSIFICATION

Most epithelial tissue is described with two names. The first name describes the number of cell layers present and the second describes the shape of the cells. One layer of epithelial cells is called simple and more than one layer of epithelial cells is called stratified. There are three basic shapes of epithelial cells, squamous, cuboidal, and columnar. Squamous cells are thin and flat; cuboidal cells have a shape of a cube; columnar cells have a shape of a pillar. For example, simple squamous epithelial tissue describes a single layer of cells that are flat and scale-like in shape.

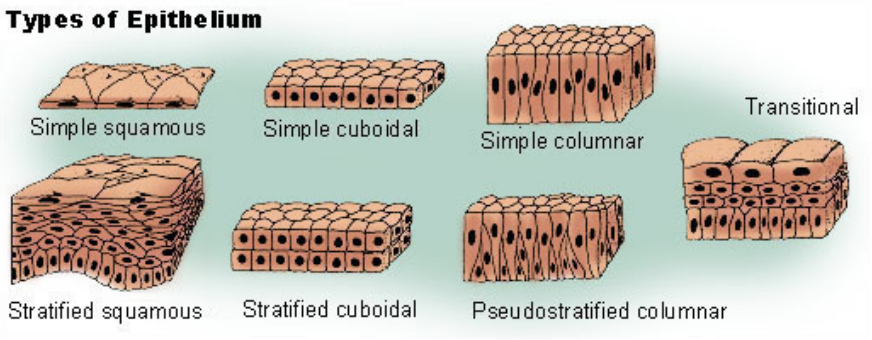


Figure **5.3.13**: Classification of Epithelial Tissues

LOCATIONS AND FUNCTIONS OF EPITHELIAL TISSUES

These tissues are found at various locations in our body and they have many functions. Some locations and functions are listed below:

- Simple squamous epithelium: This tissue is located in the sacs of the lungs and kidney where the exchange of nutrients and gas is essential.
- Simple cuboidal epithelium: This tissue is located in the glands and their ducts and kidneys. The main function of this tissue is secretion.
- Simple Columnar epithelium: This tissue lines the Gastrointestinal tract. The main function of this tissue is absorption and secretion.
- Pseudostratified epithelium: This is a simple tissue with the appearance of stratification. This tissue is located in the respiratory tract. This tissue may contain cilia to move mucus.
- Stratified squamous epithelium: This tissue is located where protection is needed such as skin.
- Stratified cuboidal epithelium: This tissue is located in the sweat glands for protection.
- Stratified columnar epithelium: This tissue is located in some sweat glands. The main function is to protect and secrete sweat components.
- Transitional epithelium: This tissue lines bladder, urethra, and ureters. The tissue allows the urinary organs to expand and stretch.

MUSCLE TISSUE

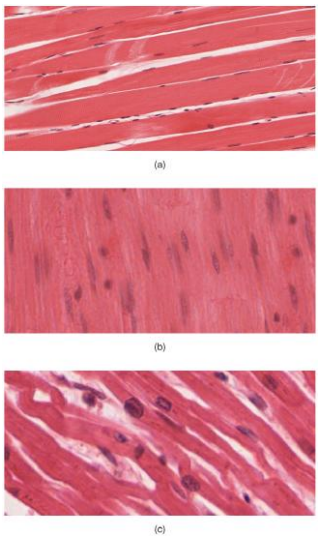


Figure **5.3.14**: The body contains three types of muscle tissue: (a) skeletal muscle, (b) smooth muscle, and (c) cardiac muscle.

Muscle tissue is made up of cells that have the unique ability to contract or become shorter. There are three major types of muscle tissue, as pictured in Figure **5.3.14**: skeletal, smooth, and cardiac muscle tissues.

1. **Skeletal muscles** are striated, or striped in appearance, because of their internal structure. Skeletal muscles are attached to bones, and when they pull on the bones, they enable the body to move. Skeletal muscles are under voluntary control.
2. **Smooth muscles** are nonstriated muscles. They are found in the walls of blood vessels and in the reproductive, gastrointestinal, and respiratory tracts. Smooth muscles are not under voluntary control.
3. **Cardiac muscles** are striated and found only in the heart. Their contractions cause the heart to beat. Cardiac muscles are not under voluntary control.

NERVOUS TISSUE

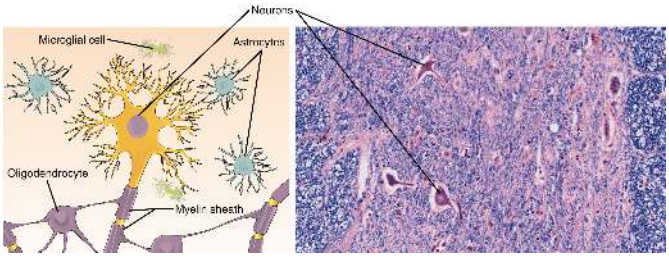


Figure **5.3.15**. This diagram shows some of the cell types that make up nervous tissues.

Nervous tissue is made up of neurons and other types of cells generally called glial cells (Figure **5.3.15**). Neurons are composed of cell body and extensions. The cell body contains the nucleus and the extensions make connections with the other tissues and neurons. Neurons transmit electrical messages and the glial cells play supporting roles. Nervous tissue makes up the central nervous system (mainly the brain and spinal cord) and peripheral nervous system (the network of nerves that runs throughout the rest of the body).

FEATURE: MY HUMAN BODY

If you are a blood donor, then you have donated tissue. Blood is a tissue that you can donate when you are alive. You may have indicated on your driver's license application that you wish to be a tissue donor in the event of your death. Deceased people can donate many different tissues, including skin, bone, heart valves, and the corneas of the eyes. If you are not already registered as a tissue donor, the information below may help you decide if you would like to register.

Each year, approximately 30,000 people donate tissues, which supply tissues for up to 1 million tissue transplants. One tissue donor can enhance or save the life of more than 50 people! Unlike organs, which generally must be transplanted immediately after the donor dies, donated tissues can be processed and stored for a long time for later use. Donated tissues can be used to replace burned skin and damaged bone and to repair ligaments. Corneal tissues can be used for corneal transplants that restore sight in blind people. In fact, each year 48,000 patients have their sight restored with corneal transplants. Unfortunately, there are not enough tissues to go around, and the need for donated tissues keeps rising.

REVIEW

1. Give an example of cells that function individually and move freely, and give an example of cells that act together and are attached to other cells of the same type.
2. What are examples of cells that can readily divide and cells that can divide only under rare circumstances?
3. Identify a type of cell that secretes an important substance and name the substance it secretes.
4. Explain how different cell types come about when all the cells in an individual human being are genetically identical.
5. Compare and contrast four subtypes of human bone cells.
6. Identify three types of human white blood cells, and state their functions.
7. Why are bone and blood both classified as connective tissues?
8. Name another type of connective tissue, and describe its role in the human body.
9. Based on the information in the table above of types of epithelial tissues, list four general functions of this type of tissue in the human body.
10. Compare and contrast the three types of muscle tissues.
11. Identify the four types of nervous tissues, where each type is found, and its basic function.
12. Of the main types of human tissue, name two that can secrete hormones.
13. Cells in a particular tissue:
    A. Are all of the same type
    B. Have different genes from cells in other tissues
    C. Work together to carry out a function
    D. Are always connected physically to each other
14. Why are mucous membranes often located in regions that interface between the body and the outside world?
15. Skin is a type of _____ tissue.
16. Body fat is a type of _____ tissue.

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5.4: HUMAN ORGANS AND ORGAN SYSTEMS

"ACHY BREAKY HEART"

Billy Ray Cyrus's song "Achy Breaky Heart" has lyrics suc as: Heartache, heartbreak...it all has to do with love. Did you ever wonder why the heart is associated with love? The heart was once thought to be the center of all thought processes, as well as the site of all emotions. This notion may have stemmed from very early anatomical dissections that found many nerves can be traced to the region of the heart. The fact that the heart may start racing when one is excited or otherwise emotionally aroused may have contributed to this idea as well. In fact, the heart is not the organ that controls thoughts or emotions. The organ that controls those functions is the brain. In this concept, you'll be introduced to the heart, brain, and other major organs of the human body.



Figure **5.4.1**: Twemoji

HUMAN ORGANS

An organ is a collection of tissues joined in a structural unit to serve a common function. Organs exist in most multicellular organisms, including not only humans and other animals but also plants. In single-celled organisms such as bacteria, the functional equivalent of an organ is an organelle.

TISSUES IN ORGANS

Although organs consist of multiple tissue types, many organs are composed of the main tissue that is associated with the organ's major function and other tissues that play supporting roles. The main tissue may be unique to that specific organ. For example, the main tissue of the heart is the cardiac muscle, which performs the heart's major function of pumping blood and is found only in the heart. The heart also includes nervous and connective tissues that are required for it to perform its major function. For example, nervous tissues control the beating of the heart, and connective tissues make up heart valves that keep blood flowing in just one direction through the heart.

VITAL ORGANS

The human body contains five organs that are considered vital for survival. They are the heart, brain, kidneys, liver, and lungs. The locations of these five organs and several other internal organs are shown in Figure **5.4.2**. If any of the five vital organs stops functioning, the death of the organism is imminent without medical intervention.

1. The heart is located in the center of the chest, and its function is to keep blood flowing through the body. Blood carries substances to cells that they need and also carries away wastes from cells.
2. The brain is located in the head and functions as the body's control center. It is the seat of all thoughts, memories, perceptions, and feelings.
3. The two kidneys are located in the back of the abdomen on either side of the body. Their function is to filter blood and form urine, which is excreted from the body.
4. The liver is located on the right side of the abdomen. It has many functions, including filtering blood, secreting bile that is needed for digestion, and producing proteins necessary for blood clotting.
5. The two lungs are located on either side of the upper chest. Their main function is exchanging oxygen and carbon dioxide with the blood.

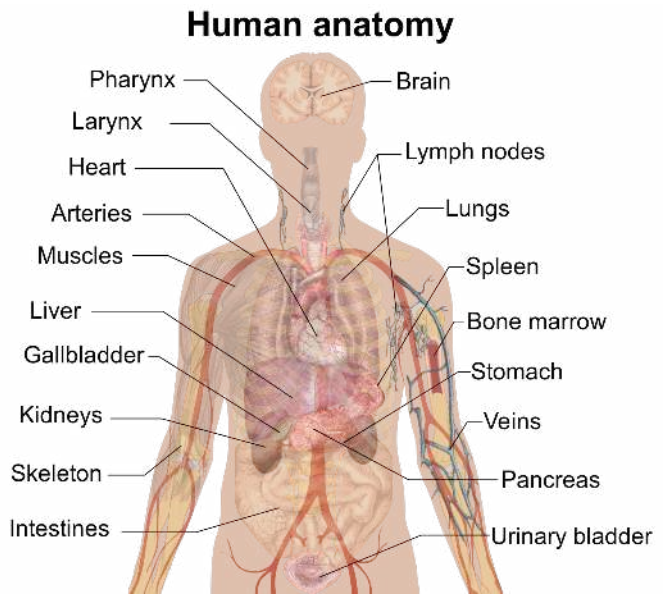


Figure **5.4.2**: Use this shadow diagram of human anatomy to locate the five organs described above: heart, brain, kidneys, liver, and lungs. Do you know the functions of any of the other organs in the diagram?

HUMAN ORGAN SYSTEMS

Functionally related organs often cooperate to form whole organ systems. Figure **5.4.3** and Figure **5.4.4** show 11 human organ systems, including separate diagrams for the male and female reproductive systems. Some of the organs and functions of the organ systems are identified in the figure. Each system is also described in more detail in the text that follows. Most of these human organ systems are also the subject of separate chapters in this book.

INTEGUMENTARY SYSTEM

Organs of the integumentary system include the skin, hair, and nails. The skin is the largest organ in the body. It encloses and protects the body and is the site of many sensory receptors. The skin is the body's first defense against pathogens, and it also helps regulate body temperature and eliminate wastes in sweat.

SKELETAL SYSTEM

The skeletal system consists of bones, joints, teeth. The bones of the skeletal system are connected by tendons, ligaments, and cartilage. Functions of the skeletal system include supporting the body and giving it shape. Along with the muscular system, the skeletal system enables the body to move. The bones of the skeletal system also protect internal organs, store calcium, and produce red and white blood cells.

MUSCULAR SYSTEM

The muscular system consists of three different types of muscles, including skeletal muscles, which are attached to bones by tendons and allow for voluntary movements of the body. Smooth muscle tissues control the involuntary movements of internal organs, such as the organs of the digestive system, allowing food to move through the system. Smooth muscles in blood vessels allow vasoconstriction and vasodilation and thereby help regulate body temperature. Cardiac muscle tissues control the involuntary beating of the heart, allowing it to pump blood through the blood vessels of the cardiovascular system.

NERVOUS SYSTEM

The nervous system includes the brain and spinal cord, which make up the central nervous system, and nerves that run throughout the rest of the body, which make up the peripheral nervous system. The nervous system controls both voluntary and involuntary responses of the human organism and also detects and processes sensory information.

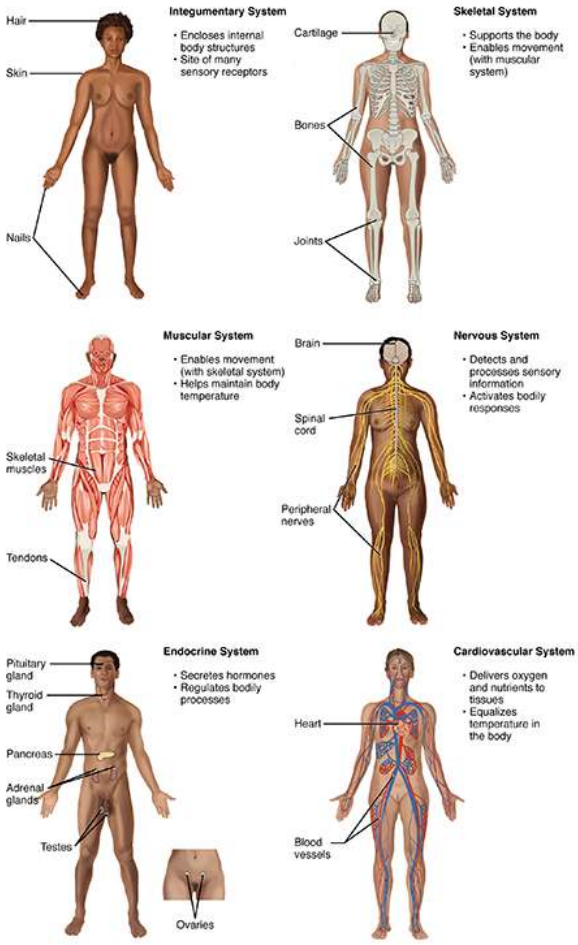


Figure **5.4.3**: Organ systems: Integumentary, Skeletal, Muscular, Nervous, Endocrine, and Cardiovascular

ENDOCRINE SYSTEM

The endocrine system is made up of glands that secrete hormones into the blood, which carries the hormones throughout the body. Endocrine hormones are chemical messengers that control many body functions, including metabolism, growth, and sexual development. The master gland of the endocrine system is the pituitary gland, which produces hormones that control other endocrine glands. Some of the other endocrine glands include the pancreas, thyroid gland, and adrenal glands.

CARDIOVASCULAR SYSTEM

The cardiovascular system (also called the circulatory system) includes the heart, blood, and three types of blood vessels: arteries, veins, and capillaries. The heart pumps blood, which travels through the blood vessels. The main function of the cardiovascular system is transport. Oxygen from the lungs and nutrients from the digestive system are transported to cells throughout the body. Carbon dioxide and other waste materials are picked up from the cells and transported to organs such as the lungs and kidneys for elimination from the body. The cardiovascular system also equalizes body

temperature and transports endocrine hormones to cells in the body where they are needed.

URINARY SYSTEM

The urinary system includes the pair of kidneys, which filter excess water and a waste product called urea from the blood and form urine. Two tubes called ureters carry the urine from the kidneys to the urinary bladder, which stores the urine until it is excreted from the body through another tube named the urethra. The kidneys also produce an enzyme called renin and a variety of hormones. These substances help regulate blood pressure, the production of red blood cells, and the balance of calcium and phosphorus in the body.

RESPIRATORY SYSTEM

Organs and other structures of the respiratory system include the nasal passages, lungs, and a long tube called the trachea, which carries air between the nasal passages and lungs. The main function of the respiratory system is to deliver oxygen to the blood and remove carbon dioxide from the body. Gases are exchanged between the lungs and blood across the walls of capillaries lining tiny air sacs (alveoli) in the lungs.

LYMPHATIC SYSTEM

The lymphatic system is sometimes considered to be part of the immune system. It consists of a network of lymph vessels and ducts that collect excess fluid (called lymph) from extracellular spaces in tissues and transport the fluid to the bloodstream. The lymphatic system also includes many small collections of tissue, called lymph nodes, and an organ called the spleen, both of which remove pathogens and cellular debris from the lymph or blood. In addition, the thymus gland in the lymphatic system produces some types of white blood cells (lymphocytes) that fight infections.

DIGESTIVE SYSTEM

The digestive system consists of several main organs — including the mouth, esophagus, stomach, and small and large intestines — that form a long tube called the gastrointestinal (GI) tract. Food moves through this tract where it is digested, its nutrients absorbed, and its waste products excreted. The digestive system also includes accessory organs (such as the pancreas and liver) that produce enzymes and other substances needed for digestion but through which food does not actually pass.

MALE AND FEMALE REPRODUCTIVE SYSTEMS

The reproductive system is the only body system that differs substantially between individuals. There is a range of Biological sex, but most books divide them into male and female. We will discuss the Biology of sex in detail in the reproductive and development chapters.

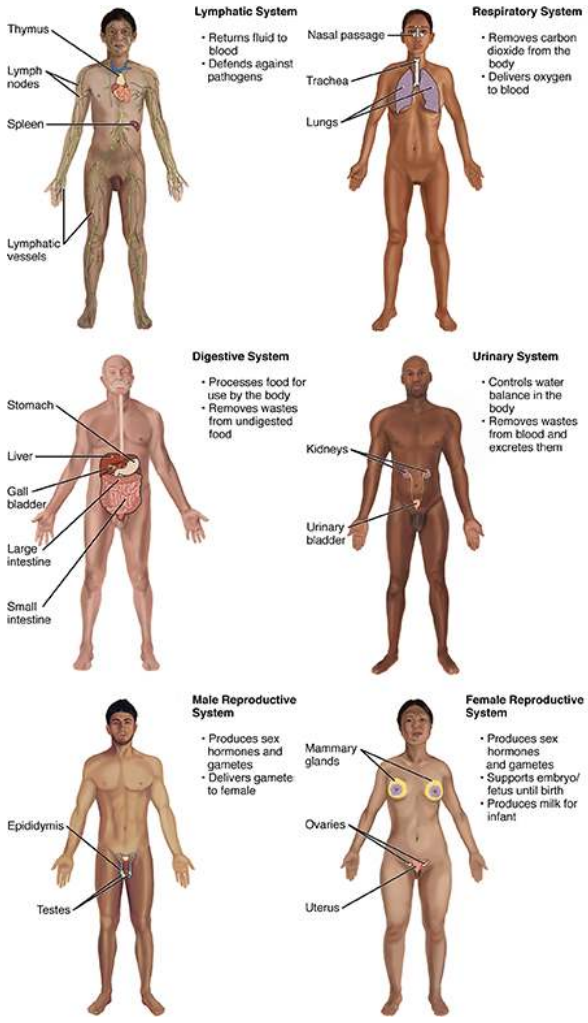


Figure **5.4.4**: Organ Systems: Lymphatic, Respiratory, Digestive, Urinary, male and female reproductive

FEATURE: HUMAN BIOLOGY IN THE NEWS

Organ transplantation has been performed by surgeons for more than six decades, and you've no doubt heard of people receiving heart, lung, and kidney transplants. However, you may have never heard of a penis transplant. The first U.S. penis transplant was performed in May of 2016 at Massachusetts General Hospital in Boston. The 15-hour procedure involved a team of more than 50 physicians, surgeons, and nurses. The patient was a 64-year-old man who had lost his penis to cancer in 2012. The surgical milestone involved grafting microscopic blood vessels and nerves of the donor organ to those of the recipient. As with most transplant patients, this patient will have to take immunosuppressing drugs for the rest of his life so his immune system will not reject the organ. The transplant team said that their success with this transplant "holds promise for patients with devastating genitourinary injuries and disease." They also hope their experiences will be helpful for gender reassignment surgery.

REVIEW

1. What is the main tissue in the heart, and what is its role?
2. What non-muscle tissues are found in the heart? What are their functions?
3. Identify two vital organs in the human body. Identify their locations and functions.
4. List three human organ systems. For each organ system, identify some of its organs and functions.
5. Compare and contrast the male and female reproductive systems.
6. For each of the following pairs of organ systems, describe one way in which they work together and/or overlap.
   A. Skeletal system and muscular system
   B. Muscular system and digestive system
   C. Endocrine system and reproductive system
   D. Cardiovascular system and urinary system
7. What is the largest organ of the human body?
8. What are the three organ systems involved in regulating human body temperature?
9. Teeth are part of which system?
   A. Integumentary
   B. Skeletal
   C. Nervous
   D. A and B
10. Hair is part of which organ system?
11. *True or False.* Organs only exist in animals.
12. *True or False.* The respiratory system helps to remove wastes from the body.

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5.5: HUMAN BODY CAVITIES

CONTAIN THE BRAIN

The brain is a delicate organ that regulates the physiology of the whole body. Figure **5.5.1** shows the brain with its superficial structures. Brain coverings and the skull provide protection to the brain. The space where the brain is located in the skull is called the cranial cavity.

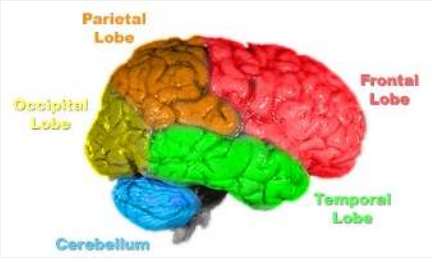


Figure **5.5.1**: Human Brain lateral view

WHAT ARE BODY CAVITIES?

The human body, like that of many other multicellular organisms, is divided into a number of body cavities. A **body cavity** is a fluid-filled space inside the body that holds and protects internal organs. Human body cavities are separated by membranes and other structures. The two largest human body cavities are the ventral cavity and the dorsal cavity. These two body cavities are subdivided into smaller body cavities. Both the dorsal and ventral cavities and their subdivisions are shown in Figure **5.5.2**.

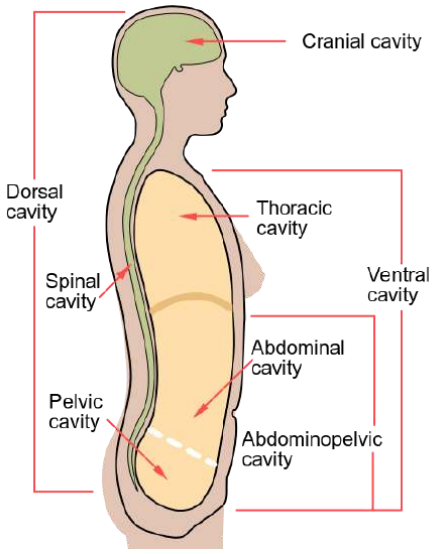


Figure **5.5.2**: The ventral cavity includes the thoracic and abdominopelvic cavities and their subdivisions. The abdominopelvic cavity is further divided into abdominal and pelvic cavities. The dorsal cavity includes the cranial and spinal cavities.

VENTRAL CAVITY

The **ventral cavity** is at the anterior, or front, of the trunk. Organs contained within this body cavity include the lungs, heart, stomach, intestines, and reproductive organs. You can see some of the organs in the ventral cavity in Figure **5.5.3**. The ventral cavity allows for considerable changes in the size and shape of the organs within it as they perform their functions. For example, organs such as the lungs, stomach, or uterus can expand or contract without distorting other tissues or disrupting the activities of nearby organs.

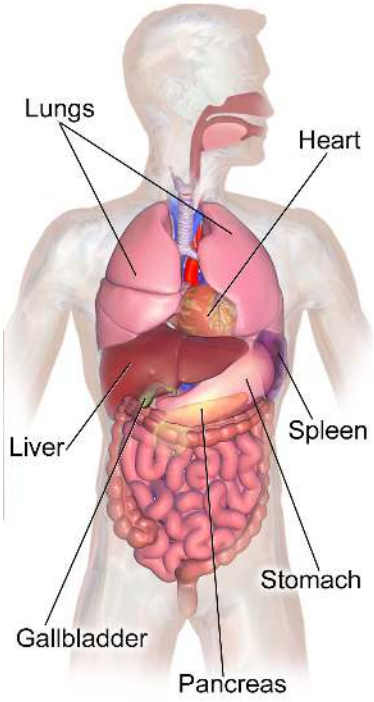


Figure **5.5.3**: Some of the major organs such as the spleen, stomach, pancreas, gallbladder, liver, lungs, and heart inside the ventral cavity of the human body

The ventral cavity is subdivided into the thoracic and abdominopelvic cavities.

- The **thoracic cavity** fills the chest and is subdivided into two pleural cavities and the pericardial cavity. The pleural cavities hold the lungs, and the pericardial cavity holds the heart.
- The **abdominopelvic cavity** fills the lower half of the trunk and is subdivided into the abdominal cavity and the pelvic cavity. The abdominal cavity holds digestive organs and the kidneys, and the pelvic cavity holds reproductive organs and organs of excretion.

DORSAL CAVITY

The **dorsal cavity** is at the posterior, or back, of the body, including both the head and the back of the trunk. The dorsal cavity is subdivided into the cranial and spinal cavities.

- The **cranial cavity** fills most of the upper part of the skull and contains the brain.
- The **spinal cavity** is a very long, narrow cavity inside the vertebral column. It runs the length of the trunk and contains the spinal cord.

The brain and spinal cord are protected by the bones of the skull and the vertebrae of the spine. They are further protected by the **meninges,** a three-layer membrane that encloses the brain and spinal cord. A thin layer of **cerebrospinal fluid** is maintained between two of the meningeal layers. This clear fluid is produced by the brain, and it provides extra protection and cushioning for the brain and spinal cord.

FEATURE: MY HUMAN BODY

The meninges membranes that protect the brain and spinal cord inside their cavities may become inflamed, generally due to a bacterial or viral infection. This condition is called meningitis. Meningitis can lead to serious long-term consequences such as deafness, epilepsy, or cognitive deficits, especially if not treated quickly. Meningitis can also rapidly become life-threatening, so it is classified as a medical emergency.

Learning the symptoms of meningitis may help you or a loved one get prompt medical attention if you ever develop the disease. Common symptoms include fever, headache, and neck stiffness. Other symptoms may include confusion or altered consciousness, vomiting, and an inability to tolerate light or loud noises. Young children often exhibit less specific symptoms, such as irritability, drowsiness, or poor feeding.

Meningitis is diagnosed with a lumbar puncture (commonly known as a "spinal tap"), in which a needle is inserted into the spinal canal to collect a sample of cerebrospinal fluid. The fluid is analyzed for the presence of pathogens in a medical lab. If meningitis is diagnosed, treatment consists of antibiotics and sometimes antiviral drugs. Corticosteroids may also be administered to reduce inflammation and the risk of complications such as brain damage. Supportive measures such as IV fluids may also be provided.

Some types of meningitis can be prevented with a vaccine. Ask your health care professional whether you have had the vaccine or should get it. Giving antibiotics to people who have had significant exposure to certain types of meningitis may reduce their risk of developing the disease. If someone you know is diagnosed with meningitis, see your doctor for advice if you are concerned about contracting the disease.

REVIEW

1. What is a body cavity?
2. Compare and contrast ventral and dorsal body cavities.
3. Identify the subdivisions of the ventral cavity and the organs each contains.
4. Describe the subdivisions of the dorsal cavity and its contents.
5. Identify and describe all the tissues that protect the brain and spinal cord.
6. What do you think might happen if fluid were to build up excessively in one of the body cavities?
7. Explain why a woman's body can accommodate a full-term fetus during pregnancy, without damage to her internal organs.
8. Which body cavity does the needle enter in a lumbar puncture?
9. What are the names given to the three body cavity divisions where the heart is located?
10. What are the names given to the three body cavity divisions where the kidneys are located?
11. *True or False.* The stomach is located in the dorsal cavity.
12. *True or False.* A body cavity must open to the outside world.
13. *True or False.* The vertebral column surrounds the spinal cavity.
14. The _____ cavity is directly below the thoracic cavity.
15. What is the name of the fluid that protects the brain and spinal cord?

    A. meningeal
    B. cerebrospinal
    C. lumbar
    D. cranial

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5.6: INTERACTION OF ORGAN SYSTEMS

TEAMWORK

Every player on a softball team has a special job to perform. Each of the orange team's players in Figure **5.6.1** has his part of the infield or outfield covered if the ball comes his way. Other players on the orange team cover other parts of the field or pitch or catch the ball. Playing softball clearly requires teamwork. The human body is like a softball team in that regard. All the organ systems of the human body must work together as a team to keep the body alive and well. Teamwork within the body begins with communication.



Figure **5.6.1**: Softball

COMMUNICATION AMONG ORGAN SYSTEMS

Communication among organ systems is vital if they are to work together as a team. They must be able to respond to each other and change their responses as needed to keep the body in balance. Communication among organ systems is controlled mainly by the autonomic nervous system and the endocrine system.

The autonomic nervous system is the part of the nervous system that controls involuntary functions. For example, the autonomic nervous system controls heart rate, blood flow, and digestion. You don't have to tell your heart to beat faster or to consciously squeeze muscles to push food through the digestive system. In fact, you don't have to even think about these functions at all. The autonomic nervous system orchestrates all the signals needed to control them. It sends messages between parts of the nervous system and between the nervous system and other organ systems via chemical messengers called neurotransmitters.

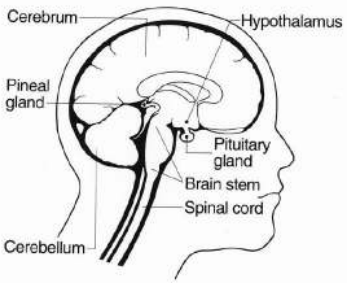


Figure **5.6.2**: The figure illustrates the hypothalamus, pituitary gland, brain stem, spinal cord, cerebellum, pineal gland, and cerebrum.

The endocrine system is the system of glands that secrete hormones directly into the bloodstream. Once in the blood, endocrine hormones circulate to cells everywhere in the body. The endocrine system is under the control of the hypothalamus, a part of the brain. The hypothalamus secretes hormones that travel directly to cells of the pituitary gland, which is located beneath it. The pituitary gland is the master gland of the endocrine system. Most of its hormones either turn on or turn off other endocrine glands. For example, if the pituitary gland secretes thyroid stimulating hormone, the hormone travels through the circulation to the thyroid gland, which is stimulated to secrete thyroid hormone. Thyroid hormone then travels to cells throughout the body, where it increases their metabolism.

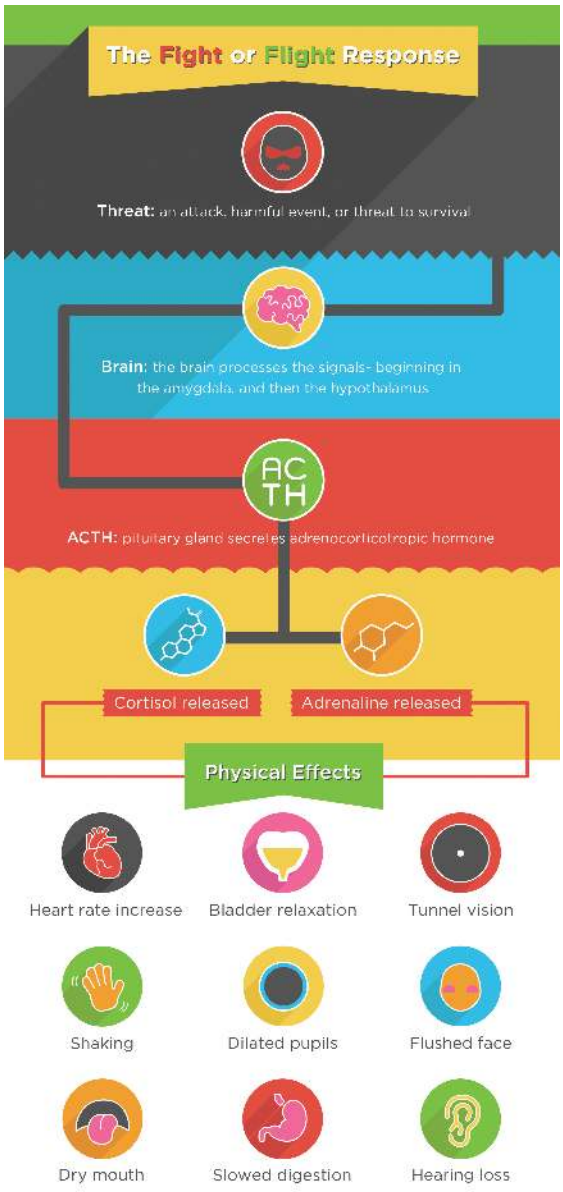


Figure **5.6.3**: The image shows a concept map of how the fight-or-flight response occurs. A treat (an attack, harmful event, or threat to survive) leads to the brain processing the signals - beginning in the amygdala, and then the hypothalamus. ACTH (adrenocorticotropic hormone) is released by the pituitary gland. This causes cortisol and adrenaline to be released. The physical effects include heart rate increase, bladder relaxation, tunnel vision, shaking, dilated pupils, flushed face, dry mouth, slowed digestion, and hearing loss.

EXAMPLES OF ORGAN SYSTEM INTERACTIONS

An increase in cellular metabolism requires more cellular respiration. Cellular respiration is a good example of organ system interactions because it is a basic life process that occurs in all living cells.

CELLULAR RESPIRATION

Cellular respiration is the intracellular process that breaks down glucose with oxygen to produce carbon dioxide and energy in the form of ATP molecules. It is the process by which cells obtain usable energy to power other cellular processes. Which organ systems are involved in cellular respiration? The glucose needed for cellular respiration comes from the digestive system via the cardiovascular system. The oxygen needed for cellular respiration comes from the respiratory system also via the cardiovascular system. The carbon dioxide produced in cellular respiration leaves the body by the opposite route. In short, cellular respiration requires at a minimum the digestive, cardiovascular, and respiratory systems.

FIGHT-OR-FLIGHT RESPONSE

The well-known **fight-or-flight response** is a good example of how the nervous and endocrine systems control other organ system responses. The fight-or-flight response begins when the nervous system perceives sudden danger, as shown in Figure **5.6.2**. The brain sends a message to the endocrine system (via the pituitary gland) for the adrenal glands to secrete their hormones cortisol and adrenaline. These hormones flood the circulation and affect other organ systems throughout the body, including the cardiovascular, urinary, sensory, and digestive systems. Specific responses include increased heart rate, bladder relaxation, tunnel vision, and a shunting of blood away from the digestive system and toward the muscles, brain, and other vital organs needed to fight or flee.

DIGESTING FOOD

Digesting food requires teamwork between the digestive system and several other organ systems, including the nervous, cardiovascular, and muscular systems. When you eat a meal, the organs of the digestive system need more blood to perform their digestive functions. Food entering the digestive systems causes nerve impulses to be sent to the brain; in response, the brain sends messages to the cardiovascular system to increase heart rate and dilate blood vessels in the digestive organs. Food passes through the organs of the digestive tract by rhythmic contractions of smooth muscles in the walls of the organs, so the muscular system is also needed for digestion. After food is digested, nutrients from the food are absorbed into the blood of the vessels lining the small intestine. Any remaining food waste is excreted through the large intestine.

PLAYING SOFTBALL

The men playing softball in Figure **5.6.1** are using multiple organ systems in this voluntary activity. Their nervous systems are focused on observing and preparing to respond to the next play. Their other systems are being controlled by the autonomic nervous system. Organ systems they are using include the muscular, skeletal, respiratory, and cardiovascular systems. Can you explain how each of these organ systems is involved in playing softball?

FEATURE: RELIABLE SOURCES

Teamwork among organ systems allows the human organism to work like a finely tuned machine. Or at least it does until one of the organ systems fails. When that happens, other organ systems interacting in the same overall process will also be affected. This is especially likely if the system affected plays a controlling role in the process. An example is type 1 diabetes.

This disorder occurs when the pancreas does not secrete the endocrine hormone insulin. Insulin normally is secreted in response to an increasing level of glucose in the blood, and it brings the level of glucose back to normal by stimulating body cells to take up insulin from the blood.

Learn more about type 1 diabetes. Use several reliable Internet sources to answer the following questions:

1. What causes the endocrine system to fail to produce insulin in type 1 diabetes?
2. Which organ systems are affected by high blood glucose levels if type 1 diabetes is not controlled? What are some of the specific effects?
3. How can blood glucose levels be controlled in patients with type 1 diabetes?

REVIEW

1. What is the autonomic nervous system?
2. How do the autonomic nervous system and endocrine system communicate with other organ systems so the systems can interact?
3. Explain how the brain communicates with the endocrine system.
4. What is the role of the pituitary gland in the endocrine system?
5. Identify organ systems that play a role in cellular respiration.
6. How does the hormone adrenaline prepare the body to fight or flee? What specific physiological changes does it bring about?
7. Explain the role of the muscular system in the digestion of food.
8. Describe how three different organ systems are involved when a player makes a particular play in softball, such as catching a fly ball.
9. *True or False*. The autonomic nervous system controls conscious movements.
10. *True or False*. Hormones travel throughout the body.
11. *True or False*. The pituitary gland directly secretes thyroid hormone.
12. What are two types of molecules that the body uses to communicate between organ systems?
13. Explain why hormones can have such a wide variety of effects on the body.
14. Heart rate can be affected by:
    A. Hormones
    B. Neurotransmitters
    C. The fight-or-flight response
    D. All of the above
15. Which gland secretes the hormone cortisol?

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5.7: HOMEOSTASIS AND FEEDBACK

STEADY AS SHE GOES

This device looks simple, but it controls a complex system that keeps a home at a steady temperature. The device is an old-fashioned thermostat. The dial shows the current temperature in the room and also allows the occupant to set the thermostat to the desired temperature. A thermostat is a commonly cited model of how living systems, including the human body, maintain a steady state called homeostasis.



Figure **5.7.1**: Thermostat for a building

WHAT IS HOMEOSTASIS?

Homeostasis is the condition in which a system such as the human body is maintained in a more-or-less steady state. It is the job of cells, tissues, organs, and organ systems throughout the body to maintain many different variables within narrow ranges that are compatible with life. Keeping a stable internal environment requires continuous monitoring of the internal environment and constantly making adjustments to keep things in balance.

SETPOINT AND NORMAL RANGE

For any given variable, such as body temperature or blood glucose level, there is a particular **setpoint** that is the physiological optimum value. For example, the setpoint for human body temperature is about 37 ºC (98.6 ºF). As the body works to maintain homeostasis for temperature or any other internal variable, the value typically fluctuates around the set point. Such fluctuations are normal as long as they do not become too extreme. The spread of values within which such fluctuations are considered insignificant is called the **normal range**. In the case of body temperature, for example, the normal range for an adult is about 36.5 to 37.5 ºC (97.7 to 99.5 ºF).

MAINTAINING HOMEOSTASIS

Homeostasis is normally maintained in the human body by an extremely complex balancing act. Regardless of the variable being kept within its normal range, maintaining homeostasis requires at least four interacting components: stimulus, sensor, control center, and effector.

1. The **stimulus** is provided by the variable that is being regulated. Generally, the stimulus indicates that the value of the variable has moved away from the set point or has left the normal range.
2. The **sensor** monitors the values of the variable and sends data on it to the control center.
3. The **control center** matches the data with normal values. If the value is not at the set point or is outside the normal range, the control center sends a signal to the effector.
4. The **effector** is an organ, gland, muscle, or other structure that acts on the signal from the control center to move the variable back toward the set point.

Each of these components is illustrated in Figure **5.7.2**. The diagram on the left is a general model showing how the components interact to maintain homeostasis. The stimulus activates the sensor. The sensor activates the control system that regulates the effector. The diagram on the right shows the example of body temperature. From the diagrams, you can see that maintaining homeostasis involves feedback, which is data that feeds back to control a response. High body temperature may stimulate the temperature regulatory center of the brain to activate the sweat glands to bring the body temperature down. When body temperature reaches normal range, it acts as negative feedback to stop the process. Feedback may be negative or positive. All the feedback mechanisms that maintain homeostasis use negative feedback. Biological examples of positive feedback are much less common.

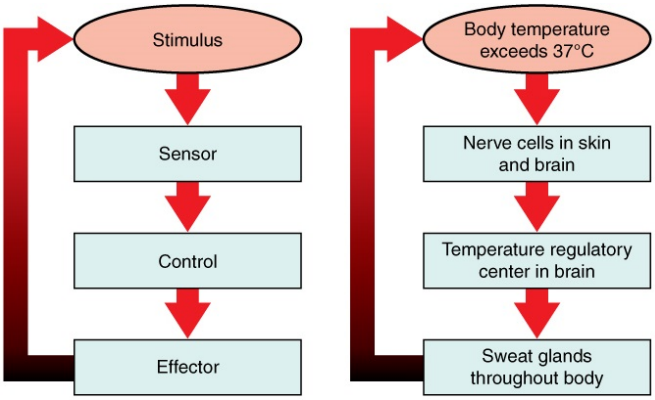


Figure **5.7.2**: Maintaining homeostasis through feedback requires a stimulus, sensor, control center, and effector

NEGATIVE FEEDBACK

In a **negative feedback loop**, feedback serves to reduce an excessive response and keep a variable within the normal range. Examples of processes controlled by negative feedback include body temperature regulation and control of blood glucose.

BODY TEMPERATURE

Body temperature regulation involves negative feedback whether it lowers the temperature or raises it (Figure **5.7.3**).

COOLING DOWN

The human body's temperature regulatory center is the hypothalamus in the brain. When the hypothalamus receives data from sensors in the skin and brain that body temperature is higher than the setpoint, it sets into motion the following responses:

- Blood vessels in the skin dilate (vasodilation) to allow more blood from the warm body core to flow close to the surface of the body, so heat can be radiated into the environment.
- As blood flow to the skin increases, sweat glands in the skin are activated to increase their output of sweat (diaphoresis). When the sweat evaporates from the skin surface into the surrounding air, it takes the heat with it.
- Breathing becomes deeper, and the person may breathe through the mouth instead of the nasal passages. This increases heat loss from the lungs.

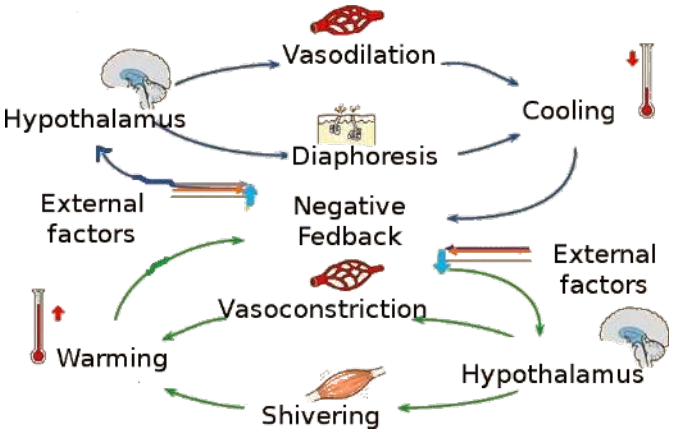


Figure 5.7.3: The hypothalamus plays a major role in temperature regulation

HEATING UP

When the brain's temperature regulatory center receives data that body temperature is lower than the setpoint, it sets into motion the following responses:

- Blood vessels in the skin contract (vasoconstriction) to prevent blood from flowing close to the surface of the body. This reduces heat loss from the surface.
- As the temperature falls lower, random signals to skeletal muscles are triggered, causing them to contract. This causes shivering, which generates a small amount of heat.
- The thyroid gland may be stimulated by the brain (via the pituitary gland) to secrete more thyroid hormones. This hormone increases metabolic activity and heat production in cells throughout the body.
- The adrenal glands may also be stimulated to secrete the hormone adrenaline. This hormone causes the breakdown of glycogen (the carbohydrate used for energy storage in animals) to glucose, which can be used as an energy source. This catabolic chemical process is exothermic, or heat producing.

BLOOD GLUCOSE

In the control of the blood glucose level, certain endocrine cells in the pancreas called alpha and beta cells, detect the level of glucose in the blood. Then they respond appropriately to keep the level of blood glucose within the normal range.

- If the blood glucose level rises above the normal range, pancreatic beta cells release the hormone insulin into the bloodstream. Insulin signals cells to take up the excess glucose from the blood until the level of blood glucose decreases to the normal range.
- If the blood glucose level falls below the normal range, pancreatic alpha cells release the hormone **glucagon** into the bloodstream. Glucagon signals cells to break down stored glycogen to glucose and release the glucose into the blood until the level of blood glucose increases to the normal range.

POSITIVE FEEDBACK

In a **positive feedback loop**, feedback serves to intensify a response until an endpoint is reached. Examples of processes controlled by positive feedback in the human body include blood clotting and childbirth.

BLOOD CLOTTING

When a wound causes bleeding, the body responds with a positive feedback loop to clot the blood and stop blood loss. Substances released by the injured blood vessel wall begin the process of blood clotting. Platelets in the blood start to cling to the injured site and release chemicals that attract additional platelets. As the platelets continue to amass, more of the chemicals are released and more platelets are attracted to the site of the clot. The positive feedback accelerates the process of clotting until the clot is large enough to stop the bleeding.

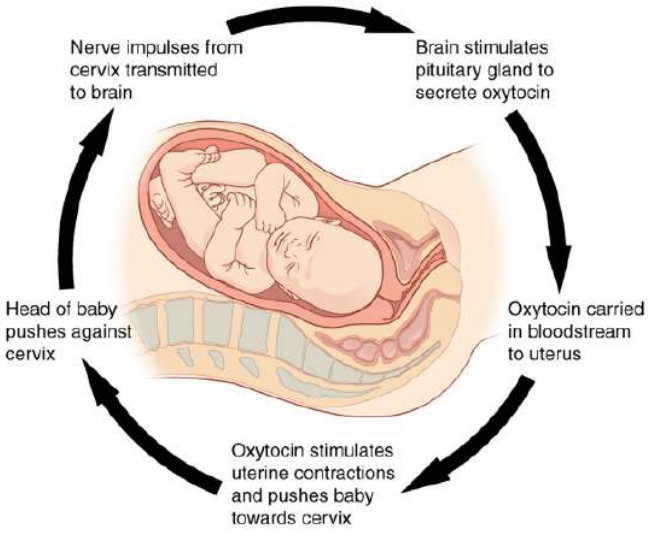


Figure 5.7.4: Normal childbirth is driven by a positive feedback loop. Positive feedback causes an increasing deviation from the normal state to a fixed endpoint rather than a return to a normal set point as in homeostasis

CHILDBIRTH

Figure **5.7.4** shows the positive feedback loop that controls childbirth. The process normally begins when the head of the infant pushes against the cervix. This stimulates nerve impulses, which travel from the cervix to the hypothalamus in the brain. In response, the hypothalamus sends the hormone **oxytocin** to the pituitary gland, which secretes it into the bloodstream so it can be carried to the uterus. Oxytocin stimulates uterine contractions, which push the baby harder against the cervix. In response, the cervix starts to dilate in preparation for the passage of the baby. This cycle of positive feedback continues, with increasing levels of oxytocin, stronger uterine contractions, and wider dilation of the cervix until the baby is pushed through the birth canal and out of the body. At that point, the cervix is no longer stimulated to send nerve impulses to the brain, and the entire process stops.

WHEN HOMEOSTASIS FAILS

Homeostatic mechanisms work continuously to maintain stable conditions in the human body. Sometimes, however, the mechanisms fail. When they do, **homeostatic imbalance** may result, in which cells may not get everything they need or toxic wastes may accumulate in the body. If homeostasis is not restored, the imbalance may lead to disease or even death. Diabetes is an example of a disease caused by homeostatic imbalance. In the case of diabetes, blood glucose levels are no longer regulated and may be dangerously high. Medical intervention can help restore homeostasis and possibly prevent permanent damage to the organism.

FEATURE: MY HUMAN BODY

Diabetes is diagnosed in people who have abnormally high levels of blood glucose after fasting for at least 12 hours. A fasting level of blood glucose below 100 is normal. A level between 100 and 125 places you in the pre-diabetes category, and a level higher than 125 results in a diagnosis of diabetes.

Of the two types of diabetes, type 2 diabetes is the most common, accounting for about 90 percent of all cases of diabetes in the United States. Type 2 diabetes typically starts after the age of 40. However, because of the dramatic increase in recent decades in obesity in younger people, the age at which type 2 diabetes is diagnosed has fallen. Even children are now being diagnosed with type 2 diabetes. Today, about 30 million Americans have type 2 diabetes, and another 90 million have pre-diabetes.

You are likely to have your blood glucose level tested during a routine medical exam. If your blood glucose level indicates that you have diabetes, it may come as a shock to you because you may not have any symptoms of the disease. You are not alone, because as many as one in four diabetics does not know they have the disease. Once the diagnosis of diabetes sinks in, you may be devastated by the news. Diabetes can lead to heart attacks, strokes, blindness, kidney failure, and loss of toes or feet. The risk of death in adults with diabetes is 50 percent greater than it is in adults without diabetes, and diabetes is the seventh leading cause of death in adults. In addition, controlling diabetes usually requires frequent blood glucose testing, watching what and when you eat and taking medications or even insulin injections. All of this may seem overwhelming.

The good news is that changing your lifestyle may stop the progression of type 2 diabetes or even reverse it. Here's how:

- Lose weight. Any weight loss is beneficial. Losing as little as seven percent of your weight may be all that is needed to stop diabetes in its tracks. It is especially important to eliminate excess weight around your waist.
- Exercise regularly. You should try to exercise five days a week for at least 30 minutes. This will not only lower your blood sugar and help your insulin work better; it will also lower your blood pressure and improve your heart health. Another bonus of exercise is that it will help you lose weight by increasing your basal metabolic rate.
- Adopt a healthy diet. Decrease your consumption of refined carbohydrates such as sweets and sugary drinks. Increase your intake of fiber-rich foods such as fruits, vegetables, and whole grains. About a quarter of each meal should consist of high-protein foods, such as fish, chicken, dairy products, legumes, or nuts.
- Control stress. Stress can increase your blood glucose and also raise your blood pressure and risk of heart disease. When you feel stressed out, do breathing exercises or take a brisk walk or jog. Also, try to replace stressful thoughts with more calming ones.
- Establish a support system. Enlist the help and support of loved ones as well as medical professionals such as a nutritionist and diabetes educator. Having a support system will help ensure that you are on the path to wellness and that you can stick to your plan.

REVIEW

1. What is homeostasis?
2. Define the setpoint and normal range for physiological measures.
3. Identify and define the four interacting components that maintain homeostasis in feedback loops.
4. Compare and contrast negative and positive feedback loops.
5. Explain how negative feedback controls body temperature.
6. Give two examples of physiological processes that are controlled by positive feedback loops.
7. A negative feedback loop:
   A. brings a variable's level back to a normal range
   B. can lower, but not raise, body temperature
   C. is the type of feedback involved in blood clotting
   D. A and B
8. During breastfeeding, the stimulus of the baby sucking on the nipple increases the amount of milk produced by the mother. The more sucking, the more milk is usually produced.

A. Is this an example of negative or positive feedback? Explain your answer.
B. What do you think might be the evolutionary benefit of the milk production regulation mechanism described in part a?

9. Explain why homeostasis is regulated by negative feedback loops, rather than positive feedback loops.
10. A setpoint is usually:
    A. the top of a normal range
    B. the bottom of a normal range
    C. in the middle of a normal range
    D. the point at which changes can no longer occur
11. The level of a sex hormone, testosterone (T), is controlled by negative feedback. Another hormone, gonadotropin-releasing hormone (GnRH), is released by the hypothalamus of the brain, which triggers the pituitary gland to release luteinizing hormone (LH). LH stimulates the gonads to produce T. When there is too much T in the bloodstream, it feeds back on the hypothalamus, causing it to produce less GnRH. While this does not describe all the feedback loops involved in regulating T, answer the following questions about this particular feedback loop.
    A. What is the stimulus in this system? Explain your answer.
    B. What is the control center in this system? Explain your answer.
    C. What is the pituitary considered in this system: stimulus, sensor, control center, or effector? Explain your answer.

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5.8: CASE STUDY CONCLUSION- PRESSURE AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: UNDER PRESSURE

As you learned in this chapter, the human body consists of many complex systems that normally work together efficiently like a well-oiled machine to carry out life's functions. For example, Figure 5.8.1 illustrates how the brain and spinal cord are protected by layers of membrane called meninges and fluid that flows between the meninges and in spaces called ventricles inside the brain. This fluid is called **cerebrospinal fluid (CSF)** and as you have learned, one of its important functions is to cushion and protect the brain and spinal cord, which make up most of the central nervous system (CNS). CSF additionally circulates nutrients and removes waste products from the CNS. CSF is produced continually in the ventricles, circulates throughout the CNS, and then is reabsorbed by the bloodstream. If too much CSF is produced, its flow blocked, or if not enough is reabsorbed, the system becomes out of balance, and CSF can build up in the ventricles. This causes an enlargement of the ventricles called hydrocephalus that can put pressure on the brain, resulting in the types of neurological problems that former professional football player, Dayo, described at the beginning of this chapter, is suffering from.

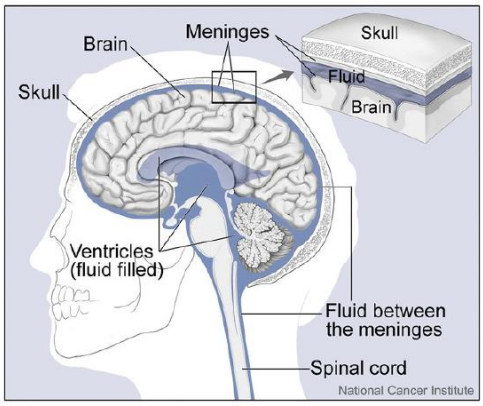


Figure 5.8.1: The brain and nearby structures (including the skull, meninges, ventricles, and spinal cord). An enlarged inset shows the skull, fluid, and brain.

Recall that Dayo's symptoms included loss of bladder control, memory loss, and difficulty walking. The cause of their symptoms was not immediately clear, although their doctors suspected that it related to the nervous system since the nervous system acts as the control center of the body, controlling and regulating many other organ systems. Dayo's memory loss directly implicated the involvement of the brain, since that is the site of thoughts and memory. The urinary system is also controlled in part by the nervous system, and the inability to hold urine appropriately can be a sign of a neurological issue. Dayo's trouble walking involved the muscular system, which works alongside the skeletal system to enable movement of the limbs. In turn, the contraction of muscles is regulated by the nervous system. You can see why a problem in the nervous system can cause a variety of different symptoms by affecting multiple organ systems in the human body.

To try to find the exact cause of Dayo's symptoms, their doctors performed a lumbar puncture, or spinal tap, which is the removal of some CSF through a needle inserted into the lower part of the spinal canal. Doctors then analyzed Dayo's CSF for the presence of pathogens such as bacteria to determine whether an infection was the cause of their neurological symptoms. When no evidence of infection was found, Doctors used an MRI to observe the structures of Dayo's brain. This is when Doctors discovered Dayo's enlarged ventricles, which are a hallmark of hydrocephalus.

To treat Dayo's hydrocephalus, a surgeon implanted a device called a shunt in Dayo's brain to remove the excess fluid (Figure 5.8.2). One side of the shunt consists of a small tube, called a **catheter**, which was inserted into Dayo's ventricles. Excess CSF is then drained through a one-way valve to the other end of the shunt, which was threaded under their skin to their abdominal cavity, where the CSF is released and can be reabsorbed by the bloodstream.

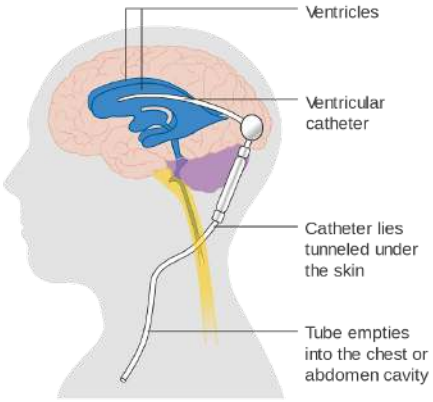


Figure 5.8.2: Tube empties CSF into the abdominal cavity.

Implantation of a shunt is the most common way to treat hydrocephalus, and for some people, it can allow them to recover almost completely. However, there can be complications associated with a brain shunt. The shunt can have mechanical problems or cause an infection. Also, the rate of draining must be carefully monitored and adjusted to balance the rate of removal of CSF with the rate of its production. If it is drained too fast, it is called overdraining, and if it is drained too slowly, it is called **underdraining**. In the case of underdraining, the pressure on the brain and associated neurological symptoms will persist. In the case of overdraining, the ventricles can collapse, which can cause serious problems such as the tearing of blood vessels and hemorrhaging. To avoid these problems, some shunts have an adjustable pressure valve where the rate of draining can be adjusted by placing a special magnet over the scalp. You can see how the proper balance between CSF production and removal is so critical – both in the causes of hydrocephalus and in its treatment.

In what other ways does your body regulate balance, or maintain a state of homeostasis? In this chapter, you learned about the feedback loops that keep body temperature and blood glucose within normal

ranges. Other important examples of homeostasis in the human body are the regulation of the pH in the blood and the balance of water in the body. You will learn more about homeostasis in different body systems in the coming chapters.

Thanks to Dayo's shunt, their symptoms are starting to improve, but they have not fully recovered. Time may tell whether the removal of the excess CSF from their ventricles will eventually allow them to recover normal functioning or whether permanent damage to their nervous system has already been done. The flow of CSF might seem simple but when it gets out of balance, it can easily wreak havoc on multiple organ systems because of the intricate interconnectedness of the systems within the human "machine."

CHAPTER SUMMARY

This chapter provided an overview of the organization and functioning of the human body. You learned that:

- The human body consists of multiple parts that function together to maintain life. The biology of the human body incorporates the body's structure, or anatomy, and the body's functioning, or physiology.
- The organization of the human body is a hierarchy of increasing size and complexity, starting at the level of atoms and molecules and ending at the level of the entire organism.
- Cells are the level of organization above atoms and molecules, and they are the basic units of structure and function of the human body. Each cell carries out basic life functions as well as other specific roles. Cells of the human body show a lot of variation.
  - Variations in cell function are generally reflected in variations in cell structure.
  - Some cells are unattached to other cells and can move freely; others are attached to each other and cannot move freely. Some cells can divide readily and form new cells; others can divide only under exceptional circumstances. Many cells are specialized to produce and secrete particular substances.
  - All the different cell types within an individual have the same genes. Cells can vary because different genes are expressed depending on the cell type.
  - Many common types of human cells consist of several subtypes of cells, each of which has a special structure and function. For example, subtypes of bone cells include osteocytes, osteoblasts, osteogenic cells, and osteoclasts.
- A tissue is a group of connected cells that have a similar function. There are four basic types of human tissues that make up all the organs of the human body: epithelial, muscle, nervous, and connective tissues.
  - Connective tissues, such as bone and blood, are made up of cells that are separated by non-living material, called the extracellular matrix.
  - Epithelial tissues, such as skin and mucous membranes, protect the body and its internal organs and secrete or absorb substances.
  - Muscle tissues are made up of cells that have the unique ability to contract. They include skeletal, smooth, and cardiac muscle tissues.
  - Nervous tissues are made up of neurons, which transmit electrical messages, and glial cells of various types, which play supporting roles. Types of nervous tissues include gray matter, white matter, nerves, and ganglia.
- An organ is a structure that consists of two or more types of tissues that work together to do the same job. Examples include the brain and heart.
  - Many organs are composed of a major tissue that performs the organ's main function, as well as other tissues that play supporting roles.
  - The human body contains five organs that are considered vital for survival. They are the heart, brain, kidneys, liver, and lungs. If any of these five organs stops functioning, the death of the organism is imminent without medical intervention.
- An organ system is a group of organs that work together to carry out a complex overall function. For example, the skeletal system provides structure to the body and protects internal organs.
  - There are 11 major organ systems in the human organism. They are the integumentary, skeletal, muscular, nervous, endocrine, cardiovascular, lymphatic, respiratory, digestive, urinary, and reproductive systems. Only the reproductive system varies significantly between males and females.
- The human body is divided into a number of body cavities. A body cavity is a fluid-filled space in the body that holds and protects internal organs. The two largest human body cavities are the ventral cavity and the dorsal cavity.
  - The ventral cavity is at the anterior, or front, of the trunk. It is subdivided into the thoracic cavity and abdominopelvic cavity.
  - The dorsal cavity is at the posterior, or back, of the body, and includes the head and the back of the trunk. It is subdivided into the cranial cavity and spinal cavity.
- Organ systems of the human body must work together to keep the body alive and functioning normally. This requires communication among organ systems. This is controlled by the autonomic nervous system and endocrine system. The autonomic nervous controls involuntary body functions, such as heart rate and digestion. The endocrine system secretes hormones into the blood that travel to body cells and influence their activities.
  - Cellular respiration is a good example of organ system interactions because it is a basic life process that occurs in all living cells. It is the intracellular process that breaks down glucose with oxygen to produce carbon dioxide and energy. Cellular respiration requires the interaction of the digestive, cardiovascular, and respiratory systems.
  - The fight-or-flight response is a good example of how the nervous and endocrine systems control other organ system responses. It is triggered by a message from the brain to the endocrine system and prepares the body for flight or a fight.

Many organ systems are stimulated to respond, including the cardiovascular, respiratory, and digestive systems.
    - Digesting food requires teamwork between the digestive system and several other organ systems, including the nervous, cardiovascular, and muscular systems.
    - Playing softball or doing other voluntary physical activities may involve the interaction of nervous, muscular, skeletal, respiratory, and cardiovascular systems.
- Homeostasis is the condition in which a system such as the human body is maintained in a more-or-less steady state. It is the job of cells, tissues, organs, and organ systems throughout the body to maintain homeostasis.
    - For any given variable, such as body temperature, there is a particular set point that is the physiological optimum value. The spread of values around the setpoint that is considered insignificant is called the normal range.
    - Homeostasis is generally maintained by a negative feedback loop that includes a stimulus, sensor, control center, and effector. Negative feedback serves to reduce an excessive response and to keep a variable within the normal range. Negative feedback loops control body temperature and blood glucose level.
    - Sometimes homeostatic mechanisms fail, resulting in homeostatic imbalance. Diabetes is an example of a disease caused by homeostatic imbalance. Aging can bring about a reduction in the efficiency of the body's control system, making the elderly more susceptible to disease.
- Positive feedback loops are not common in biological systems. Positive feedback serves to intensify a response until an endpoint is reached. Positive feedback loops control blood clotting and childbirth.

The severe and broad impact of hydrocephalus on the body's systems highlights the importance of the nervous system and its role as the master control system of the body. In the next chapter, you will learn much more about the structures and functioning of this fascinating and important system.

CHAPTER SUMMARY REVIEW

1. Compare and contrast tissues and organs.
2. Osteocyte cells are part of which type of tissue and organ system?
3. Adipose tissue, or body fat, is the same general type of tissue as:
    A. mucous membranes
    B. gray matter
    C. skin
    D. blood
4. Which type of tissue lines the inner and outer surfaces of the body?
5. *True or False.* The extracellular matrix that surrounds cells is always solid.
6. *True or False.* Skin is an organ.
7. What is a vital organ? What happens if a vital organ stops working?
8. Name three organ systems that transport or remove wastes from the body.
9. Name two types of tissue in the digestive system.
10. For each of the following body functions, choose the organ system that is most associated with the function. Organ systems: integumentary; skeletal; muscular; nervous; endocrine; cardiovascular; lymphatic; respiratory; digestive; urinary; reproductive
    A. Processes sensory information
    B. Secretes hormones
    C. Releases carbon dioxide from the body to the outside world
    D. Produces gametes
    E. Controls water balance in the body
11. The spleen is part of which organ system?
    A. Digestive
    B. Lymphatic
    C. Integumentary
    D. Urinary
12. Describe one way in which the integumentary and cardiovascular systems work together to regulate homeostasis in the human body.
13. Name the two largest body cavities in humans and describe their general locations.
14. What are the names given to the three body cavity divisions where the reproductive organs are located?
15. *True or False.* There are two pleural cavities.
16. *True or False.* Body cavities are filled with air.
17. The pituitary gland is in which organ system? Describe how the pituitary gland increases metabolism.
18. When the level of thyroid hormone in the body gets too high, it acts on other cells to reduce the production of more thyroid hormone. What type of feedback loop does this represent?
19. Hypothetical organ A is the control center in a feedback loop that helps maintain homeostasis. It secretes molecule A1 which reaches organ B, causing organ B to secrete molecule B1. B1 negatively feeds back onto organ A, reducing the production of A1 when the level of B1 gets too high.
    A. What is the stimulus in this feedback loop?
    B. If the level of B1 falls significantly below the setpoint, what do you think happens to the production of A1? Why?
    C. What is the effector in this feedback loop?
    D. If organs A and B are part of the endocrine system, what type of molecules do you think A1 and B1 are likely to be?
20. What are the two main systems that allow various organ systems to communicate with each other?
21. The hypothalamus is part of the:
    A. spinal cord
    B. thoracic cavity
    C. kidneys
    D. brain

22. What are two functions of the hypothalamus that you learned about in this chapter?

ATTRIBUTIONS

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CHAPTER OVERVIEW

6: NERVOUS SYSTEM

This chapter describes neurons and other cells of the nervous system and compares and contrasts divisions of the nervous system, including central, peripheral, somatic, and autonomic divisions. The chapter explains how nerve impulses occur and how we sense stimuli. It also describes disorders of the nervous system and the effects of psychoactive drugs on the nervous system.

6.1: Case Study- The Control Center of Your Body

6.2: Introduction to the Nervous System

6.3: Neurons

6.4: Nerve Impulses

6.5: Central Nervous System

6.6: Peripheral Nervous System

6.7: Case Study Conclusion- Memory and Chapter Summary

Thumbnail: Cerebral lobes. (CC BY SA 3.0 Unported; Gutenberg Encyclopedia).

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6.1: CASE STUDY- THE CONTROL CENTER OF YOUR BODY

CASE STUDY: FADING MEMORY

Each of these brightly colored sticky notes represents a piece of information that someone doesn't want to forget. Although we are all forgetful sometimes, most people do not have trouble remembering things that are important or routine to us, such as our friend's name or how to get to class. Our brain, the control center of the nervous system and the rest of the body, normally allows us to retain and recall information. But if the brain becomes damaged, a person may need to rely excessively on external reminders — like this wall of sticky notes — rather than being able to trust their own memory. That is if they are able to remember to write things down in the first place.

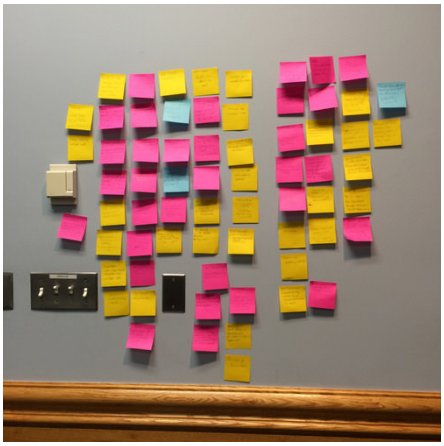


Figure **6.1.1**: Stickies

One person having trouble with their memory is Rosa, who is 68 years old. Rosa has been having difficulty remembering where she has set down objects in her house and forgot about a few doctor's appointments and lunches she planned with friends. Her family began to notice that she would sometimes not recall recent conversations, requiring them to repeat things to her. Rosa would also sometimes struggle to find the right word in a conversation and would put objects in unusual places, such as the milk in a cabinet instead of the refrigerator. While most people do things like this occasionally, it seemed to Rosa and her family that it was happening to her more often recently.

She also had some other symptoms that were impacting her life, such as having trouble paying her bills on time and managing her budget, which she had previously done well. Rosa ascribed these lapses in memory and mental functioning to the normal effects of aging, but her family was concerned. They noticed that she was also more irritable than usual and would sometimes verbally lash out at them, which was not like her. When she became disoriented on a walk around her neighborhood and a neighbor had to escort her home, her family convinced her to see a doctor.

Besides a complete physical exam and lab tests, Rosa's doctor interviewed Rosa and her family about her memory, ability to carry out daily tasks, and mood changes. He also administered a variety of tests to assess her memory and cognitive functioning, such as her ability to solve problems and use numbers and language correctly. Finally, he ordered a scan of her brain to investigate whether a tumor or some other observable cause was causing changes in the functioning of her brain.

Based on the results of these tests, Rosa's doctor came to the conclusion that she most likely has mild Alzheimer's disease (AD). AD results from abnormal changes in the molecules and cells of the brain, characterized by clumps of proteins called amyloid plaques between brain cells and tangled bundles of protein fibers called neurofibrillary tangles within certain brain cells. The affected brain cells stop functioning properly, lose their connections to other brain cells, and eventually will die. The picture below shows part of a cross-section of a brain from a patient who had severe AD compared to a similar section of a healthy brain. You can see how severely shrunken the brain with AD is, due to the death of many brain cells.

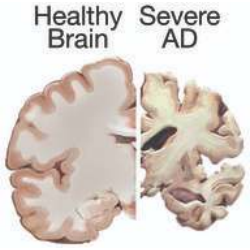


Figure **6.1.2**: The healthy brain is much larger than the brain with AD.

AD is a progressive disease, which means the damage and associated symptoms get worse over time. Clinicians have categorized the progression into three main stages — mild, moderate, and severe AD. Typically, AD cannot be definitively diagnosed until after death when the brain tissue can be directly examined for plaques and tangles. However, based on Rosa's symptoms and the results of her tests, her doctor thinks she most likely has mild AD, when the brain changes and resulting symptoms are not yet severe.

Although there is currently no cure for AD, and Rosa will eventually get worse, her doctor says that medications and behavioral therapies may improve and prolong her functioning and quality of life over the next few years. He prescribes a medication that improves communication between brain cells, which has been shown to help some people with AD.

As you read this chapter, you will learn much more about how the brain and the rest of the nervous system work, and the multitude of functions they control in the body. By the end of the chapter, you will have enough knowledge about the nervous system to learn more about why AD causes the symptoms that it does, how Rosa's medication works, and some promising new approaches that may help physicians diagnose and treat AD patients at earlier stages.

CHAPTER OVERVIEW: NERVOUS SYSTEM

In this chapter, you will learn about the human nervous system, which includes the brain, spinal cord, and nerves. Specifically, you will learn about:

- The organization of the nervous system, including the central and peripheral nervous systems and their organs and subdivisions.
- The cells of the nervous system — neurons and glia — their parts, and their functions.
- How messages are sent by neurons through the nervous system and to and from the rest of the body.
- How these messages, or nerve impulses, are transmitted by electrical changes within neurons, and through chemical molecules to other cells.
- The structure and functions of different parts of the central nervous system, which includes the brain and spinal cord, and some of the things that can go wrong when they are damaged.
- The structure and functions of the peripheral nervous system, which includes the nerves that carry motor and sensory information to and from the body to control voluntary and involuntary activities.
- The human senses and how visual information, sounds, smells, tastes, touch, and balance are detected by sensory receptor cells and then sent to the brain for interpretation.
- How legal and illegal drugs can have psychoactive effects on the brain-altering mood, perceptions, thinking, and behavior — which can sometimes lead to addiction.

As you read the chapter, think about the following questions:

1. Based on Rosa's symptoms, which parts of her brain may have been affected by Alzheimer's disease?
2. How are messages sent between cells in the nervous system? What molecules are involved in this process? What are the ways in which drugs can alter this process?
3. Why can't Rosa's brain just grow new cells to replace the ones that have died?

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6.2: INTRODUCTION TO THE NERVOUS SYSTEM

IN THE BLINK OF AN EYE

As you drive into a parking lot, a skateboarder suddenly flies in front of your car across your field of vision. You see the skateboarder in the nick of time and react immediately. You slam on the brakes and steer sharply to the right — all in the blink of an eye. You avoid a collision, but just barely. You're shaken up but thankful that no one was hurt. How did you respond so quickly? Such rapid responses are controlled by your nervous system.



Figure **6.2.1**: Skateboarder

OVERVIEW OF THE NERVOUS SYSTEM

The **nervous system**, illustrated in Figure **6.2.2**, is the human organ system that coordinates all of the body's voluntary and involuntary actions by transmitting electrical signals to and from different parts of the body. Specifically, the nervous system extracts information from the internal and external environments using sensory receptors. It then usually sends signals encoding this information to the brain, which processes the information to determine an appropriate response. Finally, the brain sends signals to muscles, organs, or glands to bring about the response. In the example above, your eyes detected the skateboarder, the information traveled to your brain, and your brain instructed your body to act so as to avoid a collision.

SIGNALS OF THE NERVOUS SYSTEM

The signals sent by the nervous system are electrical signals called nerve impulses, and they are transmitted by special nervous system cells named neurons, or nerve cells, like the one in Figure **6.2.3** (all the parts of a neuron are explained in the next section). Dendrites of a neuron receive nerve impulses from other cells. Long projection (called axons) from neurons carries nerve impulses directly to specific target cells. Schwann cells wrapped around the axon are called **glial cells**. They create a myelin sheath which allows the nerve impulse to travel very rapidly through the axons. A cell that receives nerve impulses from a neuron may be excited to perform a function, inhibited from carrying out an action, or otherwise controlled. In this way, the information transmitted by the nervous system is specific to particular cells and is transmitted very rapidly.

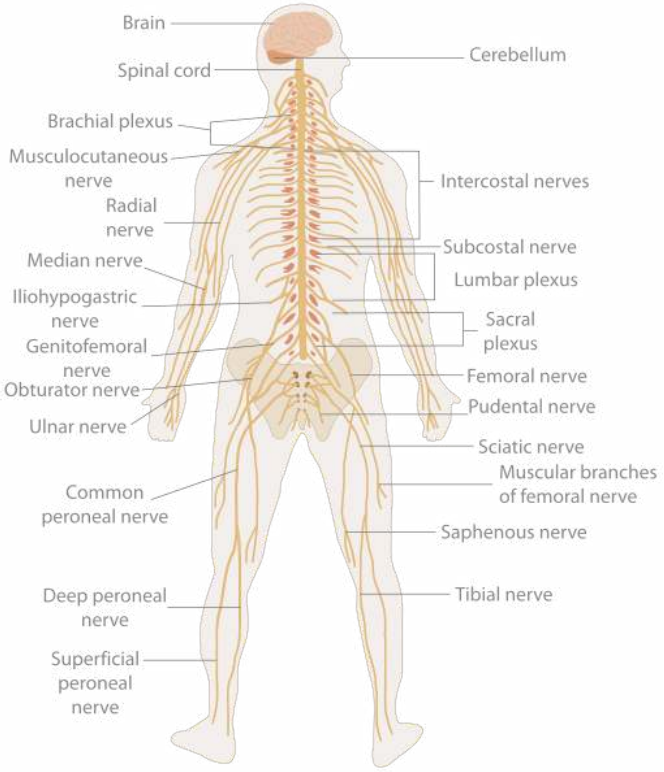


Figure **6.2.2**: The human nervous system consists of the brain and spinal cord (central nervous system) and a network of branching nerves that travel throughout the body (peripheral nervous system). Some of the major nerves in the peripheral system are identified in this drawing.

In fact, the fastest nerve impulses travel at speeds greater than 100 meters per second! Compare this to the chemical messages carried by the hormones that are secreted into the blood by endocrine glands. These hormonal messages are "broadcast" to all the cells of the body, and they can travel only as quickly as the blood flows through the cardiovascular system.

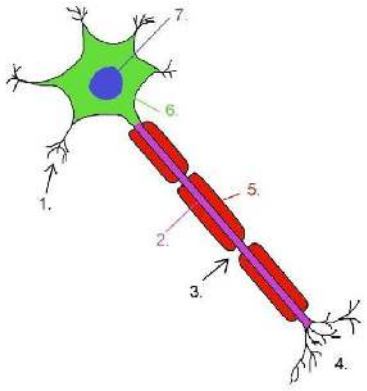


Figure **6.2.3**: This simple model of a neuron shows 1 Dendrite, 2 Axon, 3 Nodes of Ranvier, 4 Axon Terminals, 5 Schwann cell (Myelin Sheath), 6 Cell body, and 7 Nucleus

ORGANIZATION OF THE NERVOUS SYSTEM

As you might predict, the human nervous system is very complex. It has multiple divisions, beginning with its two main parts, the central nervous system (CNS) and the peripheral nervous system (PNS), as shown in Figure **6.2.4**. The CNS includes the brain and spinal cord, and the PNS consists mainly of nerves, which are bundles of axons from neurons. The nerves of the PNS connect the CNS to the rest of the body. You can learn much more about the CNS by reading the concept *Central Nervous System*.

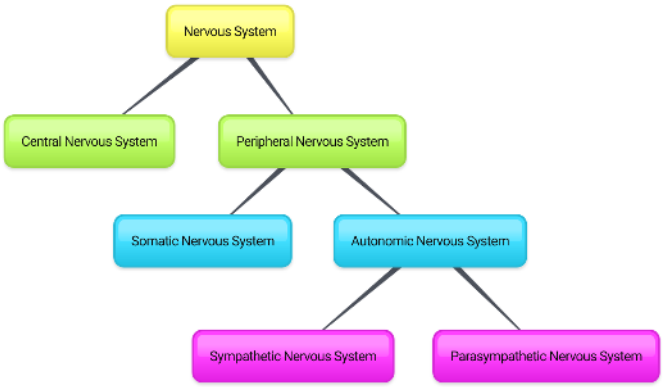


Figure **6.2.4**: The concept map illustrates that the nervous system is divided into the peripheral and central systems. The peripheral nervous system is divided into the autonomic and somatic systems. The autonomic nervous system is divided into the sympathetic and parasympathetic systems.

The PNS is divided into two major parts, called the autonomic and somatic nervous systems. The somatic nervous system controls activities that are under voluntary control, such as turning a steering wheel. The autonomic nervous system controls activities that are not under voluntary control, such as digesting a meal. The autonomic nervous system has two divisions: the sympathetic division, which controls the fight-or-flight response during emergencies, and the parasympathetic division, which controls the routine "housekeeping" functions of the body at other times. You can learn more about the PNS and its subdivisions by reading the concept *Peripheral Nervous System*.

REVIEW

1. List the general steps by which the nervous system generates an appropriate response to information from the internal and external environments.
2. What are neurons?
3. Compare and contrast the central and peripheral nervous systems.
4. Which major division of the peripheral nervous system allows you to walk to class? Which major division of the peripheral nervous system controls your heart rate?
5. Identify the functions of the three divisions of the autonomic nervous system.
6. What is an axon and what is its function?
7. *True or False*. A nerve impulse always causes the target cell to perform an action.
8. *True or False*. The spinal cord is not considered part of the peripheral nervous system.
9. Define nerve impulses.
10. Explain why signals in the nervous system are generally more targeted and specific than signals in the endocrine system.
11. Explain generally how the brain and spinal cord can interact with and control the rest of the body.
12. _____ actions are performed without the person thinking about them.
13. The fight-or-flight response is controlled by the:
    A. autonomic nervous system
    B. somatic nervous system
    C. central nervous system
    D. parasympathetic nervous system
14. How are nerves and neurons related?
15. What type of information from the outside environment do you think is detected by sensory receptors in your ears?

EXPLORE MORE

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6.3: NEURONS

LIFE AS ART

This colorful picture could be an abstract work of modern art. You might imagine it hanging in an art museum or art gallery. In fact, the picture illustrates real life rather than an artistic creation. It is a micrograph of human nervous tissue. The neon green structures in the picture are neurons. The neuron is one of two basic types of cells in the nervous system, the other type being the glial cell.

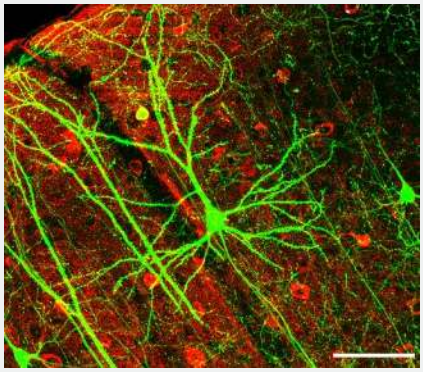


Figure **6.3.1**: Interneurons of Adult Visual Cortex

Neurons, also called nerve cells, are electrically excitable cells that are the main functional units of the nervous system. Their function is to transmit nerve impulses. They are the only type of human cells that can carry out this function.

NEURON STRUCTURE

Figure **6.3.2** shows the structure of a typical neuron. The main parts of a neuron are labeled in the figure and described below.

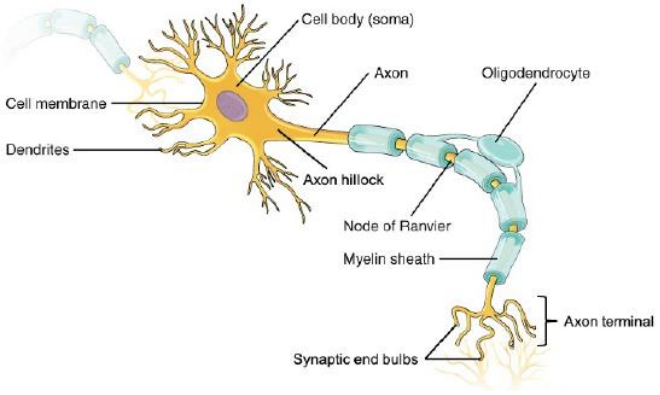


Figure **6.3.2**: Somatic Motor Neuron with cell body, axon, axon, myelin sheath, nodes of Ranvier, axon terminal, dendrites, synaptic end of the bulbs, and other associated structures.

- The **cell body** is the part of a neuron that contains the cell nucleus and other cell organelles. It is usually quite compact, and may not be much wider than the nucleus.
- **Dendrites** are thin structures that are extensions of the cell body. Their function is to receive nerve impulses from other cells and carry them to the cell body. A neuron may have many dendrites, and each dendrite may branch repeatedly to form a dendrite "tree" with more than 1,000 "branches." The end of each branch can receive nerve impulses from another cell, allowing a given neuron to communicate with tens of thousands of other cells.
- The **axon** is a long, thin extension of the cell body. It transmits nerve impulses away from the cell body and toward other cells. The axon branches at the end, forming multiple axon terminals. These are the points where nerve impulses are transmitted to other cells, often to the dendrites of other neurons. An area called a synapse occurs at each axon terminal. Synapses are complex membrane junctions that transmit signals to other cells. An axon may branch hundreds of times, but there is never more than one axon per neuron.
- Spread out along axons, especially the long axons of nerves, are many sections of the **myelin sheath.** These are lipid layers that cover sections of the axon. The myelin sheath is a very good electrical insulator, similar to the plastic or rubber that encases an electrical cord.
- Regularly spaced gaps between sections of myelin sheath occur along the axon. These gaps are called **nodes of Ranvier**, and they allow the transmission of nerve impulses along the axon. Nerve impulses skip from node to node, allowing nerve impulses to travel along the axon very rapidly.
- A Schwann cell (also on an axon) is a type of glial cell. Its function is to produce the myelin sheath that insulates axons in the peripheral nervous system. In the central nervous system, a different type of glial cell, called an oligodendrocyte, produces the myelin sheath.

NEUROGENESIS

Fully differentiated neurons, with all their special structures, cannot divide and form new daughter neurons. Until recently, scientists thought that new neurons could no longer be formed after the brain developed prenatally. In other words, they thought that people were born with all the brain neurons they would ever have, and as neurons died, they would not be replaced. However, new evidence shows that additional neurons can form in the brain, even in adults, from the division of undifferentiated neural stem cells that are found throughout the brain. The production of new neurons is called **neurogenesis.** The extent to which it can occur is not known, but it is not likely to be very great in humans.

NEURONS IN NERVOUS TISSUES

The nervous tissue in the brain and spinal cord consists of gray matter and white matter. Gray matter contains mainly the cell bodies of neurons. It is gray only in cadavers; living gray matter is actually more pink than gray (see image below). White matter consists mainly of axons covered with myelin sheath, which gives them their white color. White matter also makes up nerves of the peripheral nervous system. Nerves consist of long bundles of myelinated axons that extend to muscles, organs, or glands throughout the body. The axons in each nerve are bundled together like wires in a cable.

Axons in nerves may be more than a meter long in an adult. The longest nerve runs from the base of the spine to the toes.

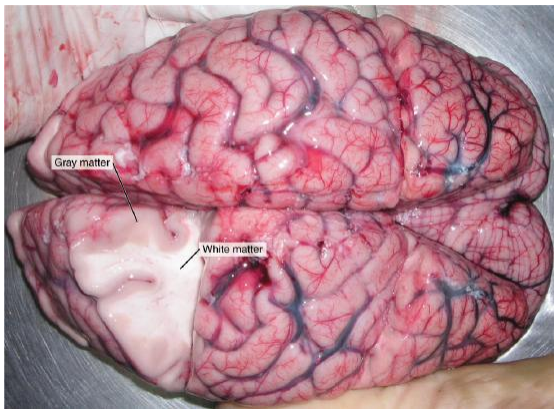


Figure **6.3.3**: You can see the layers of (pinkish) gray matter and white matter in this photo of a brain from a recently deceased human patient

TYPES OF NEURONS

There are hundreds of different types of neurons in the human nervous system. These types exhibit a variety of structures and functions. Nonetheless, many neurons can be classified functionally based on the direction in which they carry nerve impulses.

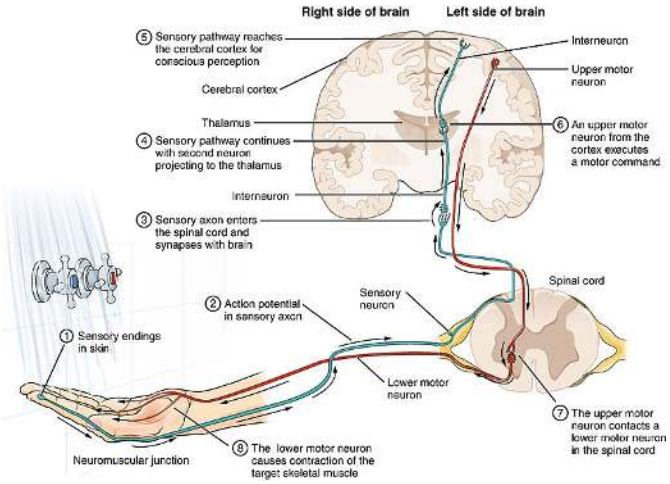


Figure **6.3.4**: Sensory neurons carry information towards the CNS. Motor neurons carry information from the CNS. Interneurons carry information between sensory and motor neurons.

- **Sensory** (also called afferent) **neurons** carry nerve impulses from sensory receptors in tissues and organs to the central nervous system. They change physical stimuli such as touch, light, and sound into nerve impulses.
- **Motor** (also called efferent) **neurons,** like the one in figure **6.3.2**, carry nerve impulses from the central nervous system to muscles and glands. They change nerve signals into the activation of these structures.
- **Interneurons** carry nerve impulses back and forth often between sensory and motor neurons within the spinal cord or brain.

GLIAL CELLS

Besides neurons, nervous tissues also consist of **glial cells** (also called neuroglia). They are now known to play many vital roles in the nervous system. There are several different types of glial cells, each with a different function. Schwann cells and Oligodendrocytes are glial cells that produce myelin sheath.

FEATURE: MY HUMAN BODY

Would you like your brain to make new neurons that could help you become a better learner? What college student wouldn't want a little more brainpower when it comes to learning new things? If research on rats applies to humans, then sustained aerobic exercise such as running can increase neurogenesis in the adult brain, and specifically in the hippocampus, a brain structure important for learning temporally and/or spatially complex tasks as well as memory. Although the research is still at the beginning stages, it suggests that exercise may actually lead to a "smarter" brain. However, even if the research results are not confirmed in the future for humans, it can't hurt to get more aerobic exercise, because it is certainly beneficial for your body if not for your brain.

REVIEW

1. Identify the three main parts of a neuron and their functions.
2. Describe the myelin sheath and nodes of Ranvier. How does their arrangement allow nerve impulses to travel very rapidly along axons?
3. What is a synapse?
4. Define neurogenesis. What is the potential for neurogenesis in the human brain?
5. Relate neurons to different types of nervous tissues.
6. Compare and contrast sensory and motor neurons.
7. Identify the role of interneurons.
8. For each type of neuron below, identify whether it is a sensory neuron, motor neuron, or interneuron.
   A. A neuron in the spinal cord receives touch information and then transmits that information to another spinal cord neuron that controls the movement of an arm muscle.
   B. A neuron that takes taste information from your tongue and sends it to your brain.
   C. A spinal cord neuron stimulates a muscle to contract.
9. The myelin sheath is made by:
   A. Sensory neurons
   B. White neurons
   C. Peripheral nervous system neurons
   D. Glial cells
10. *True or False.* Synapses often exist where a dendrite and an axon terminal meet.
11. *True or False.* There is only one axon terminal per neuron.

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6.4: NERVE IMPULSES

WHEN LIGHTNING STRIKES

This amazing cloud-to-surface lightning occurred when a difference in electrical charge built up in a cloud relative to the ground. When the buildup of charge was great enough, a sudden discharge of electricity occurred. A nerve impulse is similar to a lightning strike. Both a nerve impulse and a lightning strike occur because of differences in electrical charge, and both result in an electric current.



Figure **6.4.1**: Lightning

GENERATING NERVE IMPULSES

A **nerve impulse**, like a lightning strike, is an electrical phenomenon. A nerve impulse occurs because of a difference in electrical charge across the plasma membrane of a neuron. How does this difference in electrical charge come about? The answer involves ions, which are electrically charged atoms or molecules.

RESTING POTENTIAL

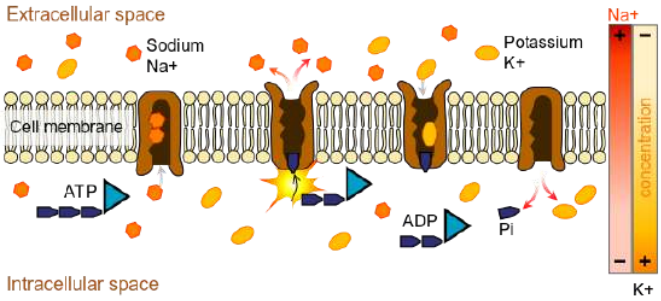


Figure **6.4.2**: The sodium-potassium pump maintains the resting potential of a neuron. There is more negative charge inside than outside the cell membrane. ATP is used to pump sodium out and potassium into the cell. There is more concentration of sodium outside the membrane and more concentration of potassium inside the cell due to the unequal movement of these ions by the pump

When a neuron is not actively transmitting a nerve impulse, it is in a resting state, ready to transmit a nerve impulse. During the resting state, the sodium-potassium pump maintains a difference in charge across the cell membrane of the neuron. The sodium-potassium pump is a mechanism of active transport that moves sodium ions out of cells and potassium ions into cells. The sodium-potassium pump moves both ions from areas of lower to higher concentration, using energy in ATP and carrier proteins in the cell membrane. Figure **6.4.3** shows in greater detail how the sodium-potassium pump works. Sodium is the principal ion in the fluid outside of cells, and potassium is the principal ion in the fluid inside of cells. These differences in concentration create an electrical gradient across the cell membrane, called **resting potential**. Tightly controlling membrane resting potential is critical for the transmission of nerve impulses.

ACTION POTENTIAL

An **action potential**, also called a nerve impulse, is an electrical charge that travels along the membrane of a neuron. It can be generated when a neuron's membrane potential is changed by chemical signals from a nearby cell. In an action potential, the cell membrane potential changes quickly from negative to positive as sodium ions flow into the cell through ion channels, while potassium ions flow out of the cell, as shown in Figure **6.4.3**.

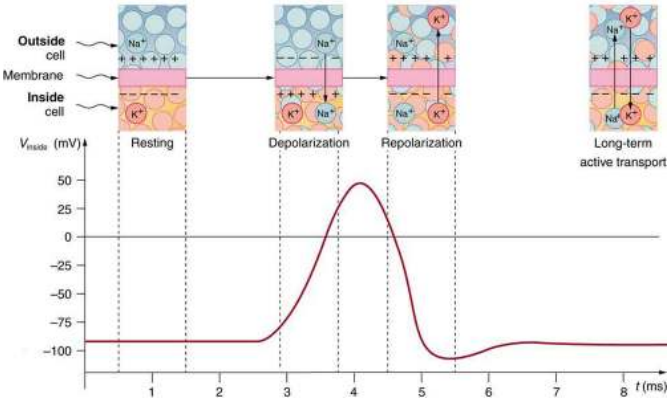


Figure **6.4.3**: An action potential speeds along an axon in milliseconds. Sodium ions flow in and cause the action potential, and then potassium ions flow out to reset the resting potential.

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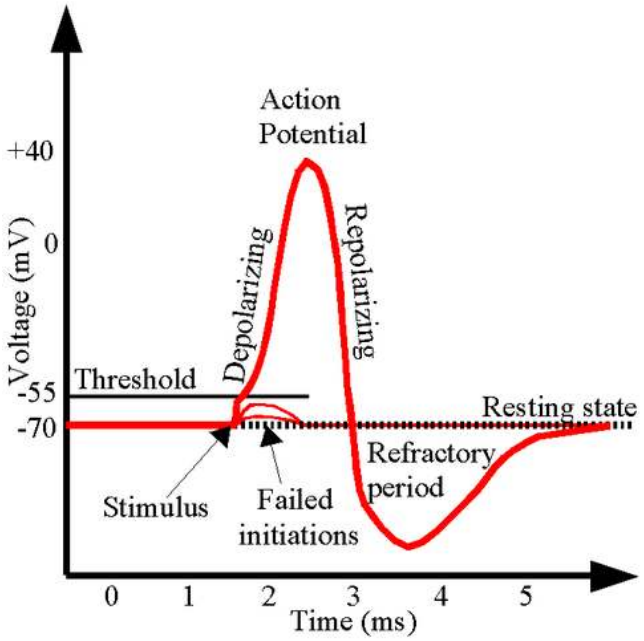


Figure **6.4.4**: An action potential graph of membrane potential over time. A neuron must reach a certain threshold in order to begin the depolarization step of reaching the action potential. The figure also shows the change in potential during the repolarization and refractory periods of the axon.

The change in membrane potential results in the cell becoming depolarized. An action potential works on an all-or-nothing basis. That is, the membrane potential has to reach a certain level of depolarization, called the threshold, otherwise, an action potential will not start. This threshold potential varies but is generally about 15 millivolts (mV) more positive than the cell's resting membrane potential. If a membrane depolarization does not reach the threshold level, an action potential will not happen. You can see in Figure **6.4.4** that two depolarizations did not reach the threshold level of -55mV.

The first channels to open are the sodium ion channels, which allow sodium ions to enter the cell. The resulting increase in positive charge inside the cell (up to about +40 mV) starts the action potential. This is called the depolarization of the membrane. Potassium ion channels then open, allowing potassium ions to flow out of the cell, which ends the action potential. The inside of the membrane becomes negative again. This is called repolarization of the membrane. Both of the ion channels then close, and the sodium-potassium pump restores the resting potential of -70 mV. The action potential will move down the axon toward the synapse like a wave would move along the surface of the water. Figure **6.4.4** shows the change in potential of the axon membrane during an action potential. The nerve goes through a brief refractory period before racing resting potential. During the refractory period, another action potential cannot be generated

In myelinated neurons, ion flows occur only at the nodes of Ranvier. As a result, the action potential signal "jumps" along the axon membrane from node to node rather than spreading smoothly along the membrane, as they do in axons that do not have a myelin sheath. This is due to a clustering of Na+ and K+ ion channels at the Nodes of Ranvier. Unmyelinated axons do not have nodes of Ranvier, and ion channels in these axons are spread over the entire membrane surface.

TRANSMITTING NERVE IMPULSES

The place where an axon terminal meets another cell is called a **synapse.** This is where the transmission of a nerve impulse to another cell occurs. The cell that sends the nerve impulse is called the presynaptic cell, and the cell that receives the nerve impulse is called the postsynaptic cell.

Some synapses are purely electrical and make direct electrical connections between neurons. However, most synapses are chemical synapses. The transmission of nerve impulses across chemical synapses is more complex.

CHEMICAL SYNAPSES

At a chemical synapse, both the presynaptic and postsynaptic areas of the cells are full of the molecular machinery that is involved in the transmission of nerve impulses. As shown in Figure **6.4.5**, the presynaptic area contains many tiny spherical vessels called synaptic vesicles that are packed with chemicals called **neurotransmitters**. When an action potential reaches the axon terminal of the presynaptic cell, it opens channels that allow calcium to enter the terminal. Calcium causes synaptic vesicles to fuse with the membrane, releasing their contents into the narrow space between the presynaptic and postsynaptic membranes. This area is called the synaptic cleft. The neurotransmitter molecules travel across the synaptic cleft and bind to **receptors**, which are proteins that are embedded in the membrane of the postsynaptic cell.

The effect of a neurotransmitter on a postsynaptic cell depends mainly on the type of receptors that it activates, making it possible for a particular neurotransmitter to have different effects on various target cells. A neurotransmitter might excite one set of target cells, inhibit others, and have complex modulatory effects on still others, depending on the type of receptors. However, some neurotransmitters have relatively consistent effects on other cells.

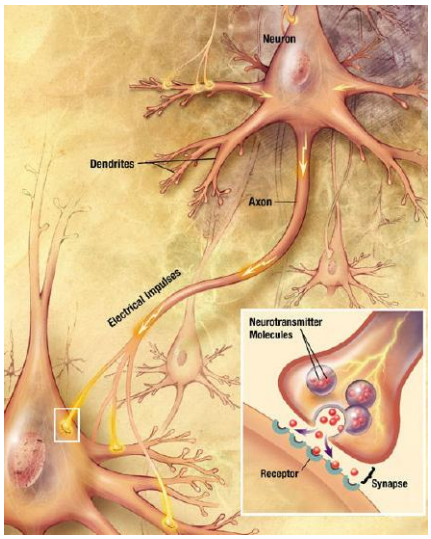


Figure 6.4.5: This diagram shows how an action potential transmits a signal across a synapse to another cell by neurotransmitter molecules. The inset diagram shows the axon terminal, synapse, and receptor of the postsynaptic cell. The neurotransmitters are released from the axon terminal, travel in the synaptic cleft, and attach to the receptors.

REVIEW

1. Define nerve impulse.
2. What is the resting potential of a neuron, and how is it maintained?
3. Explain how and why an action potential occurs.
4. Outline how a signal is transmitted from a presynaptic cell to a postsynaptic cell at a chemical synapse.
5. What generally determines the effects of a neurotransmitter on a postsynaptic cell?
6. Identify three general types of effects neurotransmitters may have on postsynaptic cells.
7. Explain how an electrical signal in a presynaptic neuron causes the transmission of a chemical signal at the synapse.
8. The flow of which type of ion into the neuron results in an action potential?
   A. How do these ions get into the cell?
   B. What does this flow of ions do to the relative charge inside the neuron compared to the outside?
9. The sodium-potassium pump:
   A. is activated by an action potential
   B. requires energy
   C. does not require energy
   D. pumps potassium ions out of cells
10. *True or False.* Some action potentials are larger than others, depending on the amount of stimulation.
11. *True or False.* Synaptic vesicles from the presynaptic cell enter the postsynaptic cell.
12. *True or False.* An action potential in a presynaptic cell can ultimately cause the postsynaptic cell to become inhibited.
13. Name three neurotransmitters.

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6.5: CENTRAL NERVOUS SYSTEM

HOMUNCULUS

Figure **6.5.1** is a very odd-looking drawing and is called a homunculus. The mass represents a cross-sectional wedge of the human brain. The drawing shows some areas of the brain associated with different parts of the body. As you can see, larger areas of the brain in this region are associated with the hands, face, and tongue than the legs and feet. Given the importance of speech, manual dexterity, and face-to-face social interactions in human beings, it is not surprising that relatively large areas of the brain are needed to control these body parts. The brain is the most complex organ in the human body and part of the central nervous system.

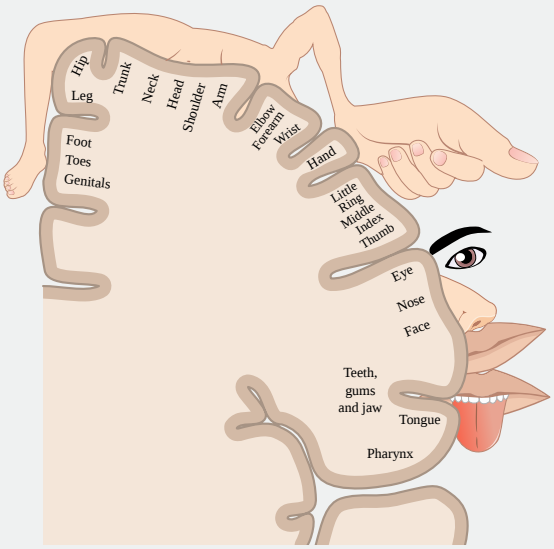


Figure **6.5.1**: Brain-Body Map. There's a map of your body on your brain's cortex, but the map is not proportional to actual space. Sensitive parts like the face and fingers are represented by more areas than less sensitive parts like the legs or back

WHAT IS THE CENTRAL NERVOUS SYSTEM?

The central nervous system (CNS) is the part of the nervous system that includes the brain and spinal cord. Figure **6.5.2** shows the central nervous system as one of the two main divisions of the total nervous system. The other main division is the peripheral nervous system (PNS). The CNS and PNS work together to control virtually all body functions. You can read much more about the PNS in the concept *Peripheral Nervous System*.

The delicate nervous tissues of the central nervous system are protected by major physical and chemical barriers. Physically, the brain and spinal cord are surrounded by tough meninges, a three-layer protective sheath that also contains cushioning cerebrospinal fluid. The bones of the skull and spinal vertebrae also contribute to physically protecting the brain and spinal cord. Chemically, the brain and spinal cord are isolated from the circulation — and most toxins or pathogens in the blood — by the **blood-brain barrier.** The blood-brain barrier is a highly selective membrane formed of endothelial cells (a type of glial cells) that separates the circulating blood from the extracellular fluid in the CNS. The barrier allows water, certain gases, glucose, and some other molecules needed by the brain and spinal cord to cross from the blood into the CNS while keeping out potentially harmful substances. These physical and chemical barriers make the CNS less susceptible to injury. However, damage to the CNS is likely to have more serious consequences.

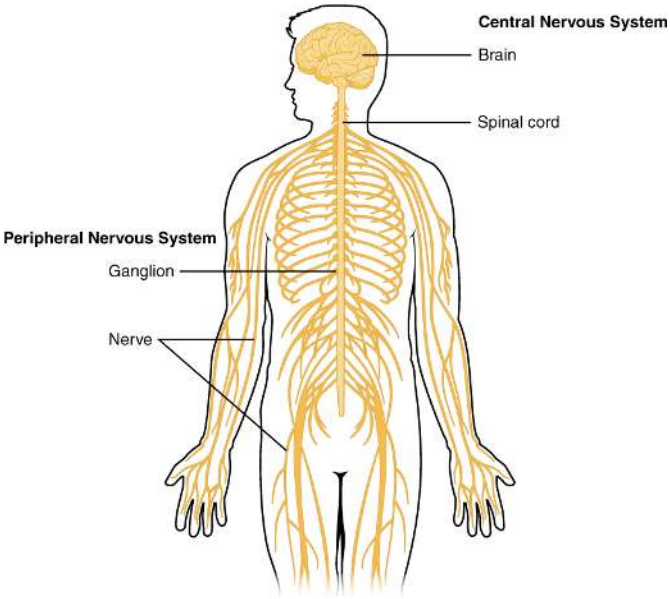


Figure **6.5.2**: The two main parts of the central nervous system are the brain and the spinal cord. Ganglions and nerves are part of the peripheral nerve system.

THE BRAIN

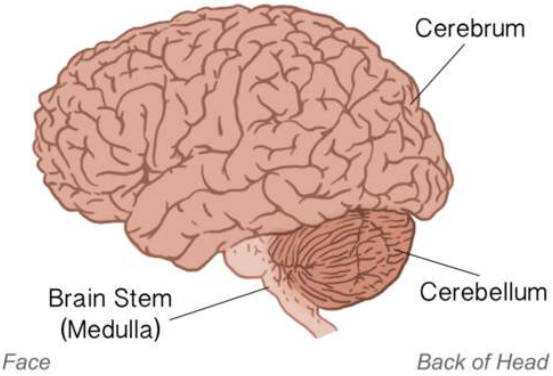


Figure **6.5.3**: Cerebrum, Cerebellum, and Brain Stem are the major parts of the brain. the medulla is part of the brain stem.

The **brain** is the control center not only of the rest of the nervous system but of the entire organism. The adult brain makes up only about 2 percent of the body's weight, but it uses about 20 percent of the body's total energy. The brain contains an estimated one hundred billion neurons, and each neuron has thousands of synaptic connections to other neurons. The brain also has about the same number of glial cells as neurons. No wonder the brain uses so much

energy! In addition, the brain uses mostly glucose for energy. As a result, if the brain is deprived of glucose, it can lead to unconsciousness. The brain is able to store some glucose in the form of glycogen, but in much smaller amounts than are found in the liver and skeletal muscles.

The brain controls such mental processes as reasoning, imagination, memory, and language. It also interprets information from the senses and commands the body how to respond. It controls basic physical processes such as breathing and heartbeat as well as voluntary activities such as walking and writing. The brain has three major parts: the cerebrum, cerebellum, and brain stem (Figure **6.5.3**). The figure shows the brain from the left side of the head. It shows how the brain would appear if the skull and meninges were removed. The brain stem via its medulla links to the spinal cord. The cerebellum is a small section at the back of the brain. The largest part of the brain is the cerebrum.

CEREBRUM

The **cerebrum** is the largest part of the brain. It controls conscious, intellectual functions. For example, it controls reasoning, language, memory, sight, touch, and hearing. When you read a book, play a video game, or recognize a classmate, you are using your cerebrum.

HEMISPHERES AND LATERALIZATION OF THE CEREBRUM

The cerebrum is divided from front to back into two halves called the left and right **hemispheres.** The two hemispheres are connected by a thick bundle of axons, known as the corpus callosum, which lies deep within the brain. The corpus callosum is the main avenue of communication between the two hemispheres. It connects each point in the cerebrum to the mirror-image point in the opposite hemisphere.

The right and left hemispheres of the cerebrum are similar in shape, and most areas of the cerebrum are found in both hemispheres. Some areas, however, show **lateralization,** or a concentration in one hemisphere or the other. For example, in most people, language functions are more concentrated in the left hemisphere, whereas abstract reasoning and visual-spatial abilities are more concentrated in the right hemisphere.

For reasons that are not yet clear, each hemisphere of the brain interacts primarily with the opposite side of the body. The left side of the brain receives messages from and sends commands to the right side of the body, and the right side of the brain receives messages from and sends commands to the left side of the body. Sensory nerves from the spinal cord to the brain and motor nerves from the brain to the spinal cord both cross the midline of the body at the level of the brain stem.

CEREBRAL CORTEX

Most of the information processing in the brain actually takes place in the **cerebral cortex.** This is a rind of gray matter and other tissues just a few millimeters thick that makes up the outer surface of the cerebrum in both hemispheres of the brain. The cerebral cortex has many folds in it that greatly increase the amount of surface area of the brain that can fit within the skull. Because of all the folds in the human cerebral cortex, it has a surface area of about 2,500 cm^2(2.5 ft^2). The size and importance of the cerebral cortex are far greater in the human brain than the brains of any other vertebrates including nonhuman primates.

LOBES OF THE CEREBRAL CORTEX

Each hemisphere of the cerebrum is further divided into the four lobes shown in Figure **6.5.4** and described below.

1. The **frontal lobes** are located at the front of the brain behind the forehead. The frontal lobes are associated with executive functions such as attention, self-control, planning, problem-solving, reasoning, abstract thought, language, and personality.

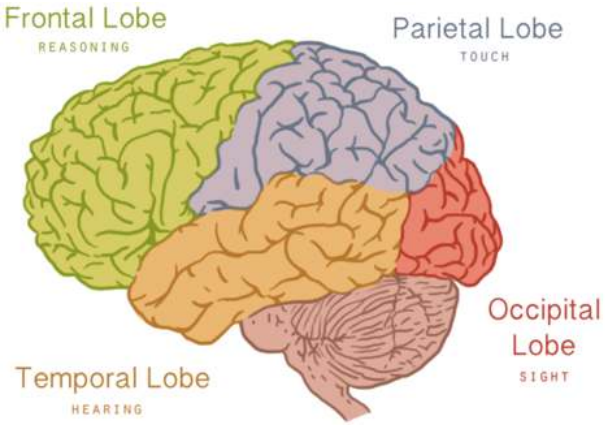


Figure **6.5.4**: Each hemisphere of the cerebrum consists of four parts, called lobes. The lobes are associated with multiple functions. The image shows one function of each lobe. Frontal, Parietal, Occipital, and Temporal lobes are associated with reasoning, touch, sight, and hearing, respectively.

2. The **parietal lobes** are located behind the frontal lobes at the top of the head. The parietal lobes are involved in sensation, including temperature, touch, and taste. Reading and arithmetic are also functions of the parietal lobes.

3. The **temporal lobes** are located at the sides of the head below the frontal and parietal lobes. The temporal lobes enable hearing, the formation and retrieval of memories, and the integration of memories and sensations.

4. The **occipital lobes** are located at the back of the head below the parietal lobes. The occipital lobes are the smallest of the four pairs of lobes. They are dedicated almost solely to vision.

INNER STRUCTURES OF THE BRAIN

Several structures are located deep within the brain and are important for communication between the brain and spinal cord or the rest of the body. These structures include the hypothalamus and thalamus. Figure **6.5.5** shows where these structures are located in the brain. The cerebrum, hypothalamus, and thalamus exist in two halves, one in each hemisphere.

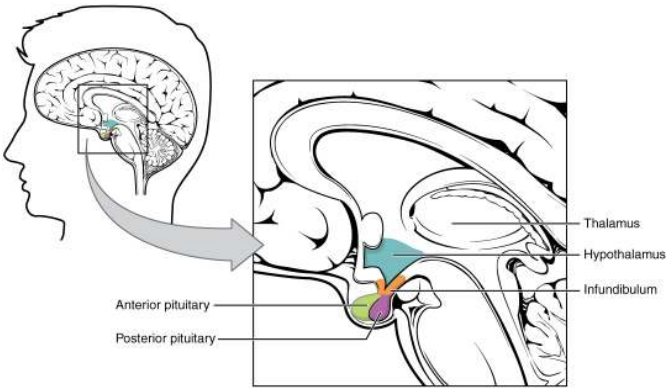


Figure **6.5.5**: Just below the cerebrum is the thalamus. Hypothalamus is located below the thalamus and a little to the anterior. The pituitary gland is attached to the hypothalamus via a tube called the infundibulum.

HYPOTHALAMUS

The **hypothalamus** is located just above the brain stem and is about the size of an almond. The hypothalamus is responsible for certain metabolic processes and other activities of the autonomic nervous system, including body temperature, heart rate, hunger, thirst, fatigue, sleep, wakefulness, and circadian (24-hour) rhythms. The hypothalamus is also an important emotional center of the brain. The hypothalamus can regulate so many body functions because it responds to many different internal and external signals, including messages from the brain, light, steroid hormones, stress, and invading pathogens, among others.

One way the hypothalamus influences body functions is by synthesizing hormones that directly influence body processes. For example, it synthesizes the hormone oxytocin, which stimulates uterine contractions during childbirth and the letdown of milk during lactation. It also synthesizes the hormone vasopressin (also called antidiuretic hormone), which stimulates the kidneys to reabsorb more water and excrete more concentrated urine. These two hormones are sent from the hypothalamus via a stalk-like structure called the infundibulum (see diagram above) directly to the posterior (back) portion of the pituitary gland, which secretes them into the blood.

The main way the hypothalamus influences body functions is by controlling the pituitary gland, known as the master gland of the endocrine system. The hypothalamus synthesizes neurohormones called releasing factors that travel through the infundibulum directly to the anterior (front) part of the pituitary gland. The releasing factors generally either stimulate or inhibit the secretion of anterior pituitary hormones, most of which control other glands of the endocrine system.

THALAMUS

The **thalamus,** which is located near the hypothalamus (Figure **6.5.5**), is a major hub for information traveling back and forth between the spinal cord and cerebrum. It filters sensory information traveling to the cerebrum. It relays sensory signals to the cerebral cortex and motor signals to the spinal cord. It is also involved in the regulation of consciousness, sleep, and alertness.

CEREBELLUM

The **cerebellum** is just below the cerebrum and at the back of the brain behind the brain stem (Figure **6.5.3**). It coordinates body movements and is involved in movements that are learned with repeated practice. For example, when you hit a softball with a bat or touch type on a keyboard you are using the cerebellum. Many nerve pathways link the cerebellum with motor neurons throughout the body.

BRAIN STEM

Sometimes called the “lower brain,” the **brain stem** is the lower part of the brain that is joined to the spinal cord. There are three parts to the brainstem: the midbrain, the pons, and the medulla oblongata, which are shown in Figure **6.5.6** below. The brain stem is primarily involved in the unconscious autonomic functions as well as several types of sensory information. It also helps coordinate large body movements such as walking and running. The **midbrain** deals with sight and sound information and translates these inputs before sending them to the forebrain. The **pons** relays messages to other parts of the brain (primarily the cerebrum and cerebellum) and helps regulate breathing. Some researchers have hypothesized that the pons plays a role in dreaming. Some of the functions of the Pons are shared by the **medulla oblongata,** also called the medulla. The medulla controls several subconscious homeostatic functions such as breathing, heart and blood vessel activity, swallowing, and digestion.

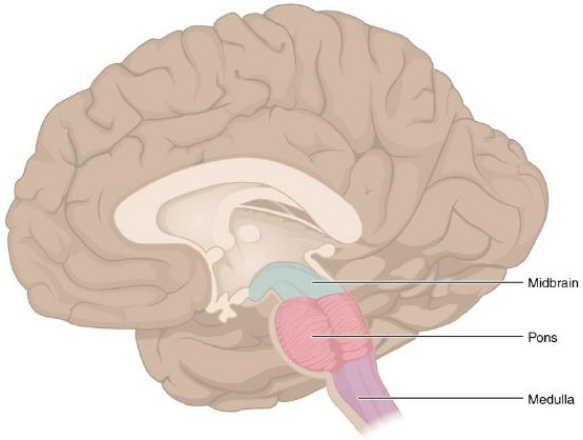


Figure **6.5.6**: Brain stem includes the midbrain, pons, and medulla oblongata

One of the brain stem’s most important roles is that of an “information highway.” That is, all of the information coming from the body to the brain and the information from the cerebrum to the body go through the brain stem. Sensory pathways for such things as pain, temperature, touch, and pressure sensation go upward to the cerebrum, and motor pathways for movement and other body processes go downward to the spinal cord. Most of the axons in the motor pathways cross from one side of the CNS to the other as they pass through the medulla oblongata. As a result, the right side of the brain controls much of the movement on the left side of the body,

and the left side of the brain controls much of the movement on the right side of the body.

SPINAL CORD



Figure **6.5.7**: The spinal cord (yellow) runs from the bottom of the brain to the lower back

The **spinal cord** is a long, thin, tubular bundle of nervous tissues that extends from the brain stem and continues down the center of the back to the pelvis. It is highlighted in yellow in Figure **6.5.7**. The spinal cord is enclosed within but is shorter than, the vertebral column.

STRUCTURE OF THE SPINAL CORD

The center of the spinal cord consists of gray matter, which is made up mainly of cell bodies of neurons, including interneurons and motor neurons. The gray matter is surrounded by white matter that consists mainly of myelinated axons of motor and sensory neurons. Spinal nerves, which connect the spinal cord to the PNS, exit from the spinal cord between vertebrae (Figure **6.5.8**).

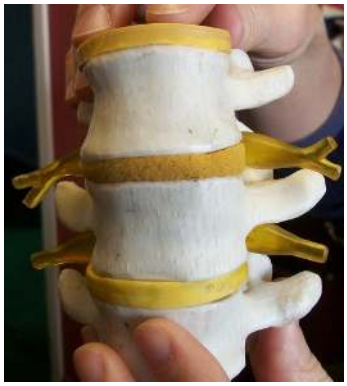


Figure **6.5.8**: This model shows three vertebrae (white) with branching spinal nerves (yellow) emerging from either side of the spinal cord between vertebrae

FUNCTIONS OF THE SPINAL CORD

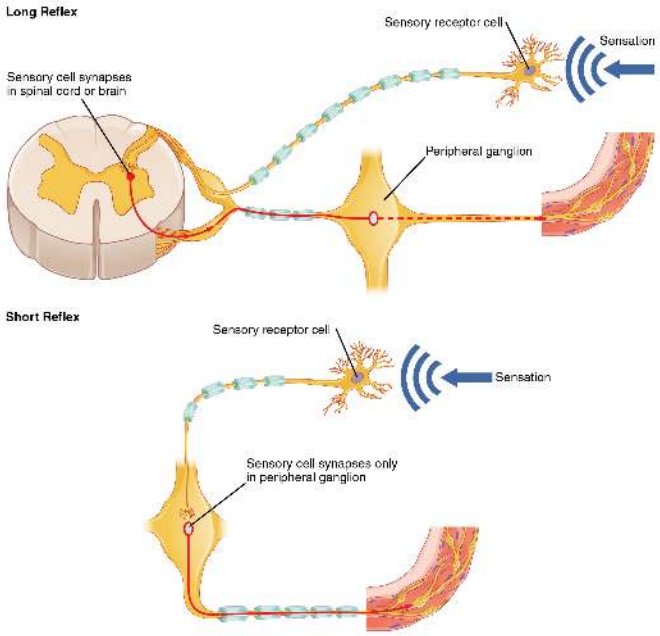


Figure **6.5.9**: This diagram shows what happens in a long reflex (top), in which sensory nerves carry the message all the way to the spinal cord; and in a short reflex (bottom), in which sensory nerves travel only to a ganglion outside the spinal cord. Note that interneurons are involved in reflexes, connecting sensory and motor neurons, but they are not actually shown in the diagram.

The spinal cord serves as an information superhighway. It passes messages from the body to the brain and from the brain to the body. Sensory (afferent) nerves carry nerve impulses to the brain from sensory receptor cells everywhere in and on the body. Motor (efferent) nerves carry nerve impulses away from the brain to glands, organs, or muscles throughout the body.

The spinal cord also independently controls certain rapid responses called **reflexes** without any input from the brain. You can see how this may happen in Figure **6.5.9**. A sensory receptor responds to a sensation and sends a nerve impulse along a sensory nerve to the spinal cord. In the spinal cord, the message passes to an interneuron and from the interneuron to a motor nerve, which carries the impulse to a muscle. The muscle contracts in response. These neuron connections form a reflex arc, which requires no input from the brain. No doubt you have experienced such reflex actions yourself. For example, you may have reached out to touch a pot on the stove, not realizing that it was very hot. Virtually at the same moment that you feel the burning heat, you jerk your arm back and remove your hand from the pot.

INJURIES TO THE SPINAL CORD

Physical damage to the spinal cord may result in **paralysis,** which is a loss of sensation and movement in part of the body. Paralysis generally affects all the areas of the body below the level of the injury because nerve impulses are interrupted and can no longer travel back and forth between the brain and body beyond that point. If an injury to the spinal cord produces nothing more than swelling, the symptoms may be transient. However, if nerve fibers (axons) in

the spinal cord are badly damaged, the loss of function may be permanent. Experimental studies have shown that spinal nerve fibers attempt to regrow, but tissue destruction usually produces scar tissue that cannot be penetrated by the regrowing nerves, as well as other factors that inhibit nerve fiber regrowth in the central nervous system.

FEATURE: MY HUMAN BODY

Each year, many millions of people have a stroke, and stroke is the second leading cause of death in adults. **Stroke,** also known as cerebrovascular accident, occurs when poor blood flow to the brain results in the death of brain cells. There are two main types of strokes:

- Ischemic strokes occur due to a lack of blood flow because of a blood clot in an artery going to the brain.
- Hemorrhagic strokes occur due to bleeding from a broken blood vessel in the brain.

Either type of stroke may result in paralysis, loss of the ability to speak or comprehend speech, loss of bladder control, personality changes, and many other potential effects, depending on the part of the brain that is injured. The effects of a stroke may be mild and transient or more severe and permanent. A stroke may even be fatal. It generally depends on the type of stroke and how extensive it is.

Are you at risk of stroke? The main risk factor for stroke is age: about two-thirds of strokes occur in people over the age of 65. There is nothing you can do about your age, but most other stroke risk factors can be reduced with lifestyle changes or medications. The risk factors include high blood pressure, tobacco smoking, obesity, high blood cholesterol, diabetes mellitus, and atrial fibrillation.

Chances are good that you or someone you know is at risk of a stroke, so it is important to recognize a stroke if one occurs. Stoke is a medical emergency, and the more quickly treatment is given, the better the outcome is likely to be. In the case of ischemic strokes, the use of clot-busting drugs may prevent permanent brain damage if administered within 3 or 4 hours of the stroke. Remembering the signs of a stroke is easy.

They are summed up by the acronym FAST, as explained in the chart below.



Figure **6.5.10**: The signs of stroke are abbreviated as FAST. Where F, A, S, and T stand for droopy face, arm weakness, slurry speech, and time to call 911, respectively.

REVIEW

1. What is the central nervous system?
2. How is the central nervous system protected?
3. What is the overall function of the brain?
4. Identify the three main parts of the brain and one function of each part.
5. Describe the hemispheres of the brain.
6. Explain and give examples of lateralization of the brain.
7. Identify one function of each of the four lobes of the cerebrum.
8. Summarize the structure and function of the cerebral cortex.
9. Explain how the hypothalamus controls the endocrine system.
10. Describe the spinal cord.
11. What is the main function of the spinal cord?
12. Explain how reflex actions occur.
13. Why do severe spinal cord injuries usually cause paralysis?
14. What do you think are some possible consequences of severe damage to the brain stem? How might this compare to the consequences of severe damage to the frontal lobe? Explain your answer.
15. Information travels very quickly in the nervous system, but generally, the longer the path between areas, the longer it takes. Based on this, explain why you think reflexes often occur at the spinal cord level and do not require input from the brain.

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6.6: PERIPHERAL NERVOUS SYSTEM

ONE PIANO, FOUR HANDS

Did you ever see two people play the same piano? How do they coordinate all the movements of their own fingers, let alone synchronize them with those of their partner? The peripheral nervous system plays an important part in this challenge.



Figure **6.6.1**: Two people playing piano together

WHAT IS THE PERIPHERAL NERVOUS SYSTEM?

The *peripheral nervous system (PNS)* consists of all the nervous tissue that lies outside of the central nervous system (CNS). The main function of the PNS is to connect the CNS to the rest of the organism. It serves as a communication relay, going back and forth between the CNS and muscles, organs, and glands throughout the body.

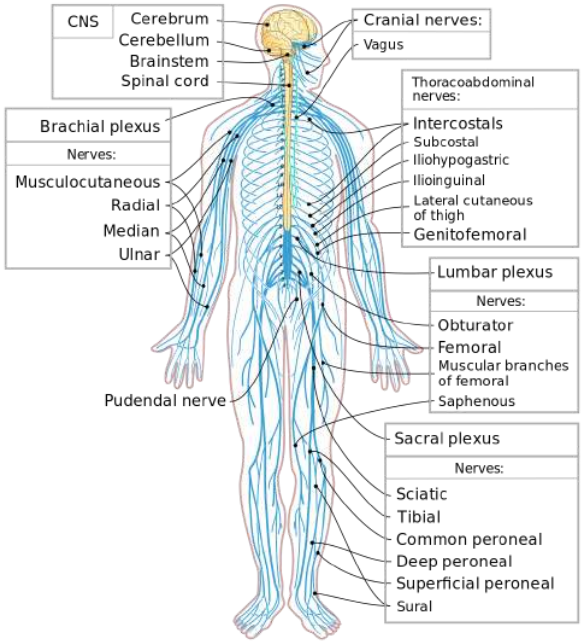


Figure **6.6.2**: The nerves of the peripheral nervous system are shown in blue in this figure.

TISSUES OF THE PERIPHERAL NERVOUS SYSTEM

The tissues that make up the PNS are nerves and ganglia. Ganglia are nervous tissues that act as relay points for messages transmitted through nerves of the PNS. Nerves are cable-like bundles of axons that make up the majority of PNS tissues. Nerves are generally classified on the basis of the direction in which they carry nerve impulses as sensory, motor, or mixed nerves. See examples of sensory and motor never in Figure **6.6.3**.

- **Sensory nerves** transmit information from sensory receptors in the body to the CNS. Sensory nerves are also called afferent nerves.
- **Motor nerves** transmit information from the CNS to muscles, organs, and glands. Motor nerves are also called efferent nerves.
- **Mixed nerves** contain both sensory and motor neurons, so they can transmit information in both directions. They have both afferent and efferent functions.

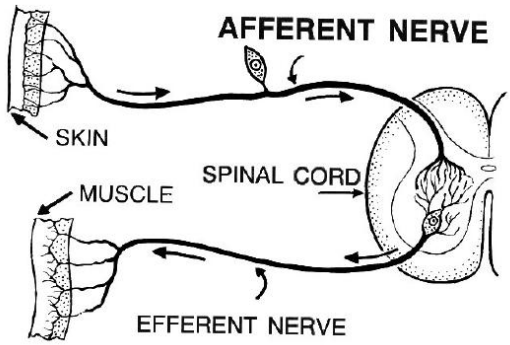


Figure **6.6.3**: An afferent nerve is a sensory nerve. The one pictured here sends nerve impulses from sensory cells in the skin to the CNS. An efferent nerve is a motor nerve. This one sends nerve impulses from the CNS to a muscle.

DIVISIONS OF THE PERIPHERAL NERVOUS SYSTEM

The PNS is divided into two major systems, called the autonomic nervous system and the somatic (or sensory-somatic) nervous system. Both systems of the PNS interact with the CNS and include sensory and motor neurons, but they use different circuits of nerves and ganglia.

SOMATIC NERVOUS SYSTEM

The **somatic nervous system** primarily senses the external environment and controls voluntary activities in which decisions and commands come from the cerebral cortex of the brain. For example, when you feel too warm, decide to turn on the air conditioner, and walk across the room to the thermostat, you are using your somatic nervous system. In general, the somatic nervous system is responsible for all of your conscious perceptions of the outside world and all of the voluntary motor activities you perform in response. Whether it's playing piano, driving a car, or playing basketball, you can thank your somatic nervous system for making it possible.

Structurally, the somatic nervous system consists of 12 pairs of cranial nerves and 31 pairs of spinal nerves (Figure **6.6.2**). Cranial nerves are in the head and neck and connect directly to the brain. Sensory cranial nerves sense smells, tastes, light, sounds, and body position. Motor cranial nerves control muscles of the face, tongue, eyeballs, throat, head, and shoulders. The motor nerves also control the salivary glands and swallowing. Four of the 12 cranial nerves participate in both sensory and motor functions as mixed nerves, having both sensory and motor neurons.

Spinal nerves of the somatic nervous system emanate from the spinal column between vertebrae. All of the spinal nerves are mixed nerves, containing both sensory and motor neurons. Spinal nerves also include motor nerves that stimulate skeletal muscle contraction, allowing for voluntary body movements.

AUTONOMIC NERVOUS SYSTEM

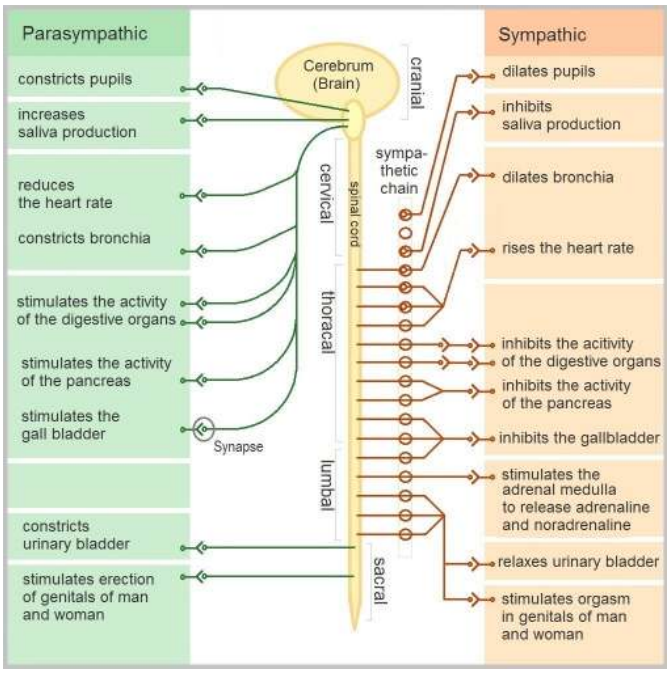


Figure **6.6.4**: This diagram summarizes the structures and functions controlled by the parasympathetic and sympathetic divisions of the autonomic nervous system. The images explained how eyes, salivary gland, bronchi, heart rate, digestive system, bladder, and genitalia are affected in opposite ways by the two systems.

The **autonomic nervous system** primarily senses the internal environment and controls involuntary activities. It is responsible for monitoring conditions in the internal environment and bringing about appropriate changes in them. In general, the autonomic nervous system is responsible for all the activities that go on inside your body without your conscious awareness or voluntary participation.

Structurally, the autonomic nervous system consists of sensory and motor nerves that run between the CNS (especially the hypothalamus in the brain) and internal organs (such as the heart, lungs, and digestive organs) and glands (such as the pancreas and sweat glands). Sensory neurons in the autonomic system detect internal body conditions and send messages to the brain. Motor nerves in the autonomic system function by controlling the contractions of smooth or cardiac muscle or glandular tissue. For example, when sensory nerves of the autonomic system detect a rise in body temperature, motor nerves signal smooth muscles in blood vessels near the body surface to undergo vasodilation, and the sweat glands in the skin secrete more sweat to cool the body.

The autonomic nervous system, in turn, has two subdivisions: the sympathetic division and parasympathetic division. The two subdivisions of the autonomic system are summarized in Figure **6.6.4**. Both affect the same organs and glands, but they generally do so in opposite ways.

- The **sympathetic division** controls the fight-or-flight response. Changes occur in organs and glands throughout the body that prepare the body to fight or flee in response to a perceived danger. For example, the heart rate speeds up, air passages in the

lungs become wider, more blood flows to the skeletal muscles, and the digestive system temporarily shuts down.

- The **parasympathetic division** returns the body to normal after the fight-or-flight response has occurred. For example, it slows down the heart rate, narrows air passages in the lungs, reduces blood flow to the skeletal muscles, and stimulates the digestive system to start working again. The parasympathetic division also maintains the internal homeostasis of the body at other times.

DISORDERS OF THE PERIPHERAL NERVOUS SYSTEM

Unlike the CNS, which is protected by bones, meninges, and cerebrospinal fluid, the PNS has no such protections. The PNS also has no blood-brain barrier to protect it from toxins and pathogens in the blood. Therefore, the PNS is more subject to injury and disease than is the CNS. Causes of nerve injury include diabetes, infectious diseases such as shingles, and poisoning by toxins such as heavy metals. Disorders of the PNS often have symptoms such as loss of feeling, tingling, burning sensations, or muscle weakness. If a traumatic injury results in a nerve being transacted (cut all the way through), it may regenerate, but this is a very slow process and may take many months.

REVIEW

1. Describe the general structure of the peripheral nervous system, and state its primary function.
2. What are ganglia?
3. Identify three types of nerves based on the direction in which they carry nerve impulses.
4. Outline all of the divisions of the peripheral nervous system.
5. Compare and contrast the somatic and autonomic nervous systems.
6. When and how does the sympathetic division of the autonomic nervous system affect the body?
7. What is the function of the parasympathetic division of the autonomic nervous system? What specific effects does it have on the body?
8. Name and describe two disorders of the peripheral nervous system.
9. Give one example of how the CNS interacts with the PNS to control a function in the body.
10. For each of the following types of information, identify whether the neuron carrying it is sensory or motor and whether it is most likely in the somatic or autonomic nervous system.
    A. Visual information
    B. Blood pressure information
    C. Information that causes muscle contraction in digestive organs after eating
    D. Information that causes muscle contraction in skeletal muscles based on the person's decision to make a movement
11. The cranial nerves:
    A. Carry sensory information
    B. Carry motor information
    C. Are part of the somatic nervous system
    D. All of the above
12. *True or False.* All of the spinal nerves carry both sensory and motor information.
13. *True or False.* The sympathetic nervous system enhances digestion to provide more energy for the body.

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6.7: CASE STUDY CONCLUSION- MEMORY AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: FADING MEMORY

Figure **6.7.1** illustrates some of the molecular and cellular changes that occur in **Alzheimer's disease** (AD), which Rosa was diagnosed with at the beginning of this chapter, after experiencing memory problems and other changes in her cognitive functioning, mood, and personality. These abnormal changes in the brain include the development of amyloid plaques between brain cells and neurofibrillary tangles inside of neurons. These hallmark characteristics of AD are associated with the loss of synapses between neurons, and ultimately the death of neurons.

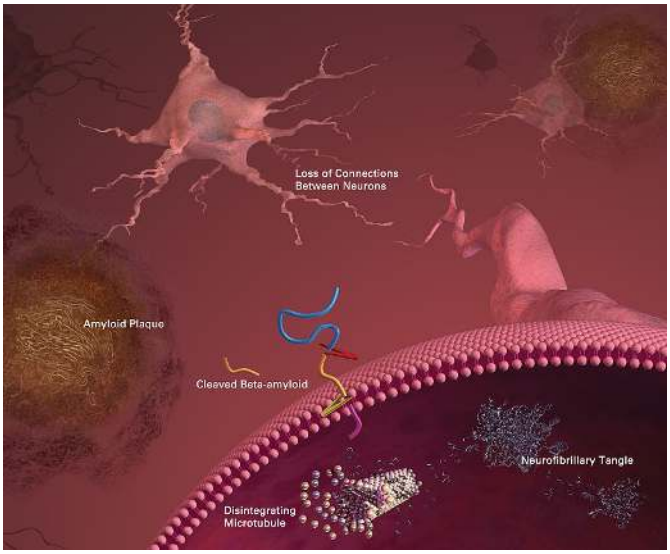


Figure **6.7.1**: Characteristics of Alzheimer's disease. On a microscopic level, some of the changes that happen are depicted above. For example, the neurons lose connections, plaque accumulates, microtubes disintegrate, and much more.

After reading this chapter, you should have a good appreciation for the importance of keeping neurons alive and communicating with each other at synapses. The nervous system coordinates all of the body's voluntary and involuntary activities. It interprets information from the outside world through sensory systems and makes appropriate responses through the motor system, through communication between the PNS and CNS. The brain directs the rest of the nervous system and controls everything from basic vital functions such as heart rate and breathing to high-level functions such as problem-solving and abstract thought. The nervous system is able to perform these important functions by generating action potentials in neurons in response to stimulation and sending messages between cells at synapses, typically using chemical neurotransmitter molecules. When neurons are not functioning properly, lose their synapses, or die, they cannot carry out the signaling that is essential for the proper functioning of the nervous system.

AD is a progressive neurodegenerative disease, meaning that the damage to the brain becomes more extensive as time goes on. Figure **6.7.2** illustrates how the damage progresses from before AD is diagnosed (preclinical AD), to mild and moderate AD, and finally to severe AD.

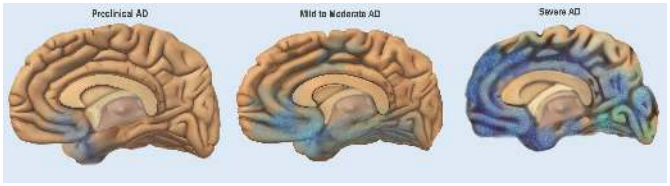


Figure **6.7.2**: Illustration showing the areas of the brain that become damaged as Alzheimer's disease (AD) progresses. This is a side view along the middle of the brain, with the front of the brain shown to the left. Damaged are (blue shade) is widespread in severe AD.

You can see that the damage starts in a relatively small location towards the bottom of the brain. One of the earliest brain areas to be affected by AD is the hippocampus. The hippocampus is important for learning and memory. This explains why many of Rosa's symptoms of mild AD involve deficits in memory, such as trouble remembering where she placed objects, recent conversations, and appointments.

As AD progresses, more of the brain is affected, including areas involved in emotional regulation, social behavior, planning, language, spatial navigation, and higher-level thought. Rosa is beginning to show signs of problems in these areas, including irritability, lashing out at family members, getting lost in her neighborhood, problems finding the right words, putting objects in unusual locations, and difficulty in managing her finances. You can see that as AD progresses, damage spreads further across the cerebrum, which you now know controls conscious functions such as reasoning, language, and interpretation of sensory stimuli. You can also see how the frontal lobe, which controls executive functions such as planning, self-control, and abstract thought, becomes increasingly damaged.

Increasing damage to the brain causes corresponding deficits in functioning. In moderate AD, patients have increased memory, language, and cognitive deficits compared to mild AD. They may not recognize their own family members, and may wander and get lost, engage in inappropriate behaviors, become easily agitated, and have trouble carrying out daily activities such as dressing. In severe AD, much of the brain is affected. Patients usually cannot recognize family members or communicate and are fully dependent on others for their care. They begin to lose the ability to control their basic functions, such as bladder and bowel control and proper swallowing. Eventually, AD causes death, usually as a result of this loss of basic functions.

For now, Rosa only has mild AD is still able to function relatively well with care from her family. The medication her doctor gave her has helped improve some of her symptoms. It is a cholinesterase inhibitor, which blocks an enzyme that normally degrades the neurotransmitter acetylcholine. With more of the neurotransmitter available, more of it can bind to neurotransmitter receptors on postsynaptic cells. Therefore, this drug acts as an agonist for

acetylcholine, which enhances communication between neurons in Rosa's brain. This increase in neuronal communication can help restore some of the functions lost in early Alzheimer's disease and may slow the progression of symptoms.

But medication such as this is only a short-term measure and does not halt the progression of the underlying disease. Ideally, the damaged or dead neurons would be replaced by new, functioning neurons. Why does this not happen automatically in the body? As you have learned, neurogenesis is very limited in adult humans, so once neurons in the brain die, they are not normally replaced to any significant extent. However, scientists are studying the ways in which neurogenesis might be able to be increased in cases of disease or injury to the brain. Also, they are investigating the possibility of using stem cell transplants to replace damaged or dead neurons with new neurons. But this research is in very early stages and is not currently a treatment for AD.

One promising area of research is in the development of methods to allow earlier detection and treatment of AD, given that the changes in the brain may actually start 10 to 20 years before the diagnosis of AD. For example, a radiolabeled chemical called Pittsburgh Compound B (PiB) binds to amyloid plaques in the brain and in the future may be used in conjunction with brain imaging techniques to detect early signs of AD. Scientists are also looking for biomarkers in bodily fluids such as blood and cerebrospinal fluid that might indicate the presence of AD before symptoms appear. Finally, researchers are also investigating possible early and subtle symptoms, such as changes in how people move or a loss of smell, to see whether they can be used to identify people who will go on to develop AD. This research is in the early stages, but the hope is that patients can be identified earlier to provide earlier and possibly more effective treatment and to allow families more time to plan.

Scientists are also still trying to fully understand the causes of AD, which affects more than 5 million Americans. Some genetic mutations have been identified that play a role, but environmental factors also appear to be important. With more research into the causes and mechanisms of AD, hopefully, a cure can be found, and people like Rosa can live a longer and better life.

CHAPTER SUMMARY

In this chapter, you learned about the human nervous system. Specifically, you learned that:

- The nervous system is the organ system that coordinates all of the body's voluntary and involuntary actions by transmitting signals to and from different parts of the body. It has two major divisions, the central nervous system (CNS) and the peripheral nervous system (PNS).
- The CNS includes the brain and spinal cord.
- The PNS consists mainly of nerves that connect the CNS with the rest of the body. It has two major divisions: the somatic nervous system and the autonomic nervous system. The somatic system controls activities that are under voluntary control. The autonomic system controls activities that are involuntary.
- The autonomic nervous system is further divided into the sympathetic division, which controls the fight-or-flight response; the parasympathetic division, which controls most routine involuntary responses; and the enteric division, which provides local control for digestive processes.
- Signals sent by the nervous system are electrical signals called nerve impulses. They are transmitted by special, electrically excitable cells called neurons, which are one of two major types of cells in the nervous system.
- Glial cells are the other major type of nervous system cells. There are many types of glial cells, and they have many specific functions. In general, glial cells function to support, protect, and nourish neurons.
- The main parts of a neuron include the cell body, dendrites, and axon. The cell body contains the nucleus. Dendrites receive nerve impulses from other cells, and the axon transmits nerve impulses to other cells at axon terminals. A synapse is a complex membrane junction at the end of an axon terminal that transmits signals to another cell.
- Axons are often wrapped in an electrically-insulating myelin sheath, which is produced by glial cells. Electrical impulses called action potentials occur at gaps in the myelin sheath, called nodes of Ranvier, which speeds the conduction of nerve impulses down the axon.
- Neurogenesis, or the formation of new neurons by cell division, may occur in a mature human brain but only to a limited extent.
- The nervous tissue in the brain and spinal cord consists of gray matter, which contains mainly the cell bodies of neurons; and white matter, which contains mainly myelinated axons of neurons. Nerves of the peripheral nervous system consist of long bundles of myelinated axons that extend throughout the body.
- There are hundreds of types of neurons in the human nervous system, but many can be classified on the basis of the direction in which they carry nerve impulses. Sensory neurons carry nerve impulses away from the body and toward the central nervous system, motor neurons carry them away from the central nervous system and toward the body, and interneurons often carry them between sensory and motor neurons.
- A nerve impulse is an electrical phenomenon that occurs because of a difference in electrical charge across the plasma membrane of a neuron.
- The sodium-potassium pump maintains an electrical gradient across the plasma membrane of a neuron when it is not actively transmitting a nerve impulse. This gradient is called the resting potential of the neuron.
- An action potential is a sudden reversal of the electrical gradient across the plasma membrane of a resting neuron. It begins when the neuron receives a chemical signal from another cell or some other type of stimulus. The action potential travels rapidly down the neuron's axon as an electric current.
- A nerve impulse is transmitted to another cell at either an electrical or a chemical synapse. At a chemical synapse, neurotransmitter chemicals are released from the presynaptic cell

into the synaptic cleft between cells. The chemicals travel across the cleft to the postsynaptic cell and bind to receptors embedded in its membrane.

- There are many different types of neurotransmitters. Their effects on the postsynaptic cell generally depend on the type of receptor they bind to. The effects may be excitatory, inhibitory, or modulatory in more complex ways. Both physical and mental disorders may occur if there are problems with neurotransmitters or their receptors.
- The CNS includes the brain and spinal cord. It is physically protected by bones, meninges, and cerebrospinal fluid. It is chemically protected by the blood-brain barrier.
- The brain is the control center of the nervous system and of the entire organism. The brain uses a relatively large proportion of the body's energy, primarily in the form of glucose.
- The brain is divided into three major parts, each with different functions: brain stem, cerebellum, and cerebrum. The cerebrum is further divided into left and right hemispheres. Each hemisphere has four lobes: frontal, parietal, temporal, and occipital. Each lobe is associated with specific senses or other functions.
- The cerebrum has a thin outer layer called the cerebral cortex. Its many folds give it a large surface area. This is where most information processing takes place.
- Inner structures of the brain include the hypothalamus, which controls the endocrine system via the pituitary gland; and the thalamus, which has several involuntary functions.
- The spinal cord is a tubular bundle of nervous tissues that extends from the head down the middle of the back to the pelvis. It functions mainly to connect the brain with the PNS. It also controls certain rapid responses called reflexes without input from the brain.
- A spinal cord injury may lead to paralysis (loss of sensation and movement) of the body below the level of the injury because nerve impulses can no longer travel up and down the spinal cord beyond that point.
- The PNS consists of all the nervous tissue that lies outside of the CNS. Its main function is to connect the CNS to the rest of the organism.
- The tissues that make up the PNS are nerves and ganglia. Ganglia act as relay points for messages that are transmitted through nerves. Nerves are classified as sensory, motor, or a mix of the two.
- The PNS is not as well protected physically or chemically as the CNS, so it is more prone to injury and disease. PNS problems include injury from diabetes, shingles, and heavy metal poisoning. Two disorders of the PNS are Guillain-Barre syndrome and Charcot-Marie-Tooth disease.
- The human body has two major types of senses, special senses, and general senses. Special senses have specialized sense organs and include vision (eyes), hearing (ears), balance (ears), taste (tongue), and smell (nasal passages). General senses are all associated with touch and lack special sense organs. Touch receptors are found throughout the body but particularly in the skin.
- All senses depend on sensory receptor cells to detect sensory stimuli and transform them into nerve impulses. Types of sensory receptors include mechanoreceptors (mechanical forces), thermoreceptors (temperature), nociceptors (pain), photoreceptors (light), and chemoreceptors (chemicals).
- Touch includes the ability to sense pressure, vibration, temperature, pain, and other tactile stimuli. The skin includes several different types of touch receptor cells.
- Vision is the ability to sense light and see. The eye is the special sensory organ that collects and focuses light, forms images, and changes them to nerve impulses. Optic nerves send information from the eyes to the brain, which processes the visual information and "tells" us what we are seeing.
- Common vision problems include myopia (nearsightedness), hyperopia (farsightedness), and presbyopia (age-related decline in close vision).
- Hearing is the ability to sense sound waves, and the ear is the organ that senses sound. It changes sound waves to vibrations that trigger nerve impulses, which travel to the brain through the auditory nerve. The brain processes the information and "tells" us what we are hearing.
- The ear is also the organ that is responsible for the sense of balance, which is the ability to sense and maintain an appropriate body position. The ears send impulses on head position to the brain, which sends messages to skeletal muscle via the peripheral nervous system. The muscles respond by contracting to maintain balance.
- Taste and smell are both abilities to sense chemicals. Taste receptors in taste buds on the tongue sense chemicals in food and olfactory receptors in the nasal passages sense chemicals in the air. The sense of smell contributes significantly to the sense of taste.
- Psychoactive drugs are substances that change the function of the brain and result in alterations of mood, thinking, perception, and/or behavior. They include prescription medications such as opioid painkillers, legal substances such as nicotine and alcohol, and illegal drugs such as LSD and heroin.
- Psychoactive drugs are divided into different classes according to their pharmacological effects. They include stimulants, depressants, anxiolytics, euphoriants, hallucinogens, and empathogens. Many psychoactive drugs have multiple effects so they may be placed in more than one class.
- Psychoactive drugs generally produce their effects by affecting brain chemistry. Generally, they act either as agonists, which enhance the activity of particular neurotransmitters; or as antagonists, which decrease the activity of particular neurotransmitters.
- Psychoactive drugs are used for various purposes, including medical, ritual, and recreational purposes.
- Misuse of psychoactive drugs may lead to addiction, which is the compulsive use of a drug despite negative consequences.

Sustained use of an addictive drug may produce physical or psychological dependence on the drug. Rehabilitation typically involves psychotherapy and sometimes the temporary use of other psychoactive drugs.

In addition to the nervous system, there is another system of the body that is important for coordinating and regulating many different functions – the endocrine system. You will learn about the endocrine system in the next chapter.

CHAPTER SUMMARY REVIEW

1. Imagine that you decide to make a movement. To carry out this decision, a neuron in the cerebral cortex of your brain (neuron A) fires a nerve impulse that is sent to a neuron in your spinal cord (neuron B). Neuron B then sends the signal to a muscle cell, causing it to contract, resulting in movement. Answer the following questions about this pathway.
   a. Which part of the brain is neuron A located in — the cerebellum, cerebrum, or brain stem? Explain how you know.
   b. The cell body of neuron A is located in a lobe of the brain that is involved in abstract thought, problem-solving and planning. Which lobe is this?
   c. Part of neuron A travels all the way down to the spinal cord to meet neuron B. Which part of neuron A travels to the spinal cord?
   d. Neuron A forms a chemical synapse with neuron B in the spinal cord. How is the signal from neuron A transmitted to neuron B?
   e. Is neuron A in the central nervous system (CNS) or peripheral nervous system (PNS)?
   f. The axon of neuron B travels in a nerve to a skeletal muscle cell. Is the nerve part of the CNS or PNS? Is this an afferent nerve or an efferent nerve?
   g. What part of the PNS is involved in this pathway — the autonomic nervous system or the somatic nervous system? Explain your answer.
2. What are the differences between a neurotransmitter receptor and a sensory receptor?
3. Which part of a postsynaptic neuron typically receives the signals from a presynaptic neuron?
   A. The axon terminal
   B. The nodes of Ranvier
   C. The dendrites
   D. The cell body
4. *True or False.* Glial cells produce action potentials.
5. *True or False.* The spinal cord consists of white matter only.
6. *True or False.* Axons may be more than a meter long in adult humans.
7. If a person has a stroke and as a result has trouble using language correctly, which hemisphere of their brain was most likely damaged? Explain your answer.
8. The right side of the brain generally controls the which side of the body?
   A. right side
   B. left side
   C. head region
   D. trunk and leg regions
9. Electrical gradients are responsible for the resting potential and action potential in neurons. Answer the following questions about the electrical characteristics of neurons.
   a. Define what an electrical gradient is, in the context of a cell.
   b. What is responsible for maintaining the electrical gradient that results in the resting potential?
   c. Compare and contrast the resting potential and the action potential.
   d. Where along a myelinated axon does the action potential occur? Why does it happen here?
10. What does it mean that the action potential is “all-or-none?”
11. What determines whether a neurotransmitter has an excitatory or inhibitory effect? Choose the best answer.
    A. The neurotransmitter itself
    B. The specific receptor for the neurotransmitter on the postsynaptic cell
    C. The number of synaptic vesicles in the axon terminal
    D. Whether it is in a sensory neuron or a motor neuron
12. Compare and contrast Schwann cells and oligodendrocytes.
13. *True or False.* The cerebellum makes up most of the brain and is divided into four lobes.
14. *True or False.* The hypothalamus is part of the brain.
15. Which lobe of the brain processes touch information?
    A. Parietal
    B. Occipital
    C. Cochlea
    D. Temporal
16. Information about sounds is mainly sent to which lobe of the brain?
    A. Parietal
    B. Occipital
    C. Cochlea
    D. Temporal
17. Rods and cones in the retina are:
    A. Mechanoreceptors
    B. Nociceptors
    C. Photoreceptors
    D. Chemoreceptors
18. For the senses of smell and hearing, name their respective sensory receptor cells, what type of receptor cells they are, and what stimuli they detect.
19. *True or False.* Sensory information such as smell, taste, and sound, are carried to the CNS by cranial nerves.
20. *True or False.* The parasympathetic nervous system is a division of the central nervous system.

ATTRIBUTIONS

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CHAPTER OVERVIEW

7: ENDOCRINE SYSTEM

This chapter describes the endocrine system and its vital roles in communication, control, and homeostasis within the human body. The focus is on the pituitary gland, as the master gland of the endocrine system, and three other endocrine glands: the thyroid gland, adrenal glands, and pancreas. The chapter also explains the differing mechanisms of steroid and non-steroid endocrine hormones.

7.1: Case Study- Hormones and Health

7.2: Introduction to the Endocrine System

7.3: Endocrine Hormones

7.4: Pituitary Gland

7.5: Thyroid Gland

7.6: Adrenal Glands

7.7: Pancreas

7.8: Case Study Conclusion- Hormonal and Chapter Summary

Thumbnail: Thyroid and parathyroid glands. (Public Domain; NIH).

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7.1: CASE STUDY- HORMONES AND HEALTH

CASE STUDY: HORMONAL HAVOC

18-year-old Gabrielle checks her calendar. It has been 42 days since her last menstrual period, two weeks later than the length of the average woman's menstrual cycle. Although many women would suspect pregnancy if their period was late, Gabrielle has not been sexually active. She is not even sure she is "late" because her period has never been regular. Ever since her first period at 13 years of age, her cycle lengths have varied greatly, and there are months where she does not get a period at all. Her mother told her that a girl's period is often irregular when it first starts, but Gabrielle's still has not become regular five years later. She decides to go to the student health center on her college campus to get it checked out.



Figure **7.1.1**: Calendar

The doctor asks her about the timing of her menstrual periods and performs a pelvic exam. She also notices that Gabrielle is overweight, has acne, and excess facial hair. As she explains to Gabrielle, while these physical characteristics can be perfectly normal, in combination with an irregular period they can be signs of a disorder of the endocrine, or hormonal, system called polycystic ovary syndrome (PCOS).

In order to check for PCOS, the doctor refers Gabrielle for a pelvic ultrasound and sends her to the lab to get blood work done. When her lab results come back, Gabrielle learns that her levels of androgens (a group of hormones) are high, and so is her blood glucose (sugar). The ultrasound showed that she has multiple fluid-filled sacs known as cysts in her ovaries. Based on Gabrielle's symptoms and test results, the doctor tells her that she does indeed have PCOS.

PCOS is common in young women. It is estimated that between 1 in 10 to 20 women of childbearing age have PCOS — as many as five million women in the United States. You may know someone with PCOS or may have it yourself.

Read the rest of this chapter to learn about the glands and hormones of the endocrine system, their functions, how they are regulated, and the disorders — such as PCOS — that can arise when hormones are not regulated properly. At the end of the chapter, you will learn more about PCOS, its possible long-term consequences including fertility problems and diabetes, and how these negative outcomes can sometimes be prevented with lifestyle changes and medications.

CHAPTER OVERVIEW: ENDOCRINE SYSTEM

In this chapter, you will learn about the endocrine system, a system of glands that secrete hormones that regulate many of the body's functions. Specifically, you will learn about:

- The glands that make up the endocrine system and how hormones act as chemical messengers in the body.
- The general types of endocrine system disorders.
- The types of endocrine hormones, including steroid hormones such as sex hormones, and non-steroid hormones such as insulin; and how they affect the functions of their target cells by binding to different types of receptor proteins.
- How the levels of hormones are regulated mostly through negative, but sometimes through positive, feedback loops.
- The master gland of the endocrine system, the pituitary gland, controls other parts of the endocrine system through the hormones that it secretes; and how the pituitary itself is regulated by hormones secreted from the hypothalamus of the brain.
- The thyroid gland and its hormones, which regulate processes such as metabolism and calcium homeostasis; how the thyroid is regulated; and the disorders that can occur when there are problems in thyroid hormone regulation, such as hyperthyroidism and hypothyroidism.
- The adrenal glands, which secrete hormones that regulate processes such as metabolism, electrolyte balance, responses to stress, and reproductive functions; and the disorders that can occur when there are problems in adrenal hormone regulation, such as Cushing's syndrome and Addison's disease.
- The pancreas, which secretes hormones that regulate blood glucose levels such as insulin; and disorders of the pancreas and its hormones including diabetes.

As you read this chapter, think about the following questions:

1. Why can hormones have such a broad-range effect on the body, such as is seen in PCOS?
2. Which hormones normally regulate blood glucose and how is this related to diabetes?
3. What are androgens? How do you think their functions relate to some of the symptoms that Gabrielle is experiencing?

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7.2: INTRODUCTION TO THE ENDOCRINE SYSTEM

MOON FACE

The patient in Figure **7.2.1** has the characteristic moon face of a disorder named Cushing's syndrome. Other signs and symptoms of this disorder include abnormal weight gain, acne, and excessive hairiness, among many other abnormalities. What can cause so many different problems in one patient? The answer is the overproduction of the endocrine system hormone cortisol.



Figure **7.2.1**: a person with Cushing's syndrome

OVERVIEW OF THE ENDOCRINE SYSTEM

The **endocrine system** is a system of glands called **endocrine glands** that release chemical messenger molecules called hormones into the bloodstream. Other glands of the body, including sweat glands and salivary glands, also secrete substances but not into the bloodstream. Instead, they secrete them through ducts that carry them to nearby body surfaces. These other glands are called **exocrine glands.**

Endocrine hormones must travel through the bloodstream to the cells they affect, and this takes time. Because endocrine hormones are released into the bloodstream, they travel throughout the body wherever blood flows. As a result, endocrine hormones may affect many cells and have body-wide effects. Endocrine hormones may cause effects that last for days, weeks, or even months.

GLANDS OF THE ENDOCRINE SYSTEM

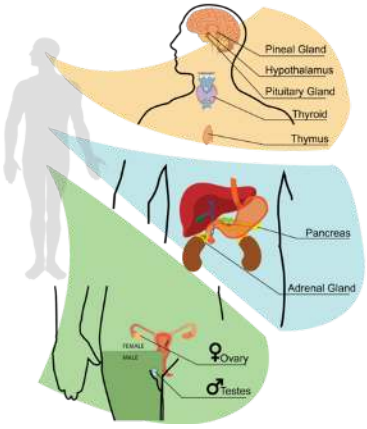


Figure **7.2.2**: Pineal gland, hypothalamus, Pituitary gland, Thyroid, Thymus, Pancreas, Adrenal gland, over and testes are part of the endocrine system. Note that the ovary and testis are the only endocrine glands that differ in males and females

The major glands of the endocrine system are shown in Figure **7.2.2**. The glands in the figure are described briefly in the rest of this section. Refer to the figure as you read about the glands in the following text.

PITUITARY GLAND

The pituitary gland is located at the base of the brain. It is controlled by the nervous system via the brain structure called the hypothalamus, to which it is connected by a thin stalk. The pituitary gland consists of two lobes, called the anterior (front) lobe and posterior (back) lobe. The posterior lobe stores and secretes hormones synthesized by the hypothalamus. The anterior lobe synthesizes and secretes its own endocrine hormones, also under the influence of the hypothalamus. One endocrine hormone secreted by the pituitary gland is growth hormone, which stimulates cells throughout the body to synthesize proteins and divide. Most of the other endocrine hormones secreted by the pituitary gland control other endocrine glands. Generally, these hormones direct the other glands to secrete either more or less of their hormones. This is why the pituitary gland is often referred to as the "master gland" of the endocrine system.

REMAINING GLANDS OF THE ENDOCRINE SYSTEM

Each of the other glands of the endocrine system is summarized below. Several of these endocrine glands are also discussed in greater detail in other concepts in the present chapter.

- The thyroid gland is a large gland in the neck. Thyroid hormones such as thyroxine increase the rate of metabolism in cells throughout the body. They control how quickly cells use energy and make proteins.
- The four parathyroid glands are located in the neck behind the thyroid gland. The parathyroid hormone helps keep the level of calcium in the blood within a narrow range. It stimulates bone cells to dissolve calcium and release it into the blood.
- The pineal gland is a tiny gland located near the center of the brain. It secretes the hormone melatonin, which controls the sleep-wake cycle and several other processes. The production of melatonin is stimulated by darkness and inhibited by light. Cells in the retina of the eye detect light and send signals to a structure in the brain named the suprachiasmatic nucleus (SCN). Nerve fibers carry the signals from the SCN to the pineal gland via the autonomic nervous system.
- The pancreas is located near the stomach. Its endocrine hormones include insulin and glucagon, which work together to control the level of glucose in the blood. The pancreas also secretes digestive enzymes into the small intestine.
- The two adrenal glands are located above the kidneys. Adrenal glands secrete several different endocrine hormones, including the hormone adrenaline, which is involved in the fight-or-flight response. Other endocrine hormones secreted by the adrenal glands have a variety of functions. For example, the hormone

aldosterone helps to regulate the balance of minerals in the body. The hormone cortisol, which causes Cushing's syndrome when it is produced in excess, is also an adrenal gland hormone.

- The gonads include the ovaries in females and testes in males. They secrete sex hormones, such as testosterone (in males) and estrogen (in females). These hormones control sexual maturation during puberty and the production of gametes (sperm or egg cells) by the gonads after sexual maturation.
- The thymus gland is located in front of the heart. It is the site where immune system cells called T cells mature. T cells are critical to the adaptive immune system, in which the body adapts to specific pathogens.

ENDOCRINE SYSTEM DISORDERS

Diseases of the endocrine system are relatively common. An endocrine system disease usually involves the secretion of too much or not enough of a hormone. When too much hormone is secreted, the condition is called **hypersecretion.** When not enough hormone is secreted, the condition is called **hyposecretion.**

HYPERSECRETION



Figure **7.2.3**: Martin Van Buren Bates

Hypersecretion by an endocrine gland is often caused by a tumor. For example, a tumor of the pituitary gland can cause hypersecretion of growth hormone. If this occurs in childhood and goes untreated, it results in very long arms and legs and abnormally tall stature by adulthood (see). This condition is commonly known as gigantism. Martin Van Buren Bates is depicted in Figure **7.2.3** standing next to a man of average size. Bates was a Civil War-era American famed for his incredibly large size. He was at least 7 feet 9 inches tall and weighed close to 500 pounds. He was normal in size at birth but started to grow very rapidly by about age 6 years, presumably because of the hypersecretion of growth hormone.

HYPOSECRETION

Hyposecretion by an endocrine gland is often caused by the destruction of the hormone-secreting cells of the gland. As a result, not enough of the hormone is secreted. An example of this is type 1 diabetes, in which the body's own immune system attacks and destroys cells of the pancreas that secrete insulin. This type of diabetes is generally treated with frequent injections of insulin.

HORMONE INSENSITIVITY

In some cases, an endocrine gland secretes a normal amount of hormone, but target cells do not respond normally to it. This may occur because target cells have become resistant to the hormone. An example of this type of endocrine disorder is Androgen Insensitivity Disorder. Individuals with this disorder are born with an X and Y chromosome but develop and raised as females. This is due to a mutation in the Androgen Receptor (AR) gene which is located on the X chromosome. Testosterone is an androgen hormone that causes testes to descend and typical male characteristics to develop. People with this form of the condition have the external sex characteristics of females but do not have a uterus and therefore do not menstruate and are unable to conceive a child (infertile). They are typically raised as females and have a female gender identity. Affected individuals have male internal sex organs (testes) that are undescended, which means they are located in the pelvis or abdomen.

REVIEW

1. What is the endocrine system? What is its general function?
2. Compare and contrast endocrine and exocrine glands.
3. How do endocrine system messages differ from those of the nervous system?
4. Describe the role of the pituitary gland in the endocrine system.
5. List three endocrine glands other than the pituitary gland, and identify their functions.
6. Which endocrine gland has an important function in the immune system? What is that function?
7. Define hypersecretion and hyposecretion.
8. Name an endocrine disorder in which too much of a hormone is produced.
9. What are two reasons people with diabetes might have signs and symptoms of inadequate insulin?
10. Choose one. Cushing's syndrome is an example of (hyposecretion/hypersecretion).
11. *True or False.* The hypothalamus is the master gland of the endocrine system.
12. *True or False.* Mammary glands that produce milk for offspring are part of the endocrine system.
13. Melatonin is produced by the:
    A. A. Pituitary gland
    B. B. Hypothalamus
    C. C. Pineal gland
    D. D. Pancreas
14. Besides location, what is the main difference between the anterior lobe of the pituitary and the posterior lobe of the pituitary?
15. Which endocrine glands differ between males and females? Which hormones do they produce?

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7.3: ENDOCRINE HORMONES

PILLS FROM PEE

The medication pictured above with the brand name Progynon was a drug used to control the effects of menopause in women. The pills first appeared in 1928 and contained the human sex hormone estrogen. Estrogen secretion declines in women around the time of menopause and may cause symptoms such as mood swings and hot flashes. The pills were supposed to ease the symptoms by supplementing estrogen in the body. The manufacturer of Progynon obtained estrogen for the pills from the urine of pregnant women because it was a cheap source of the hormone. Progynon is still used today to treat menopausal symptoms. Although the drug has been improved over the years, it still contains estrogen. Estrogen is an example of an endocrine hormone.



Figure **7.3.1**: Progynon pills bottle circa 1930 UK

HOW DO ENDOCRINE HORMONES WORK?

Endocrine hormones like estrogen are messenger molecules that are secreted by endocrine glands into the bloodstream. They travel throughout the body in the circulation. Although they reach virtually every cell in the body in this way, each hormone affects only certain cells, called target cells. A **target cell** is the type of cell on which a hormone has an effect. A target cell is affected by a particular hormone because it has receptor proteins — either on the cell surface or within the cell — that are specific to that hormone. An endocrine hormone travels through the bloodstream until it finds a target cell with a matching receptor to which it can bind. When the hormone binds to the receptor, it causes changes within the cell. The manner in which it changes the cell depends on whether the hormone is a steroid hormone or a non-steroid hormone.

STEROID HORMONES

A **steroid hormone** such as estrogen is made of lipids. It is fat soluble, so it can diffuse across a target cell's plasma membrane, which is also made of lipids. Once inside the cell, a steroid hormone binds with receptor proteins in the cytoplasm. As you can see in the diagram below, the steroid hormone and its receptor form a complex, called a steroid complex, which moves into the nucleus where it influences the expression of genes. Examples of steroid hormones include cortisol, which is secreted by the adrenal glands, and sex hormones, which are secreted by the gonads.

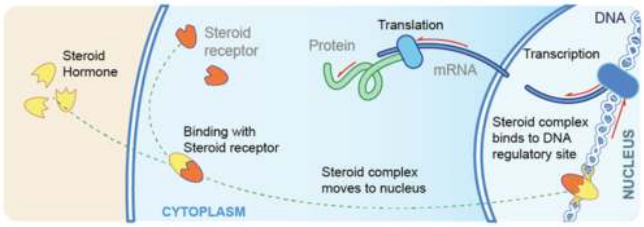


Figure **7.3.2**: A steroid hormone crosses the plasma membrane of a target cell, binds with a receptor protein within the cytoplasm, and forms a complex that moves to the nucleus where it affects gene expression.

NON-STEROID HORMONES

A **non-steroid hormone** is made of amino acids. It is not fat soluble, so it cannot diffuse across the plasma membrane of a target cell. Instead, it binds to a receptor protein on the cell membrane. In the following diagram, you can see that the binding of the hormone with the receptor activates an enzyme in the cell membrane. The enzyme then stimulates another molecule, called the second messenger, which influences processes inside the cell. Most endocrine hormones are non-steroid hormones. Examples include glucagon and insulin, both produced by the pancreas.

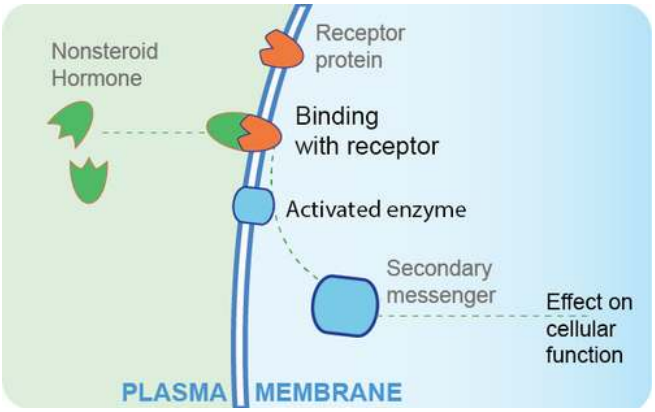


Figure **7.3.3**: A non-steroid hormone binds with a receptor protein on the plasma membrane of a target cell. This activates an enzyme, which controls a secondary messenger molecule.

REGULATION OF ENDOCRINE HORMONES

Endocrine hormones regulate many body processes, but what regulates the secretion of endocrine hormones? Most endocrine hormones are controlled by feedback mechanisms. A feedback mechanism is a loop in which a product feeds back to control its own production. Feedback loops may be either negative or positive.

- Most endocrine hormones are regulated by negative feedback loops. Negative feedback keeps the concentration of a hormone within a relatively narrow range and maintains homeostasis.
- Very few endocrine hormones are regulated by positive feedback loops. Positive feedback causes the concentration of a hormone

to become increasingly higher.

REGULATION BY NEGATIVE FEEDBACK

A negative feedback loop controls the synthesis and secretion of hormones by the thyroid gland. This loop includes the hypothalamus and pituitary gland in addition to the thyroid, as shown in Figure **7.3.4**. When the levels of thyroid hormones circulating in the blood fall too low, the hypothalamus secretes thyrotropin releasing hormone (TRH). This hormone travels directly to the pituitary gland through the thin stalk connecting the two structures. In the pituitary gland, TRH stimulates the pituitary to secrete thyroid stimulating hormone (TSH). TSH, in turn, travels through the bloodstream to the thyroid gland and stimulates it to secrete thyroid hormones. This continues until the blood levels of thyroid hormones are high enough. At that point, the thyroid hormones feedback to stop the hypothalamus from secreting TRH and the pituitary from secreting TSH. Without the stimulation of TSH, the thyroid gland stops secreting its hormones. Eventually, the levels of thyroid hormones in the blood start to fall too low again. When that happens, the hypothalamus releases TRH, and the loop repeats.

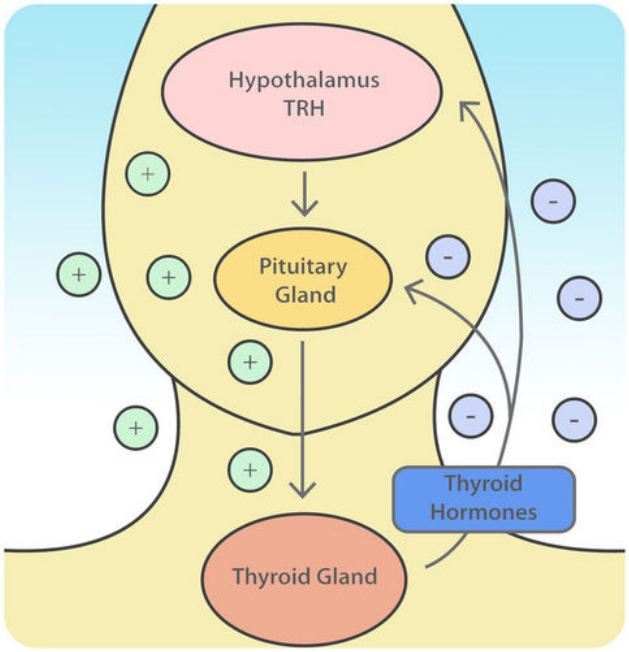


Figure **7.3.4**: This diagram shows how the thyroid gland is regulated by a negative feedback loop that also involves the hypothalamus and pituitary gland.

REGULATION BY POSITIVE FEEDBACK

Prolactin is a non-steroid endocrine hormone secreted by the pituitary gland. One of the functions of prolactin is to stimulate a nursing mother's mammary glands to produce milk. The regulation of prolactin in the mother is controlled by a positive feedback loop that involves the nipples, hypothalamus, pituitary gland, and mammary glands. Positive feedback begins when a baby suckles on the mother's nipple. Nerve impulses from the nipple reach the hypothalamus, which stimulates the pituitary gland to secrete prolactin. Prolactin travels in the blood to the mammary glands and stimulates them to produce milk. The release of milk causes the baby to continue suckling, which causes more prolactin to be secreted and more milk to be produced. The positive feedback loop continues until the baby stops suckling at the breast.

FEATURE: MYTH VS. REALITY

Anabolic steroids are synthetic versions of the naturally occurring male sex hormone testosterone. Male hormones have androgenic, or masculinizing, effects, but they also have anabolic, or muscle-building effects. The anabolic effects are the reason that synthetic steroids are used by athletes. In addition to building muscles, they also accelerate the development of bones and red blood cells, increase endurance so athletes can train harder and longer, and speed up muscle recovery. Unfortunately, these benefits of steroid use come with costs. If you ever consider taking anabolic steroids to build muscles and improve athletic performance, consider the following myths and corresponding realities.

Myth: Steroids are safe.

Reality: Steroid use may cause several serious side effects. Prolonged use may increase the risk of liver cancer, heart disease, and high blood pressure.

Myth: Steroids will not stunt your growth.

Reality: Teens who take steroids before they have finished growing in height may have their growth stunted so they remain shorter throughout life than they would otherwise have been. Such stunting occurs because steroids increase the rate at which skeletal maturity is reached. Once skeletal maturity occurs, additional growth in height is impossible.

Myth: Steroids do not cause drug dependency.

Reality: Steroid use may cause dependency as evidenced by the negative effects of stopping steroid use. These negative effects may include insomnia, fatigue, and depressed mood, among others.

Myth: There is no such thing as "roid rage."

Reality: Steroid use has been shown to increase aggressiveness in some people. It has also been implicated in a number of violent acts committed by people who had not demonstrated violent tendencies until they started using steroids.

Myth: Only males use steroids.

Reality: Although steroid use is more common in males than females, some females also use steroids. They use them to build muscle and improve physical performance, generally either for athletic competition or for self-defense.

REVIEW

1. What are endocrine hormones?
2. Define the target cell in the context of endocrine hormones.
3. Explain how steroid hormones influence target cells.
4. How do non-steroid hormones affect target cells?
5. Compare and contrast negative and positive feedback loops.

6. Outline the way feedback controls the production of thyroid hormones.
7. Describe the feedback mechanism that controls milk production by the mammary glands.
8. Why do endocrine hormones only affect some of the cells in the body? Choose the best answer.
   A. They only reach certain cells.
   B. Many hormones cannot cross the plasma membrane of cells.
   C. Some cells feedback negatively in response to a hormone.
   D. Only some cells have receptor proteins that can bind to a given hormone.
9. People with a condition called hyperthyroidism produce too much thyroid hormone. What do you think this does to the level of TSH? Explain your answer.
10. Which is more likely to maintain homeostasis — negative feedback or positive feedback? Explain your answer.
11. Does testosterone bind to receptors on the plasma membrane of target cells or in the cytoplasm of target cells? Explain your answer.
12. *True or False.* Endocrine hormones can affect the expression of genes.
13. *True or False.* Non-steroid hormones cannot affect intracellular processes.
14. *True or False.* Insulin binds to receptors on the plasma membrane of cells.
15. Which hormone is secreted by the pituitary gland?
    A. Prolactin
    B. Insulin
    C. Cortisol
    D. Thyrotropin releasing hormone

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7.4: PITUITARY GLAND

MILK ON DEMAND

This adorable nursing infant is part of a positive feedback loop. When he suckles on the nipple, it sends nerve impulses to his mother's hypothalamus, which "tell" her pituitary gland to release the hormone prolactin into her bloodstream. Prolactin travels to the mammary glands in the breasts and stimulates milk production, which motivates the infant to keep suckling.



Figure **7.4.1**: Nursing infant

WHAT IS THE PITUITARY GLAND?

The **pituitary gland** is the master gland of the endocrine system, the system of glands that secrete hormones into the bloodstream. Endocrine hormones control virtually all physiological processes. For example, they control growth, sexual maturation, reproduction, body temperature, blood pressure, and metabolism. The pituitary gland is considered the master gland of the endocrine system because it controls the rest of the endocrine system. Many pituitary hormones either promote or inhibit hormone secretion by other endocrine glands.

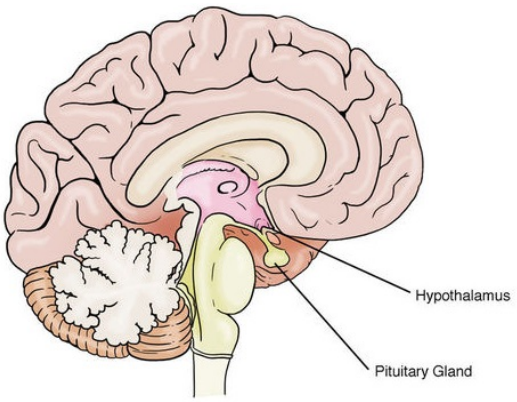


Figure **7.4.2**: The pituitary gland in the endocrine system is closely connected to the hypothalamus in the brain

STRUCTURE AND FUNCTION OF THE PITUITARY GLAND

The pituitary gland is about the size of a pea. It protrudes from the bottom of the hypothalamus at the base of the inner brain (Figure **7.4.2**). The pituitary is connected to the hypothalamus by a thin stalk (called the infundibulum). Blood vessels and nerves in the stalk allow direct connections between the hypothalamus and the pituitary gland. The pituitary gland consists of two bulb-like lobes: an anterior lobe and a posterior lobe (Figure **7.4.3**).

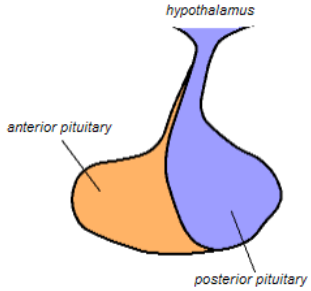


Figure **7.4.3**: Both anterior and posterior lobes of the pituitary gland are directly connected to the hypothalamus by capillaries (anterior lobe) and nerve axons (posterior lobe)

ANTERIOR LOBE

The **anterior pituitary** is at the front of the pituitary gland. It synthesizes and releases hormones into the blood. Table **7.4.1** shows some of the endocrine hormones released by the anterior pituitary, including their targets and effects.

Table **7.4.1**: Anterior Pituitary Hormones

Hormone	Target	Effect(s)
Adrenocorticotropic hormone (ACTH)	Adrenal glands	Stimulates the cortex of each adrenal gland to secrete its hormones
Thyroid-stimulating hormone (TSH)	Thyroid gland	Stimulates the thyroid gland to secrete thyroid hormone
Growth hormone (GH)	Body cells	Stimulates body cells to synthesize proteins and grow
Follicle-stimulating hormone (FSH)	Ovaries, testes	Stimulates the ovaries to develop mature eggs; stimulates the testes to produce sperm
Luteinizing hormone (LH)	Ovaries, testes	Stimulates the ovaries and testes to secrete sex hormones; stimulates the ovaries to release eggs
Prolactin (PRL)	Mammary glands	Stimulates the mammary glands to produce milk

The anterior pituitary gland is regulated mainly by hormones from the hypothalamus. The hypothalamus secretes hormones called releasing hormones and inhibiting hormones that travel through capillaries directly to the anterior lobe of the pituitary gland. The hormones stimulate the anterior pituitary to either release or stop releasing particular pituitary hormones. Several of these hypothalamic hormones and their effects on the anterior pituitary are shown in Table **7.4.2**.

Table 7.4.2: Hypothalamic Hormones and Their Effects on the Anterior Pituitary

Hypothalamic Hormone	Effect on Anterior Pituitary
Thyrotropin releasing hormone (TRH)	Release of thyroid stimulating hormone (TSH)
Corticotropin releasing hormone (CRH)	Release of adrenocorticotropic hormone (ACTH)
Gonadotropin releasing hormone (GnRH)	Release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
Growth hormone releasing hormone (GHRH)	Release of growth hormone (GH)
Growth hormone inhibiting hormone (GHIH) (Somatostatin)	Stopping of growth hormone release
Prolactin releasing hormone (PRH)	Release of prolactin
Prolactin inhibiting hormone (PIH) (Dopamine)	Stopping of prolactin release

POSTERIOR LOBE

The **posterior pituitary** is at the back of the pituitary gland. This lobe does not synthesize any hormones. Instead, the posterior lobe stores hormones that come from the hypothalamus along the axons of nerves connecting the two structures (Figure **7.4.3**). The posterior pituitary then secretes the hormones into the bloodstream as needed. Hypothalamic hormones secreted by the posterior pituitary include vasopressin and oxytocin.

- Vasopressin (also called antidiuretic hormone, or ADH) helps to maintain homeostasis in body water. It stimulates the kidneys to conserve water by producing more concentrated urine. Specifically, vasopressin targets ducts in the kidneys and makes them more permeable to water. This allows more water to be resorbed by the body rather than excreted in the urine.
- Oxytocin (OXY) targets cells in the uterus to stimulate uterine contractions, for example, during childbirth. It also targets cells in the breasts of a nursing mother to stimulate the letdown of milk.

REVIEW

1. Explain why the pituitary gland is called the master gland of the endocrine system.
2. Compare and contrast the two lobes of the pituitary gland and their general functions.
3. Identify two hormones released by the anterior pituitary, their targets, and their effects.
4. Explain how the hypothalamus influences the output of hormones by the anterior lobe of the pituitary gland.
5. Name and give the function of two hypothalamic hormones released by the posterior pituitary gland.
6. *True or False.* The pituitary gland only secretes hormones that are involved in reproduction.
7. *True or False.* The brain does not produce hormones, only glands produce hormones.
8. If a releasing hormone is secreted from the hypothalamus to the pituitary gland, which part of the pituitary receives it? Explain your answer.
9. Answer the following questions about prolactin releasing hormone (PRH) and prolactin inhibiting hormone (PIH).
   A. Where are these hormones produced?
   B. Where are their target cells located?
   C. What are their effects on their target cells?
   D. What are their ultimate effects on milk production? Explain your answer.
10. e. When a baby nurses, which of these hormones is most likely released in the mother? Explain your answer.
11. For each of the following hormones, state whether it is synthesized in the pituitary or the hypothalamus.
    A. Gonadotropin releasing hormone (GnRH)
    B. Growth hormone (GH)
    C. Oxytocin
12. d. Adrenocorticotropic hormone (ACTH)

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7.5: THYROID GLAND

TOO MUCH OF A GOOD THING

The individual in Figure **7.5.1** has a goiter. A **goiter** is an abnormal enlargement of the thyroid gland, which is located in the neck. The formation of a goiter may occur in a number of different thyroid disorders. You'll learn why in this concept.



Figure **7.5.1**: Goiter

THYROID STRUCTURE

The **thyroid gland** is one of the largest endocrine glands in the body. It is located in the front of the neck below Adam's apple (see Figure **7.5.2**). The gland is butterfly-shaped and composed of two lobes. The lobes are connected by a narrow band of thyroid tissue called an isthmus.

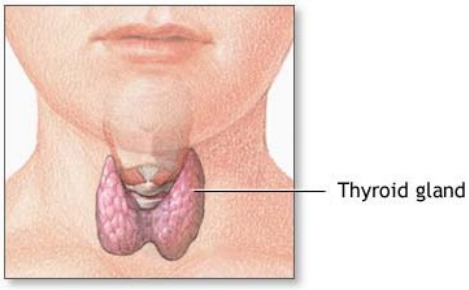


Figure **7.5.2**: The thyroid gland is a two-lobed gland in the front of the neck

Internally, the thyroid gland is composed mainly of follicles. A **follicle** is a small cluster of cells surrounding a central cavity, which stores hormones and other molecules made by the follicular cells. Thyroid follicular cells are unique in being highly specialized to absorb and use iodine. They absorb iodine as iodide ions (I^-) from the blood and use the iodide to produce thyroid hormones. The cells also use some of the iodide they absorb to form a protein called thyroglobulin, which serves to store iodide for later hormone synthesis. The outer layer of cells of each follicle secretes thyroid hormones as needed. Scattered among the follicles are another type of thyroid cells, called parafollicular cells (or C cells). These cells synthesize and secrete the hormone calcitonin.

FUNCTIONS OF THE THYROID

Like all endocrine glands, the function of the thyroid is to synthesize hormones and secrete them into the bloodstream. Once in the blood, they can travel to cells throughout the body and influence their functions.

THYROID HORMONES: T4 AND T3

There are two main thyroid hormones produced by the follicles: **thyroxine (T4),** which contains four iodide ions and is represented by the structural diagram below; and **triiodothyronine (T3),** which contains three iodide ions. T3 is much more powerful than T4, but T4 makes up about 90 percent of circulating thyroid hormone, and T3 makes up only about 10 percent. However, most of the T4 is converted to T3 by target tissues.

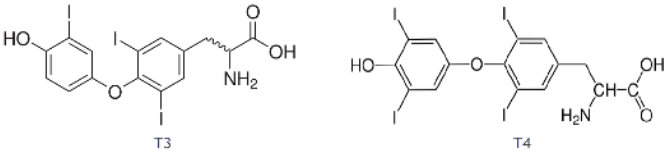


Figure **7.5.3**: This structural model represents a single molecule of triiodothyronine (T3) and thyroxine (T4). The letter I represents the iodide ions they contain. The rings consist mainly of carbon atoms

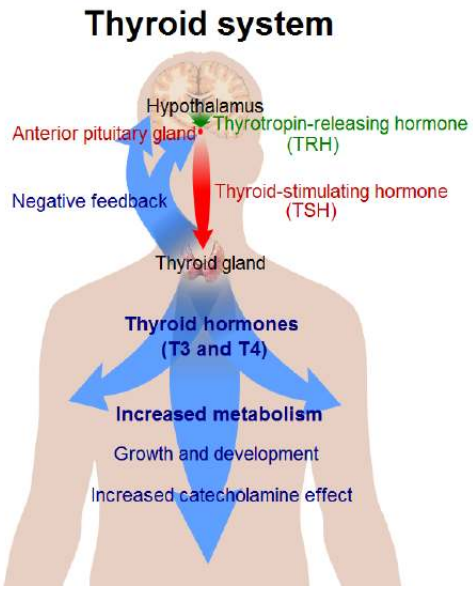


Figure **7.5.4**: The thyroid system is a negative feedback loop that includes the hypothalamus, pituitary gland, and thyroid gland. As this diagram shows, thyroid hormones increase the effect of catecholamines such as adrenaline, a fight-or-flight hormone

Like steroid hormones, T3 and T4 cross cell membranes everywhere in the body and bind to intracellular receptors to regulate gene expression. However, unlike steroid hormones, thyroid hormones can cross cell membranes only with the help of special transporter proteins. Once inside the nucleus of cells, T3 and T4 turn on genes that control protein synthesis. Thyroid hormones increase the rate of metabolism in cells, so cells absorb more carbohydrates, use more energy, and produce more heat. Thyroid hormones also increase the

rate and force of the heartbeat. In addition, they increase the sensitivity of cells to fight-or-flight hormones (that is, catecholamine hormones such as adrenaline).

The production of both T4 and T3 is regulated primarily by thyroid stimulating hormone (TSH), which is secreted by the anterior pituitary gland (see the diagram below). TSH production, in turn, is regulated by thyrotropin releasing hormone (TRH), which is produced by the hypothalamus. The thyroid gland, pituitary gland, and hypothalamus form a negative feedback loop to keep thyroid hormone secretion within a normal range. TRH and TSH production is suppressed when T4 levels start to become too high. The opposite occurs when T4 levels start to become too low.

CALCITONIN

The **calcitonin** produced by the parafollicular cells of the thyroid gland has the role of helping to regulate blood calcium levels by stimulating the movement of calcium into bone. Calcitonin is secreted in response to rising blood calcium levels. It decreases blood calcium levels by enhancing calcium absorption and deposition in bone. Calcitonin works hand-in-hand with parathyroid hormone, which is secreted by the parathyroid glands and has the opposite effects as calcitonin. Together, these two hormones maintain calcium homeostasis.

THYROID DISORDERS

As with other endocrine disorders, thyroid disorders are generally associated with either over or under-secretion of hormones. Abnormal secretion of thyroid hormones may occur for a variety of reasons.

HYPERTHYROIDISM

Hyperthyroidism occurs when the thyroid gland produces excessive amounts of thyroid hormones. The most common cause of hyperthyroidism is Graves' disease. **Graves' disease** is an autoimmune disorder in which abnormal antibodies produced by the immune system stimulate the thyroid to secrete excessive quantities of its hormones. This stimulation overrides the usual negative feedback mechanism that normally controls thyroid hormone output. Graves' disease often results in the formation of an enlarged thyroid (goiter) because of the continued stimulation to produce more hormones.

Besides a goiter, other signs and symptoms of hyperthyroidism may include protruding eyes (see photo below), heart palpitations, excessive sweating, diarrhea, weight loss despite increased appetite, muscle weakness, and unusual sensitivity to heat. Medications can be prescribed to mitigate the symptoms of the disease. Anti-thyroid drugs can also be given to decrease the production of thyroid hormones. If the drugs are ineffective, the gland can be partially or entirely removed. This can be done surgically or with the administration of radioactive iodine. Removal of the thyroid produces hypothyroidism.

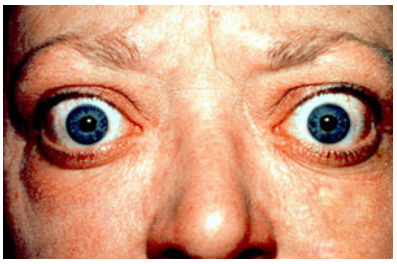


Figure **7.5.5**: Protruding eyes are one sign of hyperthyroidism, such as Graves' disease

HYPOTHYROIDISM

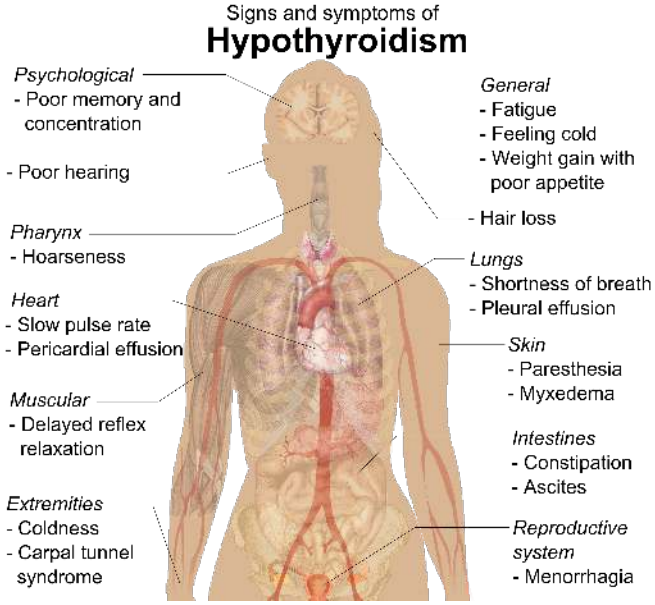


Figure **7.5.6**: the signs and symptoms of hypothyroidism may include fatigue, coldness, weight gain, shortness of breath, constipation, menorrhagia, poor memory and hearing, hoarseness, slow heart rate, delayed reflexes, and carpal tunnel syndrome.

Hypothyroidism occurs when the thyroid gland produces insufficient amounts of thyroid hormones. It can result from surgical removal of the thyroid. However, worldwide, the most common cause of hypothyroidism is dietary iodine deficiency. In cases of iodine deficiency, the negative feedback loop controlling the release of thyroid hormone causes repeated stimulation of the thyroid. This results in the thyroid gland growing in size and producing a goiter. Although the gland gets larger, it cannot increase hormone output because of the lack of iodine in the diet.

Iodine deficiency is uncommon in the Western world because iodine is added to salt. Where iodine deficiency is not a problem, the most common cause of hypothyroidism is **Hashimoto's thyroiditis.** This is another autoimmune disease, but in this case, the immune system destroys the thyroid gland, producing hypothyroidism. Hashimoto's thyroiditis tends to run in families so it is likely to have a genetic component. It usually appears after the age of 30 and is more common in females than males.

Hypothyroidism produces many signs and symptoms, as shown in Figure **7.5.6**. These may include abnormal weight gain, tiredness, baldness, cold intolerance, and slow heart rate. Hypothyroidism is

generally treated with thyroid hormone replacement therapy. This may be needed for the rest of a person's life. Hypothyroidism in a pregnant woman can have serious adverse consequences for the fetus. During the fetal period, cells of the developing brain are a major target for thyroid hormones, which play a crucial role in brain maturation. When levels of thyroid hormones are too low, the fetus may suffer permanent deficits in cognitive abilities. Deafness is also a potential outcome of hypothyroidism *in utero*.

Feature: Myth vs. Reality

Thyroid disorders are relatively common, affecting as many as 20 million people in the United States. Because the disorders are common, there are also many common myths about them.

Myth: If you have a thyroid problem, you will know something is wrong because you will have obvious symptoms.

Reality: The majority of people with a thyroid disorder are not aware they have it because the symptoms are often mild, nonspecific, and easy to ignore. Generally, blood tests of thyroid hormone levels are needed to make a conclusive diagnosis.

Myth: If you are diagnosed with a thyroid disorder, you will have to take medication for the rest of your life.

Reality: Whether you need to continue thyroid medication for life depends on the cause of the disorder. For example, some women develop hypothyroidism during pregnancy but no longer need medication after the pregnancy is over and hormone levels return to normal.

Myth: As soon as you start taking thyroid medication, your symptoms will resolve.

Reality: It often takes weeks or even months for thyroid hormone levels to return to normal and symptoms to disappear.

Myth: You can take an over-the-counter iodine supplement to correct hypothyroidism.

Reality: In the United States, where dietary iodine is almost always adequate, iodine deficiency is unlikely to be the cause of hypothyroidism. Therefore, taking supplemental iodine is not likely to correct the problem.

Myth: If thyroid symptoms are mild, you don't need to take medication.

Reality: Because thyroid hormones are responsible for so many vital body functions, failing to treat even a mild thyroid disorder may lead to a range of other problems, such as osteoporosis or infertility.

Myth: Goiter may be caused by eating "goitrogenic" vegetables, such as broccoli, Brussels sprouts, and spinach.

Reality: Although these foods can interfere with the thyroid's ability to process iodide, you would have to eat huge amounts of them to cause goiter.

Myth: Thyroid disorders occur only after middle age and only in women.

Reality: Thyroid disorders may occur at any age and in any sex. Hypothyroidism occurs more commonly in older adults, but hyperthyroidism occurs more commonly in younger adults. Although women are more likely to develop thyroid disorders, about 20 percent of cases occur in men.

REVIEW

1. Describe the structure and location of the thyroid gland.
2. Identify the types of cells within the thyroid gland that produce hormones.
3. Compare and contrast T4 and T3.
4. How do T4 and T3 affect body cells?
5. Explain how T4 and T3 production is regulated.
6. What is the function of calcitonin?
7. Identify the chief cause and effects of hyperthyroidism.
8. What are two possible causes of hypothyroidism?
9. List signs and symptoms of hypothyroidism.
10. Why may both hyperthyroidism and hypothyroidism cause goiters?
11. Choose one symptom each for hyperthyroidism and hypothyroidism and explain why they occur based on the functions of thyroid hormones.
12. Which hormone is produced by the thyroid gland?
    A. T3
    B. Calcitonin
    C. Parathyroid hormone
    D. TSH
    E. A and B
13. In cases of hypothyroidism due to Hashimoto's thyroiditis or removal of the thyroid gland to treat hyperthyroidism, patients are often given medication to replace the missing thyroid hormone. Explain why the level of replacement thyroid hormone must be carefully monitored and adjusted if needed.
14. *True or False.* T3 and T4 bind to receptors on the plasma membrane of target cells.
15. Which disease causes too much thyroid hormone to be produced?
    A. Hashimoto's thyroiditis
    B. Graves' disease
    C. Goiter
    D. Iodine deficiency

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7.6: ADRENAL GLANDS

EEK!

Being bitten on the nose by an eel certainly qualifies as a frightening experience! The fear this man is experiencing produces the same physiological responses in most people—racing heart, rapid breathing, clammy hands. These and other fight-or-flight responses prepare the body to either defend itself or run away from danger. Why does fear elicit these changes in the body? The responses occur in large part because of hormones secreted by the adrenal glands.



Figure **7.6.1**: Attack

INTRODUCTION TO THE ADRENAL GLANDS

The **adrenal glands** are endocrine glands that produce a variety of hormones. Adrenal hormones include the fight-or-flight hormone adrenaline and the steroid hormone cortisol. The two adrenal glands are located on both sides of the body, just above the kidneys, as shown in Figure **7.6.2**. The right adrenal gland (on the left in the figure) is smaller and has a pyramidal shape. The left adrenal gland (on the right in the figure) is larger and has a half-moon shape.

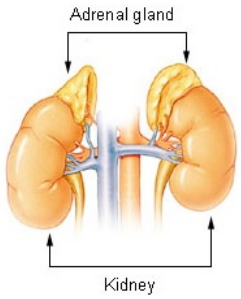


Figure **7.6.2**: Each of the two adrenal glands is found above a kidney

Each adrenal gland has two distinct parts, and each part has a different function, although both parts produce hormones. There is an outer layer, called the adrenal cortex, which produces steroid hormones including cortisol. There is also an inner layer, called the adrenal medulla, which produces non-steroid hormones including adrenaline.

ADRENAL CORTEX

The **adrenal cortex,** or the outer layer of the adrenal gland, is divided, in turn, into three additional layers, called zones (Figure **7.6.3**). Each zone has distinct enzymes that produce different hormones from the common precursor molecule cholesterol, which is a lipid.

1. Zona glomerulosa is the outermost layer of the adrenal cortex. It lies immediately under the outer fibrous capsule that encloses the adrenal gland.
2. Zona fasciculata is the middle layer of the adrenal cortex. It is the largest of the three zones, accounting for nearly 80 percent of the adrenal cortex.
3. Zona reticularis is the innermost layer of the adrenal cortex. It is directly adjacent to the medulla of the adrenal gland.

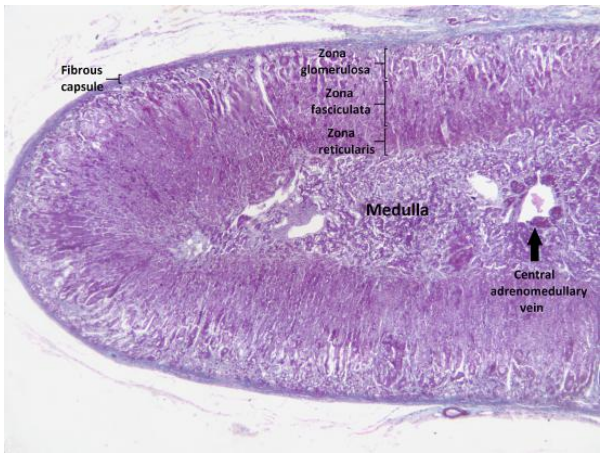


Figure **7.6.3**: The adrenal cortex is divided into three zones, zona glomerulosa, zona fasciculata, and zona reticularis. Each zone produces a different type of steroid hormone. This photomicrograph also shows the medulla of the adrenal gland.

TYPES OF ADRENAL CORTEX HORMONES

Hormones produced by the adrenal cortex are called **corticosteroids.** As steroid hormones, corticosteroids are endocrine hormones that are made of lipids and exert their effects on target cells by crossing the plasma membrane and binding with receptors within the cytoplasm. A steroid hormone and its receptor form a complex that enters the cell nucleus and affects gene expression. There are three types of corticosteroids synthesized and secreted by the adrenal cortex. Each type is produced by a different zone of the adrenal cortex, as shown in Figure **7.6.3**.

MINERALOCORTICOIDS

Mineralocorticoids are produced in the zona glomerulosa and include the hormone aldosterone. These hormones help control the balance of mineral salts (electrolytes) in the body. In the kidneys, aldosterone increases the reabsorption of sodium ions and the excretion of potassium ions. Aldosterone also stimulates the retention of sodium ions by cells in the colon and by the sweat glands. The amount of sodium in the body affects the volume of

extracellular fluids including the blood and thereby affects blood pressure. In this way, mineralocorticoids help control blood volume and blood pressure.

GLUCOCORTICOIDS

Glucocorticoids are produced in the zona fasciculata and include the hormone **cortisol,** which is released in response to stress and is considered the primary stress hormone. Glucocorticoids help control the rate of metabolism of proteins, fats, and sugars. In general, they increase the level of glucose and fatty acids circulating in the blood. Cells rely primarily on glucose for energy, but they can also use fatty acids for energy as an alternative to glucose. Glucocorticoids are also involved in the suppression of the immune system, having a potent anti-inflammatory effect. In addition, cortisol reduces the production of new bone and decreases the absorption of calcium from the gastrointestinal tract.

ANDROGENS

Androgens are produced in the zona reticularis and include the hormone DHEA (dehydroepiandrosterone). Androgens are a general term for male sex hormones, although this is somewhat misleading as adrenal cortex androgens are produced by both males and females. In adult males, they are converted to more potent androgens such as testosterone in the male gonads (testes). In adult females, they are converted to female sex hormones called estrogens in the female gonads (ovaries).

REGULATION OF ADRENAL CORTEX HORMONES

Steroid hormone production by the three zones of the adrenal cortex is regulated by hormones secreted by the anterior lobe of the pituitary gland as well as by other physiological stimuli. For example, the production of glucocorticoids such as cortisol is stimulated by adrenocorticotropic hormone (ACTH) from the anterior pituitary, which in turn is stimulated by corticotropin releasing hormone (CRH) from the hypothalamus. When levels of glucocorticoids start to rise too high, they provide negative feedback to the hypothalamus and pituitary gland to stop secreting CRH and ACTH, respectively. This negative feedback mechanism is illustrated in Figure **7.6.4**. The opposite occurs when levels of glucocorticoids start to fall too low.

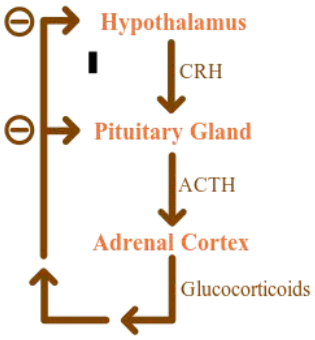


Figure **7.6.4**: The negative feedback loop that controls the production of glucocorticoids includes the pituitary gland and hypothalamus in addition to the adrenal cortex.

ADRENAL MEDULLA

The **adrenal medulla** is at the center of each adrenal gland and is surrounded by the adrenal cortex. It contains a dense network of blood vessels into which it secretes its hormones. The hormones synthesized and secreted by the adrenal medulla are called **catecholamines**, and they include **adrenaline** (also called epinephrine) and noradrenaline (also called norepinephrine). These are water-soluble, non-steroid hormones are made of amino acids. As non-steroid hormones, they cannot cross the plasma membrane of target cells. Instead, they exert their effects by binding to receptors on the surface of target cells. The binding of hormones and receptors activates an enzyme in the plasma membrane that controls a second messenger. It is the second messenger that influences processes inside the cell.

Catecholamines function to produce a rapid response throughout the body in stressful situations. They bring about such changes as increased heart rate, more rapid breathing, constriction of blood vessels in certain parts of the body, and an increase in blood pressure. The release of catecholamines by the adrenal medulla is stimulated by activation of the sympathetic division of the autonomic nervous system.

DISORDERS OF THE ADRENAL GLANDS

Disorders of the adrenal glands generally include either hypersecretion or hyposecretion of adrenal hormones. The underlying cause of the abnormal secretion may be a problem with the adrenal glands or with the pituitary gland, which controls adrenal cortex hormone production. Both adrenal and pituitary glands are subject to the formation of tumors, which may cause adrenal disorders. The adrenal gland may also be affected by infections or autoimmune diseases.

ADRENAL HYPERSECRETION: CUSHING'S SYNDROME

Hypersecretion of the glucocorticoid hormone cortisol leads to a disorder named **Cushing's syndrome.** The most common cause of Cushing's syndrome is a pituitary tumor, which causes excessive production of ACTH. The disease produces a wide variety of signs and symptoms, which may include obesity, diabetes, high blood pressure (hypertension), excessive body hair, osteoporosis, and depression. A distinctive sign of Cushing's syndrome is the appearance of stretch marks in the skin, as the skin becomes progressively thinner. Another distinctive sign is a moon face shown in the section *Introduction to the Endocrine System*, in which fat deposits give the face a rounded appearance. Treatment of Cushing's syndrome depends on its cause and may include surgery to remove a tumor or medications to suppress the activity of the adrenal glands.

ADRENAL HYPOSECRETION: ADDISON'S DISEASE



Figure **7.6.5**: Hyperpigmentation of the skin is a characteristic sign of Addison's disease. The photo on the left shows the dark skin pigmentation of an Addison's patient before treatment. The photo on the right shows the same patient after treatment.

Hyposecretion of the glucocorticoid hormone cortisol leads to a disorder named **Addison's disease**. There may also be hyposecretion of mineralocorticoids with this disorder. Addison's disease is generally an autoimmune disorder, in which the immune system produces abnormal antibodies that attack cells of the adrenal cortex. Untreated infections, especially of tuberculosis, may also damage the adrenal cortex and cause Addison's disease. A third possible cause is the decreased output of ACTH by the pituitary gland, generally due to a pituitary tumor. A distinctive sign of Addison's disease is hyperpigmentation of the skin (Figure **7.6.5**). Other symptoms tend to be nonspecific and include excessive fatigue. Addison's disease is generally treated with replacement hormones in pill form.

FEATURE: MY HUMAN BODY



Figure **7.6.6**: Base Jump

Does just looking at this photo cause you to break out in a cold sweat and experience heart palpitations? Imagine how scary it would be to fling yourself backward off a tall building like the BASE jumper in the photo. There would be very little time to use a parachute to slow your fall before you hit the ground. BASE jumping is called the most dangerous sport on Earth. In fact, it is so dangerous that it is outlawed in some places.

People who participate in such dangerous activities as BASE jumping are likely to be adrenaline "junkies." They are addicted to the adrenaline rush and euphoria, or "high," it causes when their fight-or-flight response is triggered by danger. Why does adrenaline have this effect? Adrenaline is closely related to dopamine, a chemical messenger in the brain that plays a major role in pleasure and addiction.

Adrenaline addicts don't have to participate in BASE jumping or other dangerous sports to get an adrenaline rush. They might choose a dangerous occupation such as firefighting, participate in risky behaviors such as reckless driving or bank robbing, or just pick fights with other people. They might even create their own stress by always taking on too much work or delaying projects until close to their deadline.

While some excitement in one's life is generally a good thing, always putting oneself in danger or constantly being under stress are obviously not good things. If you think you might be an adrenaline addict, note that there are healthier ways to experience a hormonal "high." Running, biking, or participating in some other form of vigorous aerobic exercise causes the pituitary gland and hypothalamus to produce opiate-like endorphins, leading to a so-called "runner's high." Like the euphoric feeling adrenaline causes, a runner's high may last for hours.

REVIEW

1. Describe the structure and location of the adrenal glands.
2. Compare and contrast the adrenal cortex and adrenal medulla.
3. Identify the three layers of the adrenal cortex and the type of hormones each layer produces.
4. Give an example of each type of corticosteroid and state its function.
5. Explain how the production of glucocorticoids is regulated.
6. What is a catecholamine? Give an example of a catecholamine and state its function.
7. Compare and contrast Cushing's syndrome and Addison's disease.
8. Cortisol is a type of:
   A. Corticosteroid
   B. Mineralocorticoid
   C. Glucocorticoid
   D. A and C
9. *True or False.* The adrenal glands help regulate the body's stress response and reproductive functions.
10. *True or False.* The left adrenal gland produces steroid hormones, while the right adrenal gland produces non-steroid hormones.
11. Would it help to give someone with Cushing's syndrome more ACTH? Explain your answer.
12. What are two ways in which the nervous system (which includes the brain, spinal cord, and nerves) controls the adrenal gland?
13. If the level of cortisol rises too high, the amount of CRH secreted will normally:
    A. not change
    B. become excessively high
    C. become slightly higher

D. decrease

14. Noradrenaline is also called:
    A. norepinephrine
    B. adrenaline
    C. adrenocorticotropin
    D. glucocorticoid
15. Explain why a pituitary tumor can cause either hypersecretion or hyposecretion of cortisol.

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7.7: PANCREAS

A SHOT IN THE ARM

Giving yourself an injection can be difficult, but for someone with diabetes, it may be a matter of life or death. The person in the photo has diabetes and is injecting himself with insulin, the hormone that helps control the level of glucose in the blood. Insulin is produced by the pancreas.



Figure **7.7.1**: Insulin Application

INTRODUCTION TO THE PANCREAS

The **pancreas** is a large gland located in the upper left abdomen behind the stomach, as shown in the figure below. The pancreas is about 15 centimeters (6 in.) long; and it has a flat, oblong shape. Structurally, the pancreas is divided into a head, body, and tail. Functionally, the pancreas serves as both an endocrine gland and an exocrine gland.

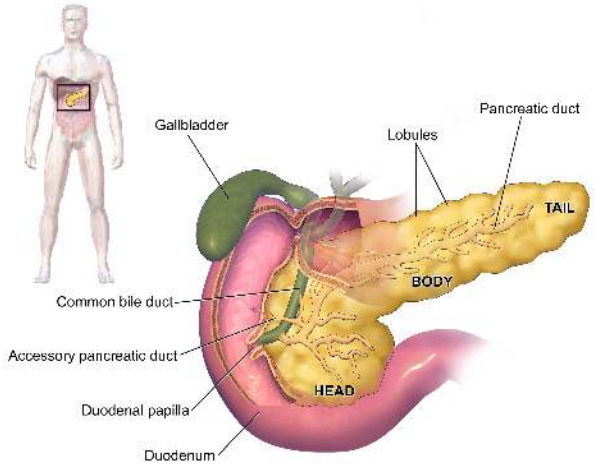


Figure **7.7.2**: The pancreas is located behind the stomach and near the upper part of the small intestine (duodenum). Its main parts are tail, body, and head. Its ducts carry digestive enzymes into the small intestine. The endocrine hormones it produces are secreted into the blood.

- As an endocrine gland, the pancreas is part of the endocrine system. As such, it releases hormones, such as insulin, directly into the bloodstream for transport to cells throughout the body.
- As an exocrine gland, the pancreas is part of the digestive system. As such, it releases digestive enzymes into ducts that carry the enzymes to the gastrointestinal tract where they assist with digestion. In this concept, the focus is on the pancreas as an endocrine gland. You can read about the pancreas as an exocrine gland in the chapter *Digestive System*.

THE PANCREAS AS AN ENDOCRINE GLAND

The tissues within the pancreas that have an endocrine role exist as clusters of cells called **pancreatic islets.** They are also called the islets of Langerhans. In Figure **7.7.3**, you can see pancreatic tissue, including islets. There are approximately 3 million pancreatic islets, and they are crisscrossed by a dense network of capillaries. The capillaries are lined by layers of islet cells that have direct contact with the blood vessels, into which they secrete their endocrine hormones.

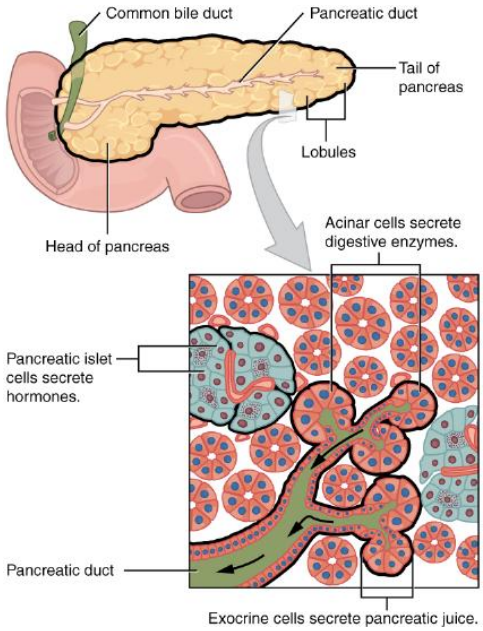


Figure **7.7.3**: Anatomy of the pancreas. The inset diagram shows pancreatic islet cells that produce endocrine hormones. It also shows the cells (called acinar cells) that secrete exocrine substances involved in digestion into pancreatic ducts.

The pancreatic islets consist of four main types of cells, each of which secretes a different endocrine hormone. However, all of the hormones produced by the pancreatic islets play crucial roles in glucose metabolism and the regulation of blood glucose levels, among other functions.

1. Islet cells called alpha (α) cells secrete the hormone glucagon. The function of glucagon is to increase the level of glucose in the blood. It does this by stimulating the liver to convert stored glycogen into glucose, which is released into the bloodstream.
2. Islet cells called beta (β) cells secrete the hormone insulin. The function of insulin is to decrease the level of glucose in the blood. It does this by promoting the absorption of glucose from the blood into fat, liver, and skeletal muscle cells. In these tissues, the absorbed glucose is converted into glycogen, fats (triglycerides), or both.
3. Islet cells called delta (δ) cells secrete the hormone **somatostatin.** This hormone is also called the growth hormone inhibiting hormone because it inhibits the anterior lobe of the pituitary gland from producing growth hormone. Somatostatin

also inhibits the secretion of pancreatic endocrine hormones and pancreatic exocrine enzymes.

4. Islet cells called gamma (γ) cells secrete the hormone pancreatic polypeptide. The function of pancreatic polypeptide is to help regulate the secretion of both endocrine and exocrine substances by the pancreas.

DISORDERS OF THE PANCREAS

There are a variety of disorders that affect the pancreas. They include pancreatitis, pancreatic cancer, and diabetes mellitus.

PANCREATITIS

Pancreatitis is inflammation of the pancreas. It has a variety of possible causes including gallstones, chronic alcohol use, infections such as measles or mumps, genetic causes, and certain medications. Pancreatitis occurs when digestive enzymes produced by the pancreas damage the gland's tissues, which causes problems with fat digestion. The disorder is usually associated with intense pain in the central abdomen, and the pain may radiate to the back. Yellowing of the skin and whites of the eyes (Figure **7.7.4**), which is called jaundice, is a common sign of pancreatitis. People with pancreatitis may also have pale stools and dark urine. Treatment of pancreatitis includes administering drugs to manage pain and addressing the underlying cause of the disease, for example, by removing gallstones.



Figure **7.7.4**: Jaundice, or yellowing of the skin and whites of the eyes, is a common sign of pancreatitis.

PANCREATIC CANCER

There are several different types of pancreatic cancer that may affect either the endocrine or the exocrine tissues of the gland. Cancers affecting the endocrine tissues are all relatively rare. However, their incidence has been rising sharply. It is unclear to what extent this reflects increased detection, especially through medical imaging techniques. Unfortunately, pancreatic cancer is usually diagnosed at a relatively late stage when it is too late for surgery, which is the only way to cure the disorder. In the United States, pancreatic cancer is the fourth most common cause of death due to cancer.

Pancreatic cancer is rare before the age of 40 and occurs most often after the age of 60. Factors that increase the risk of developing pancreatic cancer include smoking, chronic pancreatitis, and diabetes. About one in four cases of pancreatic cancer are attributable to smoking. Certain rare genetic conditions are also risk factors for pancreatic cancer.

DIABETES MELLITUS

By far the most common type of pancreatic disorder is diabetes mellitus, more commonly called simply diabetes. There are many different types of diabetes, but diabetes mellitus is the most common. It occurs in two major types, type 1 diabetes and type 2 diabetes. The two types have different causes and may also have different treatments, but they generally produce the same initial symptoms, which include excessive urination and thirst. These symptoms occur because the kidneys excrete more urine in an attempt to rid the blood of excess glucose, and loss of water in urine stimulates greater thirst. Other signs and symptoms of diabetes are listed in Figure **7.7.5**.

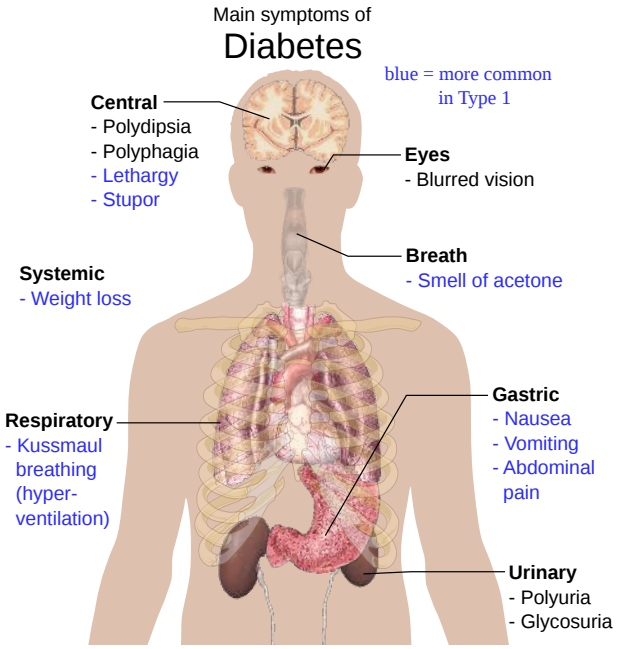


Figure **7.7.5**: Diabetes can affect many systems of the body. The symptoms shared by both type 1 and type 2 diabetes, such as blurred vision, polyuria, glycosuria, polydipsia, and polyphagia are listed in black, and the symptoms more common in type 1 diabetes, such as the smell of acetone, nausea, vomiting, abdominal pain, lethargy, stupor, weight loss, and hyperventilation are listed in blue.

When diabetes is not well controlled, it is likely to have several serious long-term consequences. Most of these consequences are due to damage to small blood vessels because of high blood levels of glucose. Damage to blood vessels, in turn, may lead to an increased risk of coronary artery disease and stroke. Damage to blood vessels in the retina of the eye can result in gradual vision loss and blindness. Damage to blood vessels in the kidneys can lead to chronic kidney disease, sometimes requiring dialysis or a kidney transplant. Long-term consequences of diabetes may also include damage to the nerves of the body, known as diabetic neuropathy. In fact, this is the most common complication of diabetes. Symptoms of diabetic neuropathy may include numbness, tingling, and pain in the extremities.

TYPE 1 DIABETES

Type 1 diabetes is a chronic autoimmune disorder in which the immune system attacks the insulin-secreting beta cells of the

pancreas. As a result, people with type 1 diabetes lack the insulin needed to keep blood glucose levels within the normal range. Type 1 diabetes may develop in people of any age but is most often diagnosed before adulthood. For type 1 diabetics, insulin injections are critical for survival.

TYPE 2 DIABETES

Type 2 diabetes is the single most common form of diabetes. The cause of high blood glucose in this form of diabetes usually includes a combination of insulin resistance and impaired insulin secretion. Both genetic and environmental factors play roles in the development of type 2 diabetes. Management of type 2 diabetes includes changes in diet and physical activity, which may increase insulin sensitivity and help reduce blood glucose levels to normal ranges. Medications may also be used as part of the treatment, as may insulin injections.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Some patients with type 1 diabetes have been given pancreatic islet cells transplants from other human donors. If the transplanted cells are not rejected by the recipient's immune system, they can cure the patient of diabetes. However, only about 1,000 such surgeries have been performed over the past 10 years because of a shortage of appropriate human donors.

In June of 2016, a research team led by Dr. David K.C. Cooper at the Thomas E. Starzl Transplantation Institute in Pittsburgh, Pennsylvania, reported on their work developing pig islet cells for transplant into human diabetes patients. The researchers genetically engineered the pig islet cells to be protected from the human immune response. As a result, patients receiving transplanted cells would require only minimal suppression of their immune system after the surgery. The pig islet cells would also be less likely to transmit pathogenic agents because the animals could be raised in a controlled environment.

The researchers have successfully transplanted the pig islet cells into monkey models of type 1 diabetes. As of June 2016, the scientists were looking for funding to undertake clinical trials in humans with type 1 diabetes. Dr. Cooper predicted then that if the human trials go as well as expected, the pig islet cells could be available for curing patients in as little as two years.

REVIEW

1. Describe the structure and location of the pancreas.
2. Distinguish between the endocrine and exocrine functions of the pancreas.
3. Identify the four types of pancreatic islet cells and the endocrine hormone each type of cell produces.
4. What is pancreatitis? What are the possible causes and effects of pancreatitis?
5. Describe the incidence, prognosis, and risk factors of cancer of the endocrine tissues of the pancreas.
6. Compare and contrast type 1 and type 2 diabetes.
7. If the alpha islet cells of the pancreas were damaged to the point that they no longer functioned, how would this affect blood glucose levels? Would the administration of insulin be more likely to help or hurt the condition? Explain your answer.
8. Explain how the pancreas is able to regulate the production of its own endocrine hormones, to some extent.
9. True or False. The pancreas is part of both the digestive system and the endocrine system.
10. Give an example of how the pancreas can regulate the production of hormones from the pituitary gland.
11. Which is the most common form of diabetes mellitus?
12. Explain why diabetes causes excessive thirst.
13. Damage to _____ is the underlying cause of many of the long-term consequences of diabetes.

    A. the adrenal gland
    B. gamma islet cells
    C. blood vessels
    D. the pituitary gland

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7.8: CASE STUDY CONCLUSION- HORMONAL AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: HORMONAL HAVOC

Gabrielle, who you read about in the beginning of this chapter, has polycystic ovary syndrome (PCOS). PCOS is named for the multiple fluid-filled sacs, or cysts, that are present in the ovaries of women with this syndrome. You can see these cysts in the illustration above, which compares a normal ovary with a polycystic ovary. The cysts result from follicles in the ovary that did not properly produce and release an egg. Mature eggs are normally released from follicles monthly during the process of ovulation, but in PCOS this often does not occur. Ovarian cysts can be common and do not necessarily mean that a woman has PCOS, but the presence of multiple ovarian cysts plus other telltale signs and symptoms may cause her physician suspect PCOS.

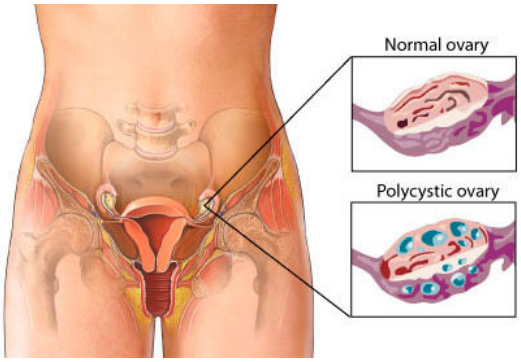


Figure **7.8.1**: Polycystic Ovary

Gabrielle's symptoms of PCOS included irregular menstrual periods, weight gain, acne, and excess facial hair. There are many other symptoms of PCOS that women can experience, such as male-pattern baldness, pelvic pain, and depression, among others. As you may recall, Gabrielle also had some abnormal blood test results, such as high levels of androgens and blood glucose. These can also be indications of PCOS.

As you have learned, androgens are a term for male sex hormones, but females also normally produce androgens, albeit to a lesser extent than males. In women with PCOS, the level of androgens is abnormally high. These androgens include testosterone, which is produced by the ovaries, and DHEA, which is produced by the adrenal glands. This increase in androgens can have a "masculinizing" effect on women, including an increase in facial and body hair, male-pattern baldness, and interference with the menstrual cycle by preventing ovulation. Androgens also can cause weight gain and acne — two of the other common symptoms of PCOS.

In addition to hypersecretion of androgens, PCOS often causes high blood glucose as a result of insulin resistance. As you have learned, insulin is a hormone secreted by the pancreas that works in conjunction with other pancreatic hormones (such as glucagon) to regulate the level of blood glucose. What is another disease involving insulin resistance? If you answered type 2 diabetes, you are correct! In fact, women with PCOS are at a high risk of developing type 2 diabetes because of their resistance to insulin. More than 50 percent of women with PCOS will develop diabetes or pre-diabetes before they are 40 years old.

Besides diabetes, women with PCOS have a higher chance of developing fertility problems, heart disease, sleep apnea (briefly stopping breathing during sleep), and uterine cancer, among other diseases and disorders. There is hope, however. Lifestyle modifications and medicines not only can help women cope with the symptoms of PCOS, but may also reduce the risk of some of the possible long-term consequences by lowering blood sugar and androgen levels. For instance, eating a healthy diet and exercising regularly can help women with PCOS lose weight. This can help lower blood glucose levels, improve insulin functioning, and can even make the menstrual cycle more regular. Medications such as birth control pills and anti-androgens can help restore a more regular menstrual cycle and reduce facial and body hair and acne. The diabetes medication metformin can be used to treat several of the symptoms of PCOS, and even may prevent type 2 diabetes, by improving insulin functioning and lowering testosterone. Finally, women with PCOS who are trying to conceive may be helped with fertility medications that stimulate ovulation.

The underlying cause of PCOS is not definitively known, although it is thought that both genetic and environmental factors play a role. PCOS tends to run in families, and women with a sister with PCOS are twice as likely to also have it. Researchers think that the insulin resistance seen in PCOS may cause an increase in androgens, illustrating how hormonal systems can influence each other.

As you have seen throughout this chapter, endocrine hormones can have a wide variety of effects on the body, including the regulation of metabolism, reproductive functions, homeostasis of different ions and molecules, and mediating responses to stressful situations. Different hormones have different effects, but even a single hormone can have multiple effects. Hormones travel throughout the bloodstream and affect any cells that have the appropriate receptors for them, known as target cells. Many hormones have target cells in multiple types of organs and tissues, or they regulate molecules, such as blood glucose, that affect many organ systems. These are some of the reasons why changes in the normal level of an endocrine hormone — either hypersecretion or hyposecretion — can result in a wide variety of symptoms, such as is seen in Cushing's syndrome, diabetes, and PCOS. By understanding what goes wrong in these disorders, you can better appreciate how important the endocrine system is for regulating the many diverse functions of the human body.

CHAPTER SUMMARY

In this chapter, you learned about the glands and hormones of the endocrine system, their functions, how they are regulated, and some diseases and disorders of the endocrine system. Specifically, you learned that:

- The endocrine system is a system of glands that release chemical messenger molecules called hormones into the bloodstream. Other glands, called exocrine glands, release substances onto nearby body surfaces through ducts.
- Endocrine hormones travel more slowly than nerve impulses, which are the body's other way of sending messages. However, the effects of endocrine hormones may be much longer lasting.
- The pituitary gland is the master gland of the endocrine system. Most of the hormones it produces control other endocrine glands. These glands include the thyroid gland, parathyroid glands, pineal gland, pancreas, adrenal glands, gonads (testes and ovaries), and thymus gland.
- Diseases of the endocrine system are relatively common. An endocrine disease usually involves hypersecretion or hyposecretion of a hormone. Hypersecretion is frequently caused by a tumor. Hyposecretion is often caused by the destruction of hormone-secreting cells by the body's own immune system.
- Endocrine hormones travel throughout the body but affect only certain cells, called target cells, which have receptors specific to particular hormones.
- Steroid hormones such as estrogen are endocrine hormones made of lipids that cross plasma membranes and bind to receptors inside target cells. The hormone-receptor complexes then move into the nucleus where they influence gene expression.
- Non-steroid hormones such as insulin are endocrine hormones made of amino acids that bind to receptors on the surface of target cells. This activates an enzyme in the plasma membrane, and the enzyme controls a second messenger molecule, which influences cell processes.
- Most endocrine hormones are controlled by negative feedback loops in which rising levels of hormone feedback to stop its own production — and vice-versa. For example, a negative feedback loop controls the production of thyroid hormones. The loop includes the hypothalamus, pituitary gland, and thyroid gland.
- Only a few endocrine hormones are controlled by positive feedback loops in which rising levels of hormone feedback to stimulate continued production of the hormone. Prolactin, the pituitary hormone that stimulates milk production by mammary glands, is controlled by a positive feedback loop. The loop includes the nipples, hypothalamus, pituitary gland, and mammary glands.
- The pituitary gland is at the base of the brain, where it is connected to the hypothalamus by nerves and capillaries. It has an anterior (front) lobe that synthesizes and secretes pituitary hormones and a posterior (back) lobe that stores and secretes hormones from the hypothalamus.
    - Hormones synthesized and secreted by the anterior pituitary include growth hormone, which stimulates cell growth throughout the body, and thyroid stimulating hormone (TSH), which stimulates the thyroid gland to secrete its hormones.
    - Hypothalamic hormones stored and secreted by the posterior pituitary include vasopressin, which helps maintain homeostasis in body water; and oxytocin, which stimulates uterine contractions during birth and the letdown of milk during lactation.
- The thyroid gland is a large endocrine gland in the front of the neck. It is composed mainly of clusters of cells called follicles, which are specialized to absorb iodine and use it to make thyroid hormones. Parafollicular cells among the follicles synthesize the hormone calcitonin.
    - The thyroid hormones thyroxine (T4) and triiodothyronine (T3) cross cell membranes and regulate gene expression to control the rate of metabolism in cells body-wide, among other functions. The production of T4 and T3 is regulated by thyroid stimulating hormone (TSH) from the pituitary, which is regulated, in turn, by thyrotropin-releasing hormone (TRH) from the hypothalamus.
    - Calcitonin helps regulate blood calcium levels by stimulating the movement of calcium into bone. It works in conjunction with parathyroid hormone to maintain calcium homeostasis.
    - Abnormal secretion of thyroid hormones may occur for a variety of reasons and may lead to the development of a goiter. The most common cause of hyperthyroidism is Graves' disease, an autoimmune disorder. Iodine deficiency is a common cause of hypothyroidism worldwide. In the United States, the most common cause of hypothyroidism is Hashimoto's thyroiditis, another autoimmune disorder. Hypothyroidism in pregnant women may cause permanent cognitive deficits in children.
- The adrenal glands are endocrine glands that produce a variety of hormones. The two adrenal glands are located on both sides of the body, just above the kidneys. Each gland has two layers: an outer layer called the adrenal cortex and an inner layer called the adrenal medulla.
    - The adrenal cortex produces steroid hormones called by the general term corticosteroids, of which there are three types: mineralocorticoids such as aldosterone, which helps control electrolyte balance; glucocorticoids such as cortisol, which helps control the rate of metabolism and suppresses the immune system; and androgens such as DHEA, which is converted to sex hormones in the gonads.
    - The adrenal medulla produces non-steroid catecholamine hormones including adrenaline and noradrenaline. These hormones stimulate the fight-or-flight response.
    - Disorders of the adrenal glands generally include either hypersecretion or hyposecretion of adrenal hormones. The cause may be a problem with the adrenal glands or with the pituitary gland, which controls adrenal cortex hormone production. Examples include Cushing's syndrome, in which there is hypersecretion of cortisol; and Addison's disease, in which there is hyposecretion of cortisol and mineralocorticoids.
- The pancreas is a gland located in the upper left abdomen behind the stomach that functions as both an endocrine gland and an exocrine gland. As an endocrine gland, the pancreas releases

hormones, such as insulin, directly into the bloodstream. As an exocrine gland, the pancreas releases digestive enzymes into ducts that carry them to the gastrointestinal tract.

- Tissues in the pancreas that have an endocrine role exist as clusters of cells called pancreatic islets. The islets consist of four main types of cells, each of which secretes a different endocrine hormone. Alpha (α) cells secrete glucagon, beta (β) cells secrete insulin, delta (δ) cells secrete somatostatin, and gamma (γ) cells secrete pancreatic polypeptide.
- The endocrine hormones secreted by the pancreatic islets all play a role, either directly or indirectly, in glucose metabolism and homeostasis of blood glucose levels. For example, insulin stimulates the uptake of glucose by cells and decreases the level of glucose in the blood, whereas glucagon stimulates the conversion of glycogen to glucose and increases the level of glucose in the blood.
- Disorders of the pancreas include pancreatitis, pancreatic cancer, and diabetes mellitus. Pancreatitis is a painful inflammation of the pancreas that has many possible causes. Pancreatic cancer of the endocrine tissues is rare but increasing in frequency. It is generally discovered too late to cure surgically. Smoking is a major risk factor for pancreatic cancer.
- Diabetes mellitus is the most common type of pancreatic disorder. In diabetes, the inadequate activity of insulin results in high blood levels of glucose. Type 1 diabetes is a chronic autoimmune disorder in which the immune system attacks the insulin-secreting beta cells of the pancreas. Type 2 diabetes is usually caused by a combination of insulin resistance and impaired insulin secretion due to a variety of environmental and genetic factors.

CHAPTER SUMMARY REVIEW

1. The pituitary gland is considered the master gland of the endocrine system because its hormones control other endocrine glands. For each of the glands below, describe one way in which it is controlled by the pituitary gland.
   A. The thyroid gland
   B. The adrenal gland
   C. The gonads (ovaries and testes)
2. What is the name of the main brain structure that secretes hormones that control the pituitary gland?
3. Define hyposecretion and give an example of an endocrine disorder involving hyposecretion. Be sure to include the name of the hormone involved.
4. Define hypersecretion and give an example of an endocrine disorder involving hypersecretion. Be sure to include the name of the hormone involved.
5. Which hormone plays a role in regulating metabolism in some way?
   A. Cortisol
   B. Thyroid hormone
   C. Glucagon
   D. All of the above
6. Which endocrine gland plays an important role in the fight-or-flight response?
7. *True or False*. Sex hormones, such as androgens, are only produced by the gonads.
8. *True or False*. Estrogen can travel to the nucleus of a cell.
9. Explain why non-steroid hormones typically require the activation of second messenger molecules to have their effects, instead of directly affecting intracellular processes themselves.
10. Explain what it means that endocrine hormones are "chemical messengers."
11. If you were a physician, and a patient came to you complaining of excessive thirst and urination, what endocrine disorder might you suspect the patient has?
    A. In order to diagnose this disorder, what would you want to check for in the patient's blood? Explain your answer.
12. Pancreatic islet cells all produce:
    A. Insulin
    B. Glucagon
    C. Endocrine hormones
    D. Digestive enzymes
13. Give one example of negative feedback in the endocrine system.
14. Explain the circumstances in which organs and hormones in a negative feedback loop can actually increase the level of a hormone.
15. *True or False*. The hormone vasopressin is synthesized by the hypothalamus.
16. *True or False*. Like most other hormones, prolactin is regulated by a negative feedback loop.
17. Identify the gland that secretes each of the following hormones:
    A. Melatonin
    B. Growth hormone
    C. Thyroid stimulating hormone
    D. Aldosterone
18. A goiter is an enlargement of which structure?
19. Explain why giving iodine can treat some cases of hypothyroidism, but it is not usually helpful when someone has hypothyroidism due to Hashimoto's thyroiditis.
20. For each disease below, identify the hormone involved and whether the problem involves hyposecretion or hypersecretion of this hormone.
    A. Addison's disease
    B. Graves' disease
    C. Cushing's syndrome
    D. Type 1 diabetes
21. What is an example of a disease that is due to hormone resistance?
22. *True or False*. Adrenaline is an exocrine hormone.
23. Steroid hormones:
    A. always increase muscle mass

B. are fat soluble
C. bind to receptors on the plasma membrane
D. include insulin

24. Explain generally how autoimmune disorders can disrupt the endocrine system, and give one example.

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CHAPTER OVERVIEW

8: SKELETAL SYSTEM

This chapter describes the structure and functions of the skeletal system and its two major divisions, the axial skeleton and the appendicular skeleton. It details the structure of bone, how bones grow, and how they are remodeled and repaired. The chapter also explains how joints work and how they are classified as well as the causes and effects of major skeletal system disorders.

8.1: Case Study- Your Support System

8.2: Introduction to the Skeletal System

8.3: Divisions of the Skeletal System

8.4: Structure of Bone

8.5: Bone Growth, Remodeling, and Repair

8.6: Joints

8.7: Disorders of the Skeletal System

8.8: Case Study Conclusion- Heels and Chapter Summary

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8.1: CASE STUDY- YOUR SUPPORT SYSTEM

CASE STUDY: A PAIN IN THE FOOT

Amari loves wearing high heels when they go out at night, like the stiletto heels shown in Figure **8.1.1**. Amari uses gender-neutral pronouns, such as they, them, and their. They know high heels are not the most practical shoes, but they like how they look. Lately, Amari has been experiencing pain in the balls of their feet—the area just behind the toes. Even when they trade heels for comfortable sneakers, it still hurts when they stand or walk.



Figure **8.1.1**: high heels

What could be going on? Amari searches online to try to find some answers. They find a reputable source for foot pain information—a website from a professional organization of physicians that peer reviews the content by experts in the field. There, Amari reads about a condition called metatarsalgia, which produces pain in the ball of the foot that sounds very similar to what they are experiencing.

Amari learns that a common cause of metatarsalgia is the wearing of high heels because they push the foot into an abnormal position. This results in excessive pressure being placed onto the ball of the foot. Looking at the photograph above, you can imagine how much of the body weight is focused on the ball of the foot because of the shape of the high heels. If they were not wearing high heels, the weight would be more evenly distributed across the foot.

As they read more about the hazards of high heels, Amari learns that heels can also cause foot deformities such as hammertoes and bunions, small cracks in the bone called stress fractures, and may even contribute to the development of osteoarthritis of the knees at an early age.

These conditions caused by high heels are all problems of the skeletal system, which includes bones and connective tissues that hold bones together and cushion them at joints such as the knee. The skeletal system supports the body's weight and protects internal organs, but as you will learn as you read this chapter, it also carries out a variety of other important physiological functions.

At the end of the chapter, you will find out why high heels can cause these skeletal system problems and the steps Amari takes to recover from their foot pain and prevent long-term injury.

CHAPTER OVERVIEW: SKELETAL SYSTEM

In this chapter, you will learn about the structure, functions, growth, repair, and disorders of the skeletal system. Specifically, you will learn about:

- The components of the skeletal system, which include bones, ligaments, and cartilage.
- The functions of the skeletal system, which include supporting and giving shape to the body, protecting internal organs, facilitating movement, producing blood cells, helping maintain homeostasis, and producing endocrine hormones.
- The organization and functions of the two main divisions of the skeletal system: the axial skeletal system, which includes the skull, spine, and rib cage; and the appendicular skeletal system, which includes the limbs and girdles that attach the limbs to the axial skeleton.
- The tissues and cells that make up bones and their specific functions, including making new bone, breaking down bone, producing blood cells, and regulating mineral homeostasis.
- The different types of bones in the skeletal system, based on shape and location.
- How bones grow, remodel, and repair themselves.
- The different types of joints between bones, where they are located, and the ways in which they allow different types of movement depending on their structure.
- The causes, risk factors, and treatments for the two most common disorders of the skeletal system: osteoporosis and osteoarthritis.

As you read this chapter, think about the following questions:

1. Amari suspects they have a condition called metatarsalgia. This term is related to the term "metatarsals." What are metatarsals, where are they located, and how do you think they are related to metatarsalgia?
2. High heels can cause stress fractures, which are small cracks in the bone that usually appear after repeated mechanical stress, instead of after a significant acute injury. What other condition described in this chapter involves a similar process?
3. What are bunions and osteoarthritis of the knee? Why do you think they can be caused by wearing high heels?

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8.2: INTRODUCTION TO THE SKELETAL SYSTEM

SKULL AND CROSS-BONES

The skull and cross-bones symbol has been used for a very long time to represent death, perhaps because after death and decomposition, bones are all that remain. Many people think of bones as being dead, dry, and brittle. These adjectives may correctly describe the bones of a preserved skeleton, but the bones of a living human being are very much alive. Living bones are also strong and flexible. Bones are the major organs of the skeletal system.



Figure **8.2.1**: skull and cross-bones flag

The **skeletal system** is the organ system that provides an internal framework for the human body. Why do you need a skeletal system? Try to imagine what you would look like without it. You would be a soft, wobbly pile of skin containing muscles and internal organs but no bones. You might look something like a very large slug. Not that you would be able to see yourself — folds of skin would droop down over your eyes and block your vision because of your lack of skull bones. You could push the skin out of the way if you could only move your arms, but you need bones for that as well!

COMPONENTS OF THE SKELETAL SYSTEM

In adults, the skeletal system includes 206 bones, many of which are shown in Figure **8.2.2**. Bones are organs made of dense connective tissues, mainly the tough protein collagen. Bones contain blood vessels, nerves, and other tissues. Bones are hard and rigid due to deposits of calcium and other mineral salts within their living tissues. Locations, where two or more bones meet, are called joints. Many joints allow bones to move like levers. For example, your elbow is a joint that allows you to bend and straighten your arm.

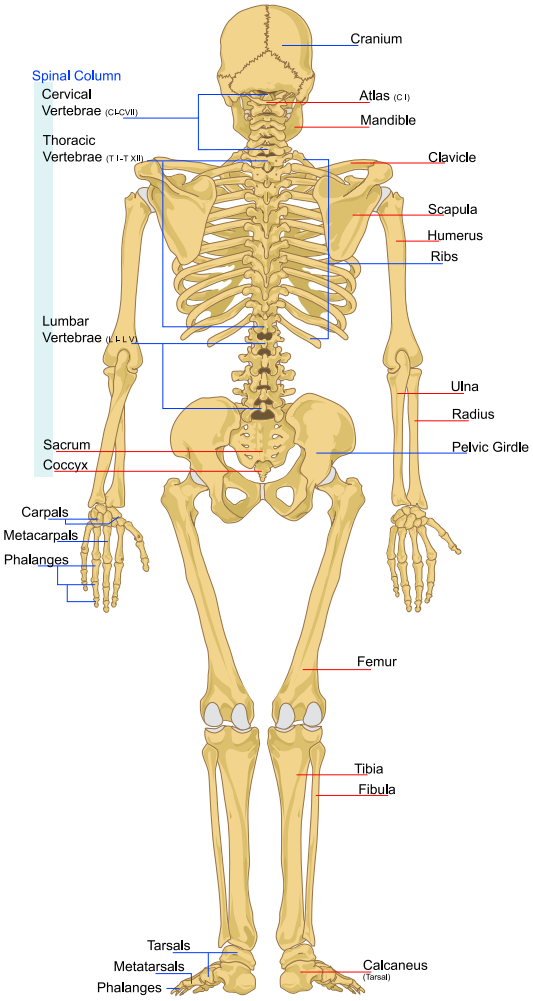


Figure **8.2.2**: Some of the 206 bones are labeled on the adult human skeleton.

Besides bones, the skeletal system includes cartilage and ligaments.

- **Cartilage** is a type of dense connective tissue, made of tough protein fibers. It is strong but flexible and very smooth. It covers the ends of bones at joints, providing a smooth surface for bones to move over.
- **Ligaments** are bands of fibrous connective tissue that hold bones together. They keep the bones of the skeleton in place.

AXIAL AND APPENDICULAR SKELETONS

The skeleton is traditionally divided into two major parts: the axial skeleton and the appendicular skeleton, both of which are pictured in Figure **8.2.3**.

- The axial skeleton forms the axis of the body. It includes the skull, vertebral column (spine), and rib cage. The bones of the axial skeleton, along with ligaments and muscles, allow the human body to maintain its upright posture. The axial skeleton also transmits weight from the head, trunk, and upper extremities

down the back to the lower extremities. In addition, the bones protect the brain and organs in the chest.

- The appendicular skeleton forms the appendages and their attachments to the axial skeleton. It includes the bones of the arms and legs, hands and feet, and shoulder and pelvic girdles. The bones of the appendicular skeleton make possible locomotion and other movements of the appendages. They also protect the major organs of digestion, excretion, and reproduction.

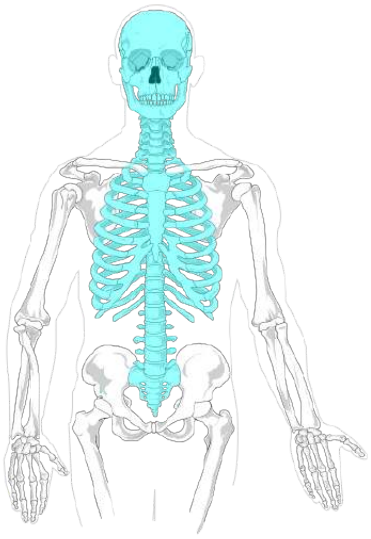


Figure **8.2.3**: Axial skeleton represented in blue

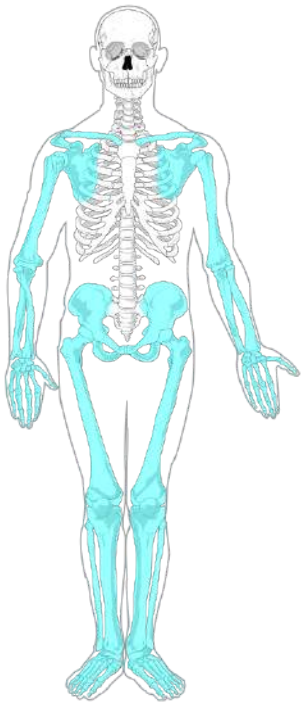


Figure **8.2.3**: Appendicular skeleton represented in blue

FUNCTIONS OF THE SKELETAL SYSTEM

The skeletal system has many different functions that are necessary for human survival. Some of the functions, such as supporting the body, are relatively obvious. Other functions are less obvious but no less important. For example, three tiny bones (hammer, anvil, and stirrup) inside the middle ear transfer sound waves into the inner ear.

SUPPORT, SHAPE, AND PROTECTION

The skeleton supports the body and gives it shape. Without the rigid bones of the skeletal system, the human body would be just a bag of soft tissues, as described above. The bones of the skeleton are very hard and provide protection to the delicate tissues of internal organs. For example, the skull encloses and protects the soft tissues of the brain, and the vertebral column protects the nervous tissues of the spinal cord. The vertebral column, ribs, and sternum (breast bone) protect the heart, lungs, and major blood vessels. Providing protection to these latter internal organs requires the bones to be able to expand and contract. The ribs and the cartilage that connects them to the sternum and vertebrae are capable of small shifts that allow breathing and other internal organ movements.

MOVEMENT

The bones of the skeleton provide attachment surfaces for skeletal muscles. When the muscles contract, they pull on and move the bones. The figure below, for example, shows the muscles attached to the bones at the knee. They help stabilize the joint and allow the leg to bend at the knee. The bones at joints act like levers moving at a fulcrum point, and the muscles attached to the bones apply the force needed for movement.

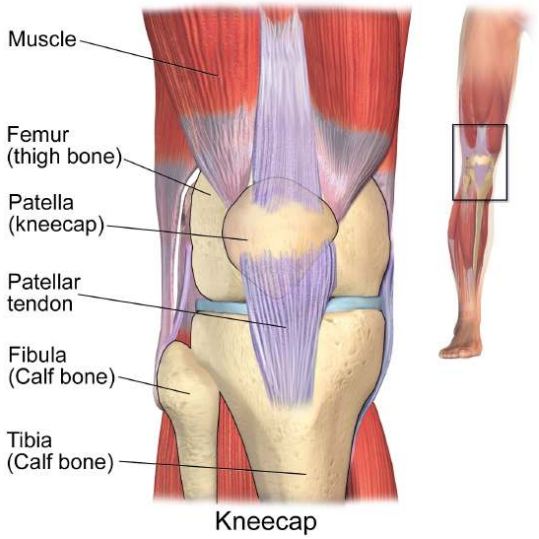


Figure **8.2.4**: Bones that meet at the knee joint include the tibia and fibula in the lower leg, the femur in the upper leg, and the kneecap at the front of the knee. These bones provide attachment surfaces for muscles that move the bones at the joint. Muscles are attached to the bones via tendons.

HEMATOPOIESIS

Hematopoiesis is the process in which blood cells are produced. This process occurs in a tissue called red marrow, which is found

inside some bones, including the pelvis, ribs, and vertebrae. Red marrow synthesizes red blood cells, white blood cells, and platelets. Billions of these blood cells are produced inside the bones every day.

MINERAL STORAGE AND HOMEOSTASIS

Another function of the skeletal system is storing minerals, especially calcium and phosphorus. This storage function is related to the role of bones in maintaining mineral homeostasis. Just the right levels of calcium and other minerals are needed in the blood for the normal functioning of the body. When mineral levels in the blood are too high, bones absorb some of the minerals and store them as mineral salts, which is why bones are so hard. When blood levels of minerals are too low, bones release some of the minerals back into the blood. Bone minerals are alkaline (basic), so their release into the blood buffers the blood against excessive acidity (low pH), whereas their absorption back into bones buffers the blood against excessive alkalinity (high pH). In this way, bones help maintain acid-base homeostasis in the blood.

Another way bones help to maintain homeostasis is by acting as an endocrine organ. One endocrine hormone secreted by bone cells is **osteocalcin,** which helps regulate blood glucose and fat deposition. It increases insulin secretion and also the sensitivity of cells to insulin. In addition, it boosts the number of insulin-producing cells and reduces fat stores.

REVIEW

1. What is the skeletal system? How many bones are there in the adult skeleton?
2. Describe the composition of bones.
3. Besides bones, what other organs are included in the skeletal system?
4. Identify the two major divisions of the skeleton.
5. List several functions of the skeletal system.
6. Discuss sexual dimorphism in the human skeleton.
7. Bones, cartilage, and ligaments are all made of types of _____ tissue.
8. *True or False.* Bones contain living tissue and can affect processes in other parts of the body.
9. *True or False.* Bone cells contract to pull on muscles in order to initiate a movement.
10. If a person has a problem with blood cell production, what type of bone tissue is most likely involved? Explain your answer.
11. Are the pelvic girdles part of the axial or appendicular skeleton?
12. What are three forms of homeostasis that the skeletal system regulates? Briefly explain how each one is regulated by the skeletal system.
13. What do you think would happen to us if we did not have ligaments? Explain your answer.
14. a. Define a joint in the skeletal system.

    b. How is cartilage related to joints?

    c. Identify one joint in the human body and describe its function.

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8.3: DIVISIONS OF THE SKELETAL SYSTEM

SKULLS ON DISPLAY

This somewhat macabre display can be viewed at the Slovak National Museum in Bratislava, Slovakia. The skulls are meant to represent normal human skeletal anatomy. The skull is part of the axial skeleton, which is one of the two major divisions of the human skeleton. The other division is the appendicular skeleton.



Figure **8.3.1**: Skulls on Display

AXIAL SKELETON

The **axial skeleton,** shown in blue in Figure **8.3.2**, consists of a total of 80 bones. Besides the skull, it includes the rib cage and vertebral column. It also includes the three tiny ossicles (hammer, anvil, and stirrup) in the middle ear and the hyoid bone in the throat, to which the tongue and some other soft tissues are attached.

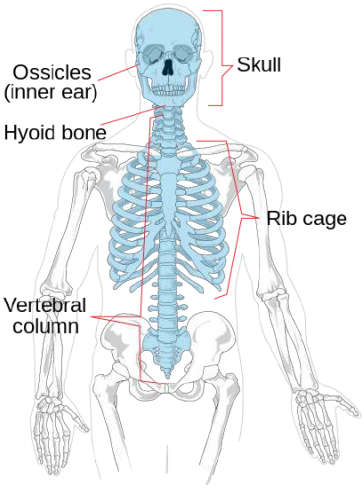


Figure **8.3.2**: The bones of the axial skeleton are shown here in blue.

SKULL

The **skull** is the part of the human skeleton that provides a bony framework for the head. It consists of 22 different bones. There are 8 bones in the cranium, which encloses the brain, and 14 bones in the face.

CRANIUM

The **cranium,** sometimes called the braincase, forms the entire upper portion of the skull. As shown in Figure **8.3.3**, it consists of eight bones: one frontal bone, two parietal bones, two temporal bones, one occipital bone, one sphenoid bone, and one ethmoid bone. The ethmoid bone separates the nasal cavity from the brain. The sphenoid bone is one of several bones, including the frontal bone, that helps form the eye sockets. The other bones of the cranium are large and plate-like. They cover and protect the brain. The bottom of the skull has openings for major blood vessels and nerves. A large opening, called the foramen magnum, allows the spinal cord and brain to connect.

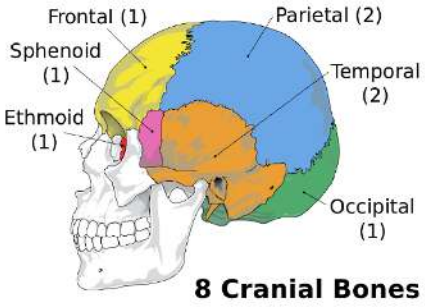


Figure **8.3.3**: The cranium consists of eight bones that are fused together at their joints.

FACIAL BONES

The 14 facial bones of the skull are located below the frontal bone of the cranium. They are depicted in Figure **8.3.4**. Large bones in the face include the upper jawbones, or **maxillae (singular, maxilla),** which form the middle part of the face and the bottom of the two eye sockets. The maxillae are fused together except for an opening between them for the nose. The lower edge of the maxillae contains sockets for the upper teeth. The lower jaw bone, or **mandible,** is also large. The top edge of the mandible contains sockets for the lower teeth. The mandible opens and closes to chew food and is controlled by strong muscles. There are two zygomatic or cheekbones and two nasal bones. The nasal region also contains seven smaller bones, as indicated in the figure.

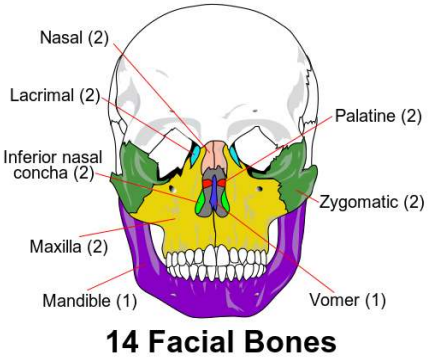


Figure **8.3.4**: The 14 bones that make up the face are labeled in this drawing of the skull.

VERTEBRAL COLUMN

The **vertebral column,** also called the spine or backbone, is the flexible column of **vertebrae (singular, vertebra)** that connects the trunk with the skull and encloses the spinal cord. It consists of 33 vertebrae that are divided into five regions, as shown in Figure **8.3.5**: the cervical, thoracic, lumbar, sacral, and coccygeal regions. From

the neck down, the first 24 vertebrae (cervical, thoracic, and lumbar) are individual bones. The five sacral vertebrae are fused together, as are the four coccygeal vertebrae.

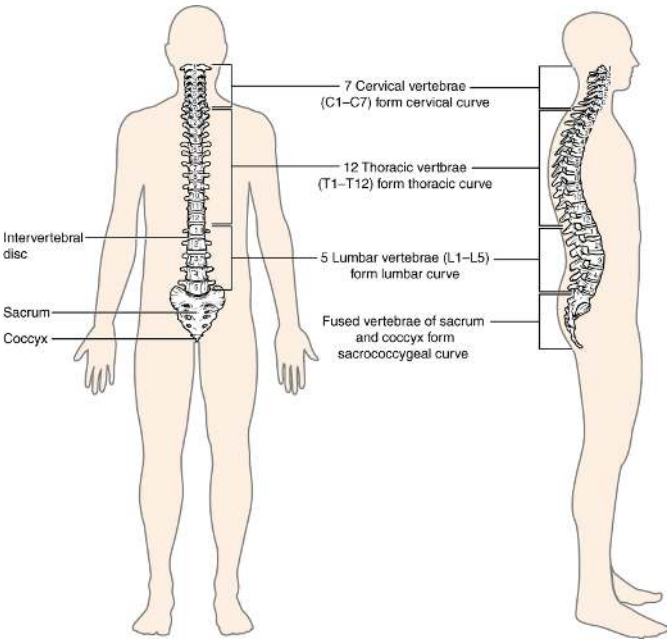


Figure **8.3.5**: The vertebral column consists of 24 individual vertebrae that are separated by intervertebral discs of cartilage. An additional 9 vertebrae are fused together at the base of the spine. Note the S-shaped curve of the vertebral column in the profile view on the right.

The human vertebral column reflects adaptations for upright bipedal locomotion. For example, the vertebral column is less like a rigid column than an S-shaped spring (see a profile view in the figure above). Although newborn infants have a relatively straight spine, the curves develop as the backbone starts taking on its support functions, such as keeping the trunk erect, holding up the head, and helping to anchor the limbs. The S shape of the vertebral column allows it to act as a shock absorber, absorbing much of the jarring of walking and running so the forces are not transmitted directly from the pelvis to the skull. The S shape also helps protect the spine from breaking, which would be more likely with a straight, more rigid vertebral column. In addition, the S shape helps to distribute the weight of the body, and particularly of the internal organs, so the weight load is not all at the bottom, as would occur with a straight spine.

RIB CAGE

The **rib cage** (also called thoracic cage) is aptly named because it forms a sort of cage that holds within it the organs of the upper part of the trunk, including the heart and lungs (Figure **8.3.6**). The rib cage includes the 12 thoracic vertebrae and the breastbone (or sternum) as well as 12 pairs of ribs, which are attached at joints to the vertebrae. The ribs are divided into three groups, called true ribs, false ribs, and floating ribs. The top seven pairs of ribs are true ribs. They are attached by cartilage directly to the sternum. The next three pairs of ribs are false ribs. They are attached by cartilage to the ribs above them, rather than directly to the sternum. The lowest two pairs of ribs are floating ribs. They are attached by cartilage to muscles in the abdominal wall. The attachments of false and floating ribs let the lower part of the rib cage expand to accommodate the internal movements of breathing.

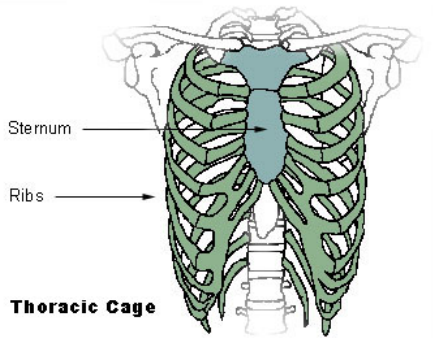


Figure **8.3.6**: The rib cage encloses and protects the thoracic cavity

APPENDICULAR SKELETON

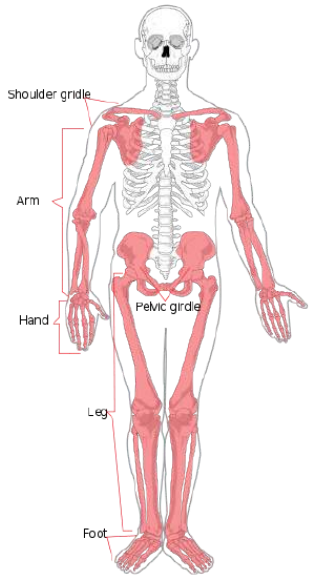


Figure **8.3.7**. The appendicular skeleton (in red) includes the upper and lower appendages and girdles.

The appendicular skeleton, shown in red in Figure **8.3.7**, consists of a total of 126 bones. It includes all the bones of the limbs (arms, legs, hands, and feet) as well as the bones of the shoulder (shoulder girdle) and pelvis (pelvic girdle).

UPPER LIMBS

Each upper limb consists of 30 bones. As shown in Figure **8.3.8**, there is one bone, called the humerus, in each of the upper arms, and there are two bones, called the ulna and radius, in each of the lower arms.

The remaining bones of the upper limb are shown in Figure **8.3.9**. Each wrist contains eight carpal bones, which are arranged in two rows of four bones each; and each hand contains five metacarpal bones. The bones in the fingers of each hand include 14 phalanges (three in each finger except the thumb, which has two phalanges). The thumb has the unique ability to move into opposition with the palm of the hand and with each of the fingers when they are slightly

bent. This allows the hand to handle and manipulate objects such as tools.

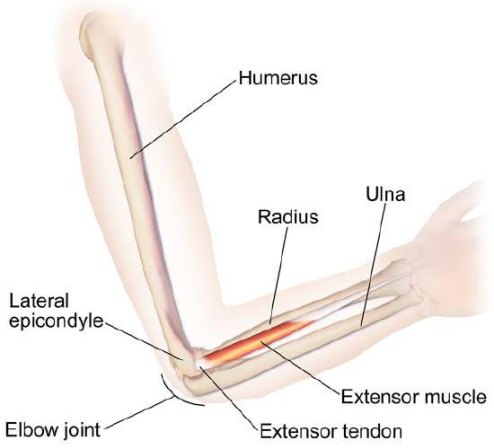


Figure **8.3.8**: In the upper limb, the upper arm contains one bone, Humerus, and the lower arm contains two bone, Ulna and Radius.

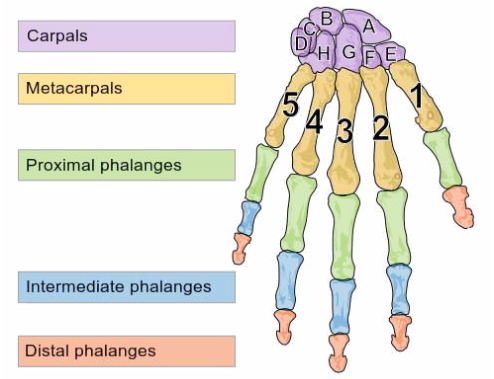


Figure **8.3.9**: Bones of the wrist (carpals A-E) and hand (metacarpals 1-5 and phalanges).

LOWER LIMBS

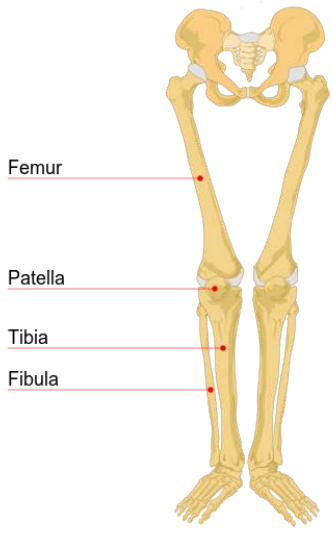


Figure **8.3.10**: Bones of the legs.

Each lower limb consists of 30 bones. As shown in Figure **8.3.10**, there is one bone, called the femur, in each of the upper legs, and there are two bones, called the tibia and fibula, in each of the lower legs. The knee cap, or patella, is an additional leg bone at the front of each knee, which is the largest joint in the human body.

The remaining bones of the lower limbs are shown in Figure **8.3.11**. Each ankle contains seven tarsal bones (including the talus and calcaneus), and each foot contains five metatarsal bones. The tarsals and metatarsals form the ankle, heel, and arch of the foot. They give the foot strength while allowing flexibility. The bones in the toes of each foot consist of 14 phalanges (three in each toe except the big toe, which has two phalanges)

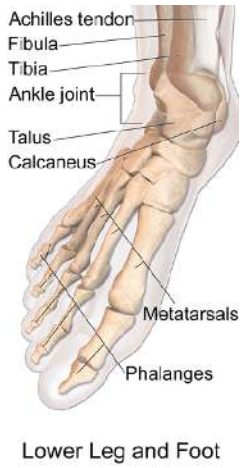


Figure **8.3.11**: Bones of the lower leg (fibula and tibia), ankle (talus), heel (calcaneus), foot (metatarsals), and toes (phalanges).

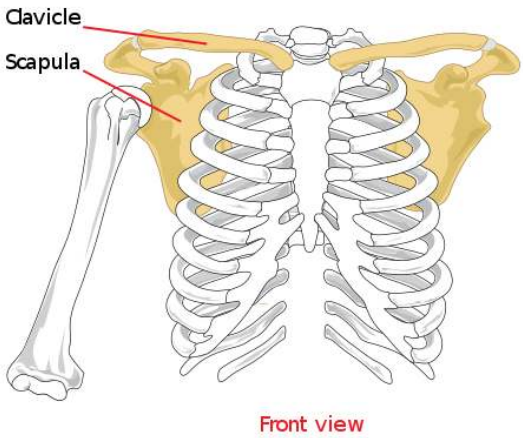


Figure **8.3.12**: Bones of the shoulder girdle are clavicle and scapula.

The pectoral girdle (also called shoulder girdle) attaches the upper limbs to the trunk of the body. Its connection with the axial skeleton is by muscles alone. This allows a considerable range of motion in the upper limbs. The shoulder girdle consists of just two pairs of bones, with one of each pair on opposite sides of the body (Figure **8.3.12**). There is a right and left clavicles (collarbone) and right and left scapulae (shoulder blade). The scapula is a pear-shaped flat bone that helps to form the shoulder joint. The clavicle is a long bone that serves as a strut between the shoulder blade and the sternum.

PELVIC GIRDLE

The **pelvic girdle** attaches the legs to the trunk of the body and also provides a basin to contain and support the organs of the abdomen. It is connected to the vertebral column of the axial skeleton by ligaments. The pelvic girdle consists of two halves, one half for each leg, but the halves are fused with each other in adults at a joint called the pubic symphysis. Each half of the pelvic girdle includes three bones, as shown in the figure below: the ilium (flaring upper part of the pelvic girdle), pubis (lower front), and ischium (lower back). Each of these bones helps form the acetabulum, which is a depression into which the top of the femur (thigh bone) fits. When the body is in a seated position, it rests on protrusions (called tuberosities) of the two ischial bones.

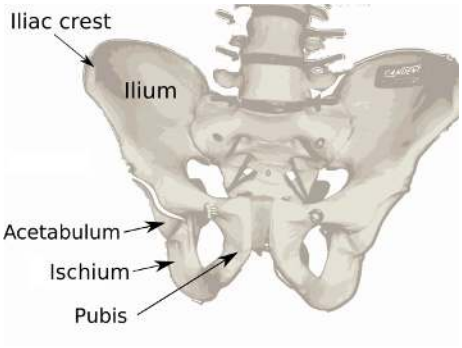


Figure **8.3.13**: Bones of the pelvic girdle.

REVIEW

1. What bones are included in the axial skeleton?
2. Identify the two main parts of the skull. How many bones does each part contain?
3. Describe the vertebral column.
4. What are the advantages of an S-shaped vertebral column?
5. What is the rib cage, and what is its function?
6. What bones are included in the appendicular skeleton?
7. How many bones are found in each upper limb? What are they?
8. Identify the bones in each of the lower limbs.
9. What is the shoulder girdle, and why does it allow considerable upper limb mobility?
10. Describe the pelvic girdle and the bones it contains.
11. *True or False.* False ribs are made of cartilage and are not true rib bones.
12. *True or False.* The jaw contains two maxillae and one mandible.
13. Describe some of the similarities between the upper limbs and the lower limbs.
14. Explain the advantage of having some ribs that are not attached directly to the sternum.
15. Put the following vertebral regions in order, from the closest to the head to the farthest from the head:

    sacral; lumbar; cervical; coccygeal; thoracic

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8.4: STRUCTURE OF BONE

ROASTED BONE MARROW

Do you recognize the food item in the top left of this photo in Figure **8.4.1**? It's roasted bone marrow, still inside the bones. It's considered a delicacy in some cuisines. Marrow is a type of tissue found inside many animal bones, including our own. It's a soft tissue that in adults may be mostly fat. You'll learn more about bone marrow and other tissues that make up bones when you read this concept.



Figure **8.4.1**:Roasted Bone Marrow

Bones are organs that consist primarily of bone tissue, also called osseous tissue. **Bone tissue** is a type of connective tissue consisting mainly of a collagen matrix that is mineralized with calcium and phosphorus crystals. The combination of flexible collagen and hard mineral crystals makes bone tissue hard without making it brittle.

BONE ANATOMY

There are several different types of tissues in bones, including two types of osseous tissues.

TYPES OF OSSEOUS TISSUE

The two different types of osseous tissue are compact bone tissue (also called hard or cortical bone) tissue and spongy bone tissue (also called cancellous or trabecular bone).

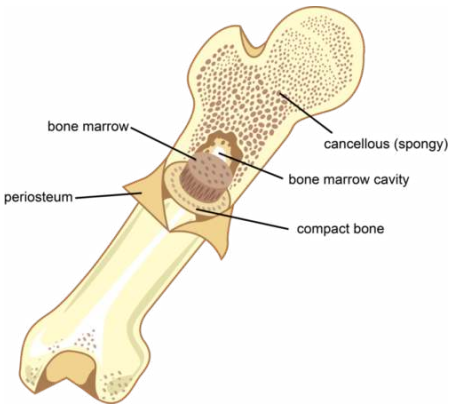


Figure **8.4.2**: Bones are more complex on the inside than you would expect from their outer appearance. There is bone marrow in the hollow part of the long bone. The outer boundary of bone is composed of compact bone tissue, and from the ends, and the rest of the bone interior is composed of cancellous or spongy bone tissue. The bone is covered in connecting tissue called the periosteum.

Compact bone tissue forms the extremely hard outside layer of bones. Cortical bone tissue gives bone its smooth, dense, solid appearance. It accounts for about 80 percent of the total bone mass of the adult skeleton. **Spongy bone tissue** fills part or all of the interior of many bones. As its name suggests, spongy bone is porous like a sponge, containing an irregular network of spaces. This makes spongy bone much less dense than compact bone. Spongy bone has a greater surface area than cortical bone but makes up only 20 percent of bone mass.

Both compact and spongy bone tissues have the same types of cells, but they differ in how the cells are arranged. The cells in the compact bone are arranged in multiple microscopic columns, whereas the cells in the spongy bone are arranged in a looser, more open network. These cellular differences explain why cortical and spongy bone tissues have such different structures.

OTHER TISSUES IN BONES

Besides cortical and spongy bone tissues, bones contain several other tissues, including blood vessels and nerves. In addition, bones contain bone marrow and periosteum. You can see these tissues in Figure **8.4.2**.

- **Bone marrow** is a soft connective tissue that is found inside a cavity, called the marrow cavity. There are two types of marrow in adults, yellow bone marrow, which consists mostly of fat, and red bone marrow. All marrow is red in newborns, but by adulthood, much of the red marrow has changed to yellow marrow. In adults, red marrow is found mainly in the femur, ribs, vertebrae, and pelvic bones. Red bone marrow contains hematopoietic stem cells that give rise to red blood cells, white blood cells, and platelets in the process of hematopoiesis.
- **Periosteum** is a tough, fibrous membrane that covers the outer surface of bones. It provides a protective covering for cortical bone tissue. It is also the source of new bone cells.

BONE CELLS

As shown in Figure **8.4.3**, bone tissues are composed of four different types of bone cells: osteoblasts, osteocytes, osteoclasts, and osteogenic cells.

- **Osteoblasts** are bone cells with a single nucleus that make and mineralize bone matrix. They make a protein mixture that is composed primarily of collagen and creates the organic part of the matrix. They also release calcium and phosphate ions that form mineral crystals within the matrix. In addition, they produce hormones that also play a role in the mineralization of the matrix.
- **Osteocytes** are mainly inactive bone cells that form from osteoblasts that have become entrapped within their own bone matrix. Osteocytes help regulate the formation and breakdown of bone tissue. They have multiple cell projections that are thought to be involved in communication with other bone cells.
- **Osteoclasts** are bone cells with multiple nuclei that resorb bone tissue and break down bone. They dissolve the minerals in bone and release them into the blood.

- **Osteogenic cells** are undifferentiated stem cells. They are the only bone cells that can divide. When they do, they differentiate and develop into osteoblasts.

Bone is a very active tissue. It is constantly remodeled by the work of osteoblasts and osteoclasts. Osteoblasts continuously make new bone, and osteoclasts keep breaking down bone. This allows for minor repair of bones as well as homeostasis of mineral ions in the blood.

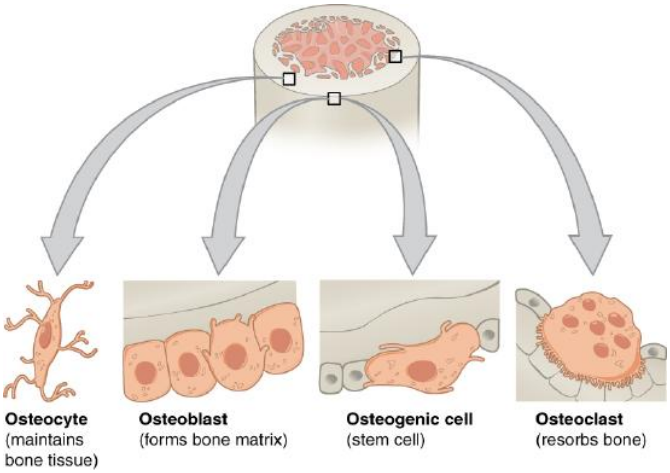


Figure **8.4.3**: Different types of bones cells have different functions.

MICROSCOPIC ANATOMY OF THE COMPACT BONE

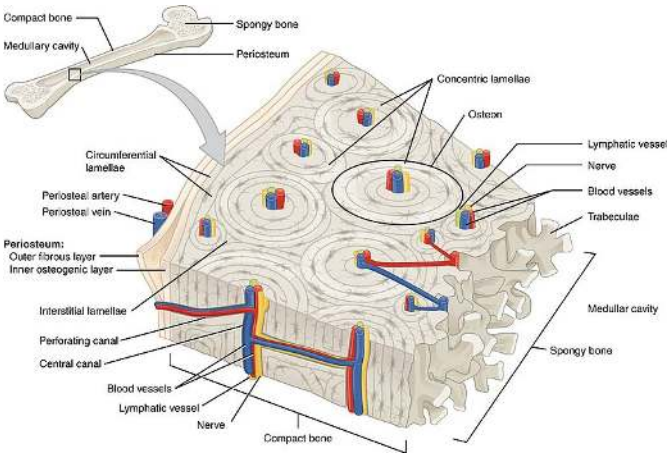


Figure **8.4.4**: Macroscopic and microscopic structures of the compact bone tissue.

The basic microscopic unit of bone is an osteon (or Haversian system). Osteons are roughly cylindrical structures that can measure several millimeters long and around 0.2 mm in diameter. Each osteon consists of lamellae of compact bone tissue that surround a central canal (Haversian canal). The Haversian canal contains the bone's blood supplies. The boundary of an osteon is called the cement line. Osteons can be arranged into woven bone or lamellar bone. Osteoblasts make the matrix of bone which calcifies hardens. This entraps the mature bone cells, osteocytes, in a little chamber called lacunae. The osteocytes receive their nutrition from the central (Haversian) canal via little canals called canaliculi. All of these structures plus more are visible in Figure **8.4.4**.

TYPES OF BONES

There are six types of bones in the human body based on their shape or location: long, short, flat, sesamoid, sutural, and irregular bones. You can see an example of each type of bone in Figure **8.4.5**.

- Long bones are characterized by a shaft that is much longer than it is wide and by a rounded head at each end of the shaft. Long bones are made mostly of compact bone, with lesser amounts of spongy bone and marrow. Most bones of the limbs, including those of the fingers and toes, are long bones.
- Short bones are roughly cube-shaped and have only a thin layer of cortical bone surrounding a spongy bone interior. The bones of the wrists and ankles are short bones.
- Flat bones are thin and generally curved, with two parallel layers of compact bone sandwiching a layer of spongy bone. Most of the bones of the skull are flat bones, as is the sternum (breast bone).
- Sesamoid bones are embedded in tendons, the connective tissues that bind muscles to bones. Sesamoid bones hold tendons farther away from joints so the angle of the tendons is increased, thus increasing the leverage of muscles. The patella (knee cap) is an example of a sesamoid bone.
- Sutural bones are very small bones that are located between the major bones of the skull, within the joints (sutures) between the larger bones. They are not always present.
- Irregular bones are those that do not fit into any of the above categories. They generally consist of thin layers of cortical bone surrounding a spongy bone interior. Their shapes are irregular and complicated. Examples of irregular bones include the vertebrae and the bones of the pelvis.

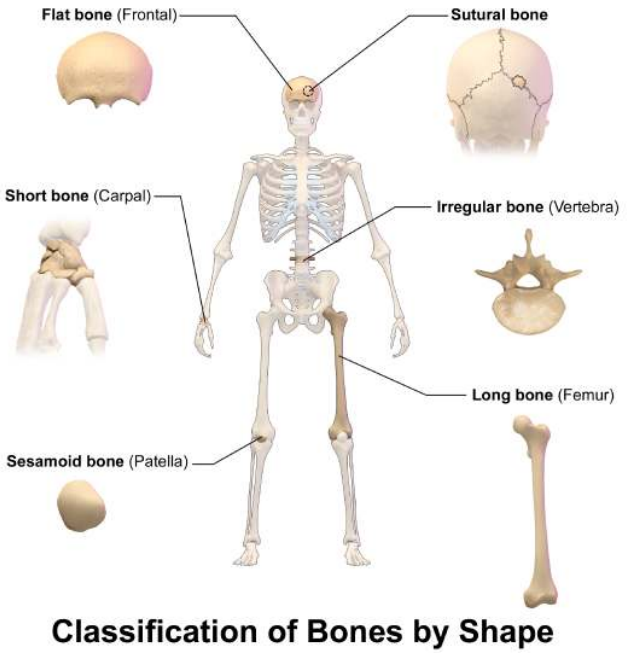


Figure **8.4.5**: six types of bones classified by shape or location.

FEATURE: RELIABLE SOURCES

Diseased or damaged bone marrow can be replaced by donated bone marrow cells, which help treat and often cure many life-threatening conditions, including leukemia, lymphoma, sickle cell anemia, and thalassemia. If a bone marrow transplant is successful, the new bone marrow will start making healthy blood cells and improve the patient's condition.

Learn more about bone marrow donation, and consider whether you might want to do it yourself. Find reliable sources to answer the following questions:

1. How does one become a potential bone marrow donor?
2. Who can and who cannot donate bone marrow?
3. How is a bone marrow donation made?
4. What risks are there in donating bone marrow?

REVIEW

1. Describe osseous tissue.
2. Why are bones hard but not brittle?
3. Compare and contrast the two main types of osseous tissue.
4. What non-osseous tissues are found in bones?
5. List four types of bone cells and their functions.
6. Identify six types of bones, and give an example of each type.
7. *True or False.* Spongy bone tissue is another name for bone marrow.
8. *True or False.* Periosteum covers osseous tissue.
9. Compare and contrast yellow bone marrow and red bone marrow.
10. Which bone is mostly made of cortical bone tissue?

    A. Pelvis

    B. Vertebrae

    C. Femur

    D. Carpal
11. a. Which type of bone cell divides to produce new bone cells?

    b. Where is this cell type located?
12. Where do osteoblasts and osteocytes come from, and how are they related to each other?
13. Which type of bone is embedded in tendons?
14. *True or False.* Calcium is the only mineral in bones.

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8.5: BONE GROWTH, REMODELING, AND REPAIR

BREAK A LEG

Did you ever break a leg or other bone, like the man looking longingly at the water in this swimming pool? Having a broken bone can really restrict your activity. Bones are very hard, but they will break, or fracture if enough force is applied to them. Fortunately, bones are highly active organs that can repair themselves if they break. Bones can also remodel themselves and grow. You'll learn how bones can do all of these things in this concept.



Figure 8.5.1: Broken leg

BONE GROWTH

Early in the development of a human fetus, the skeleton is made almost entirely of cartilage. The relatively soft cartilage gradually turns into hard bone through ossification. **Ossification** is a process in which bone tissue is created from cartilage. The steps in which bones of the skeleton form from cartilage are illustrated in Figure 8.5.2. The steps include the following:

1. Cartilage "model" of bone forms; this model continues to grow as ossification takes place.
2. Ossification begins at a primary ossification center in the middle of the bone.
3. Ossification then starts to occur at secondary ossification centers at the ends of the bone.
4. The medullary cavity forms and will contain red bone marrow.
5. Areas of ossification meet at epiphyseal plates, and articular cartilage forms. Bone growth ends.

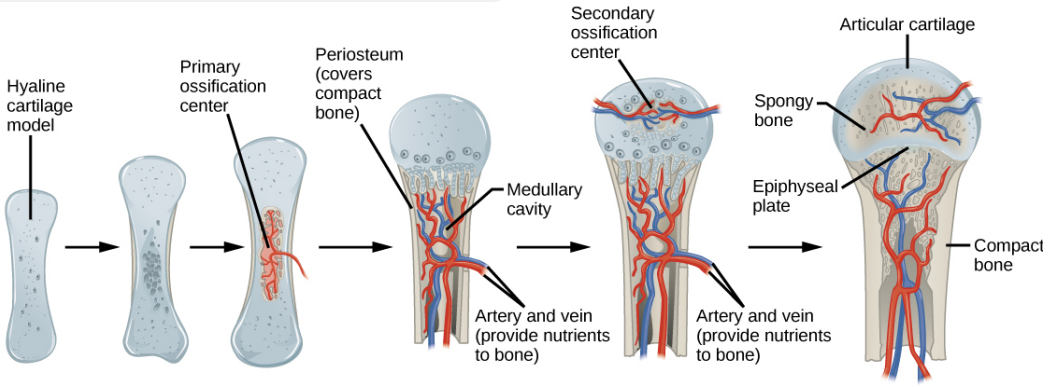


Figure 8.5.2: The ossification of cartilage in the human skeleton is a process that lasts throughout childhood in some bones.

PRIMARY AND SECONDARY OSSIFICATION CENTERS

When bone forms from cartilage, ossification begins with a point in the cartilage called the primary ossification center. This generally appears during fetal development, although a few short bones begin their primary ossification after birth. Ossification occurs toward both ends of the bone from the primary ossification center, and it eventually forms the shaft of the bone in the case of long bones.

Secondary ossification centers form after birth. Ossification from secondary centers eventually forms the ends of the bones. The shaft and ends of the bone are separated by a growing zone of cartilage until the individual reaches skeletal maturity.

SKELETAL MATURITY

Throughout childhood, the cartilage remaining in the skeleton keeps growing and allows for bones to grow in size. However, once all of the cartilage has been replaced by bone and fusion has taken place at epiphyseal plates, bones can no longer keep growing in length. This is the point at which skeletal maturity has been reached. It generally takes place by age 18 to 25.

The use of anabolic steroids by teens can speed up the process of skeletal maturity, resulting in a shorter period of cartilage growth before fusion takes place. This means that teens who use steroids are likely to end up shorter as adults than they would otherwise have been.

BONE REMODELING

Even after skeletal maturity has been attained, bone is constantly being resorbed and replaced with new bone in a process known as **bone remodeling**. In this lifelong process, mature bone tissue is continually turned over, with about 10 percent of the skeletal mass of an adult being remodeled each year. Bone remodeling is carried

out through the work of osteoclasts, which are bone cells that resorb bone and dissolve its minerals; and osteoblasts, which are bone cells that make the new bone matrix.

Bones remodeling serves several functions. It shapes the bones of the skeleton as a child grows, and it repairs tiny flaws in the bone that result from everyday movements. Remodeling also makes bones thicker at points where muscles place the most stress on them. In addition, remodeling helps regulate mineral homeostasis because it either releases minerals from bones into the blood or absorbs minerals from the blood into bones. The figure below shows how osteoclasts in bones are involved in calcium regulation.

The action of osteoblasts and osteoclasts in bone remodeling and calcium homeostasis is controlled by a number of enzymes, hormones, and other substances that either promote or inhibit the activity of the cells. In this way, these substances control the rate at which bone is made, destroyed, and changed in shape. For example, the rate at which osteoclasts resorb bone and release calcium into the blood is promoted by parathyroid hormone (PTH) and inhibited by calcitonin, which is produced by the thyroid gland (Figure 8.5.3). The rate at which osteoblasts create new bone is stimulated by growth hormone, which is produced by the anterior lobe of the pituitary gland. Thyroid hormone and sex hormones (estrogens and androgens) also stimulate osteoblasts to create new bone.

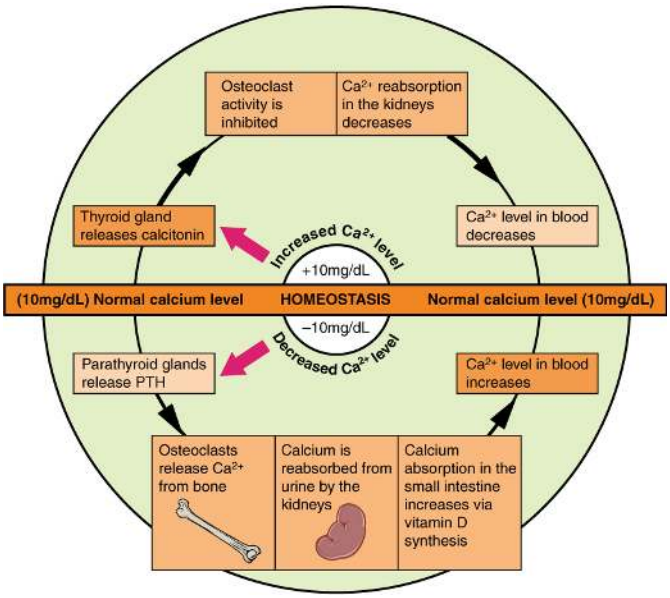


Figure 8.5.3: Keeping the calcium level in homeostasis includes the work of osteoclasts, the bone cells that resorb bone and release calcium into the blood. If calcium levels increase, the thyroid releases calcitonin which inhibits osteoclast activity. This results in less calcium be reabsorbed in the kidneys which results in the lowering of calcium in the blood. If calcium levels decrease below homeostasis, the parathyroid gland releases PTH. This causes osteoclasts to release calcium from bones and increases calcium absorption in the kidney and small intestines. This brings calcium back to homeostasis.

BONE REPAIR

Bone repair, or healing, is the process in which a bone repairs itself following a bone fracture. You can see an X-ray of bone fracture in Figure 8.5.4. In this fracture, the humerus in the upper arm has been completely broken through its shaft. Before this fracture heals, a physician must push the displaced bone parts back into their correct positions. Then the bone must be stabilized — for example, with a cast and/or pins surgically inserted into the bone — until the bone's natural healing process is completed. This process may take several weeks.

The process of bone repair is mainly determined by the periosteum, which is the connective tissue membrane covering the bone. The periosteum is the primary source of precursor cells that develop into osteoblasts, which are essential to the healing process. Bones heal as osteoblasts form new bone tissue.

Although bone repair is a natural physiological process, it may be promoted or inhibited by several factors. For example, fracture repair is likely to be more successful with adequate nutrient intake. Age, bone type, drug therapy, and pre-existing bone disease are additional factors that may affect healing. Bones that are weakened by diseases, such as osteoporosis or bone cancer, are not only likely to heal more slowly but are also more likely to fracture in the first place.



Figure 8.5.4: A bone fracture does not always involve a complete break in the bone, as in this X-ray. Sometimes a fracture is just a crack in the bone. In other cases, the bone not only breaks all the way through, as here but also breaks through the soft tissues around it so it protrudes from the skin. This is called an open fracture.

FEATURE: MYTH VS. REALITY

Bone fractures are fairly common, and there are many myths about them. Knowing the facts is important because fractures generally require emergency medical treatment.

Myth: A bone fracture is a milder injury than a broken bone.

Reality: A bone fracture is the same thing as a broken bone.

Myth: If you still have a full range of motion in a limb, then it must not be fractured.

Reality: Even if a bone is fractured, the muscles and tendons attached to it may still be able to move the bone normally. This

is especially likely if the bone is cracked but not broken into two pieces. Even if a bone is broken all the way through, the range of motion may not be much affected if the bones on either side of the fracture remain properly aligned.

Myth: A fracture always produces a bruise.

Reality: Many but not all fractures produce a bruise. If a fracture does produce a bruise, it may take several hours or even a day or more for the bruise to appear.

Myth: Fractures are so painful that you will immediately know if you break a bone.

Reality: Ligament sprains and muscle strains are also very painful, sometimes more painful than fractures. Additionally, every person has a different pain tolerance. People with high pain tolerance may continue using a broken bone in spite of the pain.

Myth: You can tell when a bone is fractured because there will be very localized pain over the break.

Reality: A broken bone is often accompanied by injuries to surrounding muscles or ligaments. As a result, the pain may extend far beyond the location of the fracture. The pain may be greater directly over the fracture, but the intensity of the pain may make it difficult to pinpoint exactly where the pain originates.

REVIEW

1. Outline how bone develops from early in the fetal stage through the age of skeletal maturity.
2. Describe the process of bone remodeling. When does it occur?
3. What purposes does bone remodeling serve?
4. Define bone repair. How long does this process take?
5. Explain how bone repair occurs.
6. Identify factors that may affect bone repair.
7. Parts of bone that have not yet become ossified are made of _____.
8. If there is a large region between the primary and secondary ossification centers in a bone, is the person young or old? Explain your answer.
9. The region where the primary and secondary ossification centers meet is called the _____.
10. *True or False.* Most bones are made entirely of cartilage at birth.
11. *True or False.* A broken bone is the same as a bone fracture.
12. If bones can repair themselves, why are casts and pins sometimes needed?
13. Which bone cell type causes the release of calcium to the bloodstream when calcium levels are low?
14. Which tissue and bone cell type are mainly involved in bone repair after a fracture?
15. Describe one way in which hormones are involved in bone remodeling.

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8.6: JOINTS

DOUBLE JOINTED?

Is this person double jointed? No; there is no such thing, at least as far as humans are concerned. However, some people, like the individual pictured here, are much more flexible than others, generally because they have looser ligaments. Physicians call the condition joint hypermobility. Regardless of what it's called, the feats of people with highly mobile joints can be quite impressive.



Figure **8.6.1**: Yoga

WHAT ARE JOINTS?

Joints are locations at which bones of the skeleton connect with one another. A joint is also called an articulation. The majority of joints are structured in such a way that they allow movement. However, not all joints allow movement. Of joints that do allow movement, the extent, and direction of the movements they allow also vary.

CLASSIFICATION OF JOINTS

Joints can be classified as structurally or functionally. The structural classification of joints depends on the manner in which the bones connect to each other. The functional classification of joints depends on the nature of the movement the joints allow. There is significant overlap between the two types of classifications because function depends largely on the structure.

STRUCTURAL CLASSIFICATION OF JOINTS

The structural classification of joints is based on the type of tissue that binds the bones to each other at the joint. There are three types of joints in the structural classification: fibrous, cartilaginous, and synovial joints.

1. **Fibrous joints** are joints in which bones are joined by dense connective tissue that is rich in collagen fibers. These joints are also called sutures. The joints between bones of the cranium are fibrous joints.
2. **Cartilaginous joints** are joints in which bones are joined by cartilage. The joints between most of the vertebrae in the spine are cartilaginous joints.
3. **Synovial joints** are characterized by a fluid-filled space, called a synovial cavity, between the bones of the joints. You can see a drawing of a typical synovial joint in Figure **8.6.2**. The cavity is enclosed by a membrane and filled with a fluid, called the synovial fluid, which provides extra cushioning to the ends of the bones. Cartilage covers the articulating surfaces of the two bones, but the bones are actually held together by ligaments. The knee is a synovial joint.

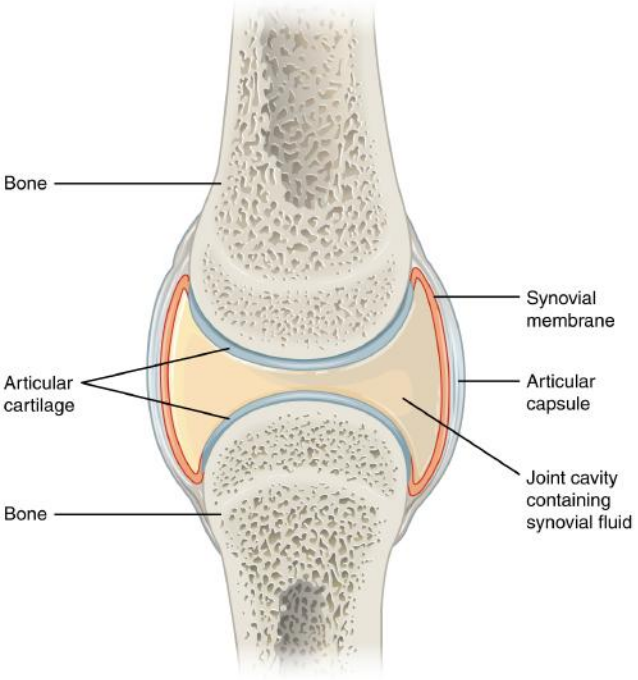


Figure **8.6.2**: The synovial membrane, articular capsule, joint cavity with synovial fluid, articular cartilage, and bone ends are the main components of a typical synovial joint.

FUNCTIONAL CLASSIFICATION OF JOINTS

The functional classification of joints is based on the type and degree of movement that they allow. There are three types of joints in the functional classification: immovable, partly movable, and movable joints.

1. Immovable joints allow little or no movement at the joint. Most immovable joints are fibrous joints. Besides the bones of the cranium, immovable joints include joints between the tibia and fibula in the lower leg and between the radius and ulna in the lower arm.
2. Partly movable joints permit slight movement. Most partly movable joints are cartilaginous joints. Besides the joints between vertebrae, they include the joints between the ribs and sternum (breast bone).
3. Movable joints allow bones to move freely. All movable joints are synovial joints. Besides the knee, they include the shoulder, hip, and elbow. Movable joints are the most common type of joints in the body.

TYPES OF MOVABLE JOINTS

Movable joints can be classified further according to the type of movement they allow. There are six classes of movable joints: pivot, hinge, saddle, plane, condyloid, and ball-and-socket joints. An example of each class, as well as the type of movement it allows, is shown in Figure **8.6.3**.

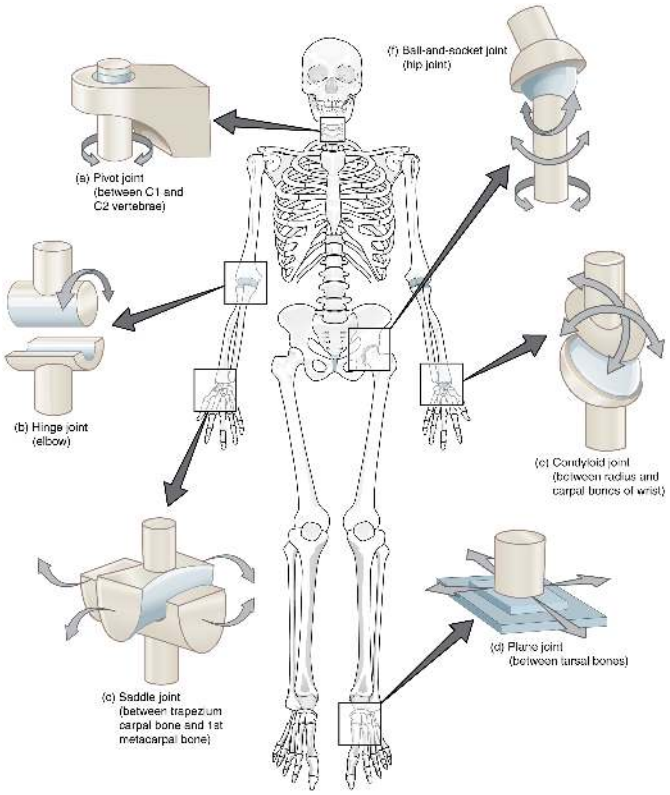


Figure **8.6.3**: This diagram shows the six classes of movable joints in the human body. All of these joints are synovial joints.

- A pivot joint allows one bone to rotate around another. An example of a pivot joint is the joint between the first two vertebrae in the spine. This joint allows the head to rotate from left to right and back again.
- A hinge joint allows back and forth movement like the hinge of a door. An example of a hinge joint is the elbow. This joint allows the arm to bend back and forth.
- A saddle joint allows two different types of movement. An example of a saddle joint is the joint between the first metacarpal bone in the hand and one of the carpal bones in the wrist. This joint allows the thumb to move toward and away from the index finger and also to cross over the palm toward the little finger.
- A plane joint also called a gliding joint, allows two bones that glide over one another. The joints between the tarsals in the ankles and between the carpals in the wrists are mainly gliding joints. In the wrist, this type of joint allows the hand to bend upward at the wrist and also to wave from side to side while the lower arm is held steady.
- A condyloid joint is one in which an oval-shaped head on one bone moves in an elliptical cavity in another bone, allowing movement in all directions except rotation around an axis. The joint between the radius in the lower arm and carpal bones of the wrist is a condyloid joint as is the joint at the base of the index finger.
- A ball-and-socket joint allows the greatest range of movement of any movable joint. It allows forward and backward as well as upward and downward motions. It also allows rotation in a circle. The hip and shoulder are the only two ball-and-socket joints in the human body.

FEATURE: MY HUMAN BODY

Of all the parts of the skeletal system, the joints are generally the most fragile and subject to damage. If the cartilage that cushions bones at joints wears away, it does not grow back. Eventually, all of the cartilage may wear away. This is the cause of osteoarthritis, which can be both painful and debilitating. In serious cases, people may lose the ability to climb stairs, walk long distances, perform routine daily activities, or participate in activities they love such as gardening or playing sports. If you protect your joints, you can reduce your chances of joint damage, pain, and disability. If you already have joint damage, it is equally important to protect your joints and limit further damage. Follow these five tips:

1. Maintain a normal, healthy weight. The higher your weight is, the more force you exert on your joints. When you walk, each knee has to bear a force equal to as much as six times your body weight. If a person weighs 200 pounds, each knee bears more than half a ton of weight with every step. Seven in ten knee replacement surgeries for osteoarthritis can be attributed to obesity.
2. Avoid too much high-impact exercise. Examples of high-impact activities include volleyball, basketball, and tennis. These activities generally involve running or jumping on hard surfaces, which puts tremendous stress on weight-bearing joints, especially the knees. Replace some or all of your high-impact activities with low-impact activities, such as biking, swimming, yoga, or lifting light weights.
3. Reduce your risk of injury. Don't be a weekend warrior, sitting at a desk all week and then crowding all your physical activity into two days. Get involved in a regular, daily exercise routine that keeps your body fit and your muscles toned. Building up muscles will make your joints more stable and spread stress across them. Be sure to do some stretching every day to keep the muscles around joints flexible and less prone to injury.
4. Distribute work over your body, and use your largest, strongest joints. Use your shoulder, elbow, and wrist to lift heavy objects, not just your fingers. Hold small items in the palm of your hand, rather than by the fingers. Carry heavy items in a backpack rather than in your hands. Hold weighty objects close to your body rather than at arms' length. Lift with your hips and knees, not your back.
5. Respect pain. If it hurts, stop doing it. Take a break from the activity at least until the pain stops. Try to use joints only to the point of mild fatigue, not pain.

REVIEW

1. What are the joints?
2. What are the two ways that joints are commonly classified?

3. How are joints classified structurally?
4. Describe the functional classification of joints.
5. How are movable joints classified?
6. Name the six classes of movable joints, and describe how they move.
7. Give an example of a joint in each of the classes of movable joints.
8. *True or False.* The skull is one smooth bone and has no joints.
9. *True or False.* A plane joint is a type of synovial joint.
10. Which specific type of moveable joint do you think your knee joint is? Explain your reasoning.
11. Explain the difference between cartilage in a cartilaginous joint and cartilage in a synovial joint.
12. Why are fibrous joints immovable?
13. Which type of joint has ligaments?

    A. Ball-and-socket
    B. Fibrous
    C. Cartilaginous
    D. None of the above

14. Which type of joint allows for the greatest range of motion?
15. What is the function of synovial fluid?

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8.7: DISORDERS OF THE SKELETAL SYSTEM

DOWAGER'S HUMP

The individual on the right in Figure **8.7.1** has a deformity in her back commonly called dowager's hump because it occurs most often in elderly women. Its medical name is kyphosis, and it is defined as excessive curvature of the spinal column in the thoracic region. The curvature generally results from fractures of thoracic vertebrae. As the inset drawings suggest, these fractures may occur due to a significant decrease in bone mass, which is called osteoporosis. Osteoporosis is one of the most prevalent disorders of the skeletal system.



Figure **8.7.1**: Kyphosis

COMMON SKELETAL SYSTEM DISORDERS

A number of disorders affect the skeletal system, including bone fractures and bone cancers. However, the two most common disorders of the skeletal system are osteoporosis and osteoarthritis. At least ten million people in the United States have osteoporosis, and more than 8 million of them are women. Osteoarthritis is even more common, affecting almost 30 million people in the United States. Because osteoporosis and osteoarthritis are so common, they are the focus of this concept. These two disorders are also good examples to illustrate the structure and function of the skeletal system.

OSTEOPOROSIS

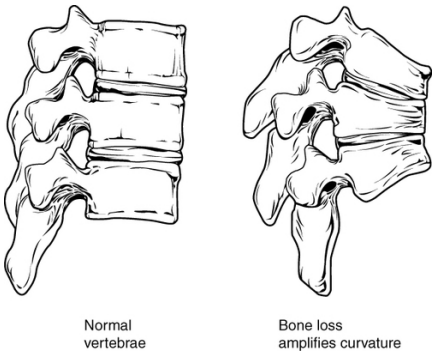


Figure **8.7.2**: Compression fractures of thoracic vertebrae are relatively common in people with osteoporosis.

Osteoporosis is an age-related disorder in which bones lose mass, weaken, and break more easily than normal bones. Bones may weaken so much that a fracture can occur with minor stress — or even spontaneously, without any stress at all. Osteoporosis is the most common cause of broken bones in the elderly, but until a bone fracture occurs, it typically causes no symptoms. The bones that break most often include those in the wrist, hip, shoulder, and spine. When the thoracic vertebrae are affected, there can be a gradual collapse of the vertebrae due to compression fractures, as shown in Figure **8.7.2**. This is what causes kyphosis, as pictured in Figure **8.7.1**.

CHANGES IN BONE MASS WITH AGE

As shown in the graph below, bone mass in both males and females generally peaks when people are in their thirties. Bone mass usually decreases after that, and this tends to occur more rapidly in individuals with XX chromosomes, especially after menopause. This is generally attributable to low levels of estrogen in the post-menopausal years.

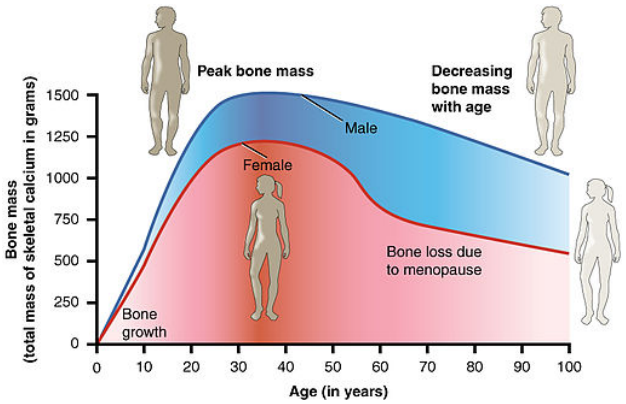


Figure **8.7.3**: Bone mass is a measure of the total mass of calcium in the bones of the skeleton. The chart shows that the bone mass peaks around age 30 in males and females. Then it starts to decrease.

WHAT CAUSES OSTEOPOROSIS?

Osteoporosis is due to an imbalance between bone formation by osteoblasts and bone resorption by osteoclasts. Normally, bones are constantly being remodeled by these two processes, with up to ten percent of all bone mass undergoing remodeling at any point in time. If these two processes are in balance, no net loss of bone occurs. There are three main ways that an imbalance between bone formation and bone resorption can occur and lead to a net loss of bone.

1. **An individual never develops normal peak bone mass during the young adult years:** If the peak level is lower than normal, then there is less bone mass, to begin with, making osteoporosis more likely to develop.
2. **There is greater than normal bone resorption:** Bone resorption normally increases after peak bone mass is reached, but age-related bone resorption may be greater than normal for a variety of reasons. One possible reason is calcium or vitamin D

deficiency, which causes the parathyroid gland to release PTH, the hormone that promotes resorption by osteoclasts.

3. **There is the inadequate formation of new bone by osteoblasts during remodeling:** Lack of estrogen may decrease the normal deposition of new bone. Inadequate levels of calcium and vitamin D also lead to the impaired bone formation by osteoblasts.

An imbalance between bone building and bone destruction leading to bone loss may also occur as a side effect of other disorders. For example, people with alcoholism, anorexia nervosa, or hyperthyroidism have an increased rate of bone loss. Some medications — including anti-seizure medications, chemotherapy drugs, steroid medications, and some antidepressants — also increase the rate of bone loss.

OSTEOPOROTIC FRACTURES

Fractures are the most dangerous aspect of osteoporosis, and osteoporosis is responsible for millions of fractures annually. Debilitating pain among the elderly is often caused by fractures from osteoporosis, and it can lead to further disability and early mortality. Fractures of the long bones (such as the femur) can impair mobility and may require surgery. A hip fracture usually requires immediate surgery, as well. The immobility associated with fractures — especially of the hip — increases the risk of deep vein thrombosis, pulmonary embolism, and pneumonia. Osteoporosis is rarely fatal, but these complications of fractures often are. Older people tend to have more falls than younger people, due to such factors as poor eyesight and balance problems, increasing their risk of fractures even more. The likelihood of falls can be reduced by removing obstacles and loose carpets or rugs in the living environment.

RISK FACTORS FOR OSTEOPOROSIS

There are a number of factors that increase the risk of osteoporosis. Eleven of them are listed below. The first five factors cannot be controlled, but the remaining factors generally can be controlled by changing behaviors.

1. older age
2. XX chromosome
3. European or Asian ancestry
4. family history of osteoporosis
5. short stature and small bones
6. smoking
7. alcohol consumption
8. lack of exercise
9. vitamin D deficiency
10. poor nutrition
11. consumption of soft drinks

TREATMENT AND PREVENTION OF OSTEOPOROSIS

Osteoporosis is often treated with medications that may slow or even reverse bone loss. Medications called bisphosphonates, for example, are commonly prescribed. Bisphosphonates slow down the breakdown of bone, allowing bone rebuilding during remodeling to keep pace. This helps maintain bone density and decreases the risk of fractures. The medications may be more effective in patients who have already broken bones than in those who have not, significantly reducing their risk of another fracture. Generally, patients are not recommended to stay on bisphosphonates for more than three or four years. There is no evidence for continued benefit after this time — in fact, there is a potential for adverse side effects.



Figure **8.7.4**: Hiking is an enjoyable way to help keep bones strong and reduce the risk of osteoporosis.

Preventing osteoporosis includes eliminating any risk factors that can be controlled through changes of behavior. If you smoke, stop. If you drink, reduce your alcohol consumption — or cut it out altogether. Eat a nutritious diet and make sure you are getting adequate amounts of vitamin D. You should also avoid drinking carbonated beverages.

If you're a couch potato, get involved in regular exercise. Aerobic, weight-bearing and resistance exercises can all help maintain or increase bone mineral density. Exercise puts stress on bones, which stimulates bone building. Good weight-bearing exercises for bone-building include weight training, dancing, stair climbing, running, and hiking (Figure **8.7.4**). Biking and swimming are less beneficial because they don't stress the bones. Ideally, you should exercise for at least 30 minutes a day on most days of the week.

OSTEOARTHRITIS

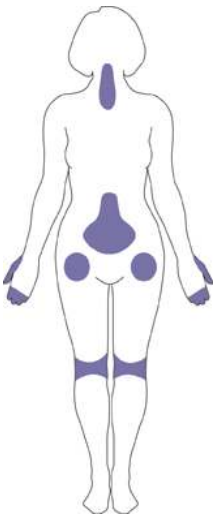


Figure **8.7.5**: The areas shaded in blue indicate the joints most commonly affected by OA.

Osteoarthritis (OA) is a joint disease that results from the breakdown of joint cartilage and bone. The most common symptoms are joint pain and stiffness. Other symptoms may include joint swelling and decreased range of motion. Initially, symptoms may

occur only after exercise or prolonged activity, but over time, they may become constant, negatively affecting work and normal daily activities. As shown in Figure 8.7.5, the most commonly involved joints are those near the ends of the fingers, at the bases of the thumbs, and in the neck, lower back, hips, and knees. Often, joints on one side of the body are affected more than those on the other side.

WHAT CAUSES OSTEOARTHRITIS?

OA is thought to be caused by mechanical stress on the joints with insufficient self-repair of cartilage. The stress may be exacerbated by low-grade inflammation of the joints, as cells lining the joint attempt to remove breakdown products from cartilage in the synovial space. OA develops over decades as stress and inflammation cause an increasing loss of articular cartilage. Eventually, bones may have no cartilage to separate them, so bones rub against one another at joints. This damages the articular surfaces of the bones and contributes to the pain and other symptoms of OA. Because of the pain, movement may be curtailed, leading to loss of muscle, as well.

DIAGNOSING OSTEOARTHRITIS

Diagnosis of OA is typically made on the basis of signs and symptoms. Signs include joint deformities, such as bony nodules on the finger joints or bunions on the feet (Figure 8.7.6). Symptoms include joint pain and stiffness. The pain is usually described as a sharp ache or burning sensation, which may be in the muscles and tendons around the affected joints, as well as in the joints themselves. The pain is usually made worse by prolonged activity, and it typically improves with rest. Stiffness is most common when first arising in the morning, and it usually improves quickly as daily activities are undertaken.



Figure 8.7.6. A bunion is a common sign of osteoarthritis. It is typically located at the base of the big toe.

X-rays or other tests are sometimes used to either support the diagnosis of OA or to rule out other disorders. Blood tests might be done, for example, to look for factors that indicate rheumatoid arthritis (RA), an autoimmune disease in which the immune system attacks the body's joints. If these factors are not present in the blood, then RA is unlikely, and a diagnosis of OA is more likely to be correct.

RISK FACTORS FOR OSTEOARTHRITIS

Age is the chief risk factor for osteoarthritis. By age 65, as many as 80 percent of all people have evidence of osteoarthritis. However, people are more likely to develop OA — especially at younger ages — if they have had a joint injury. A high school football player might have a bad knee injury that damages the joint, leading to OA in the knee by the time he is in his thirties. If people have joints that are misaligned due to congenital malformations or disease, they are also more likely to develop OA. Excess body weight is another factor that increases the risk of OA, because of the added stress it places on weight-bearing joints.

Researchers have found that people with a family history of OA have a heightened risk of developing the disorder, which suggests that genetic factors are also involved in OA. It is likely that many different genes are needed for normal cartilage and cartilage repair. If such genes are defective and cartilage is abnormal or not normally repaired, OA is more likely to result.

TREATMENT AND PREVENTION OF OSTEOARTHRITIS

OA cannot be cured, but the symptoms — especially the pain — can often be treated successfully to maintain a good quality of life for people with OA. Treatments include exercise, efforts to decrease stress on joints, pain medications, and surgery.

DESTRESSING JOINTS

Efforts to decrease stress on joints include resting and using mobility devices such as canes, which reduce the weight placed on weight-bearing joints and also improve stability. In people who are overweight, losing weight may also reduce joint stress.

EXERCISE

Exercise helps maintain joint mobility and also increases muscle strength. Stronger muscles may help keep the bones in joints correctly aligned, and this can reduce joint stress. Good exercises for OA include swimming, water aerobics (see Figure 8.7.7), and biking. These activities are recommended for OA because they put relatively little stress on the joints.



Figure 8.7.7: Exercising in water provides buoyancy that places less stress on joints than the same exercises would on the ground or other hard surfaces.

PAIN MEDICATIONS

The first type of pain medication likely to be prescribed for OA is acetaminophen (e.g., Tylenol). When taken as prescribed, it has a relatively low risk of serious side effects. If this medication is inadequate to relieve the pain, non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen) may be prescribed. NSAIDs, however, are more likely to cause serious side effects, such as gastrointestinal bleeding, elevated blood pressure, and increased risk of stroke. Opioids usually are reserved for patients who have suffered serious side effects or for whom other medications have failed to relieve pain. Due to the risk of addiction, the short-term use of opioids is generally recommended.

SURGERY

Joint replacement surgery is the most common treatment for serious OA in the knee or hip. In fact, knee and hip replacement surgeries are among the most common of all surgeries. Although they require a long period of healing and physical rehabilitation, the results are usually worth it. The replacement "parts" are usually pain-free and fully functional for at least a couple of decades. Quality, durability, and customization of artificial joints are constantly improving.

FEATURE: MYTH VS. REALITY

About one out of every two Americans will develop osteoarthritis in his or her lifetime. The more you know about this disease, the more you can do to avoid it or slow its progression. That means knowing the facts, rather than believing the myths about osteoarthritis.

Myth: Cracking my knuckles will cause osteoarthritis.

Reality: Cracking your knuckles may lead to inflammation of your tendons, but it will not cause osteoarthritis.

Myth: My diet has no effect on my joints.

Reality: What and how much you eat *does* affect your body weight, and every pound you gain translates into an additional four pounds (or more!) of stress on your knees. Being overweight, therefore, increases the chances of developing osteoarthritis — and also the rate at which it progresses.

Myth: Exercise causes osteoarthritis or makes it worse, so I should avoid it.

Reality: This is one of the biggest myths about osteoarthritis. Low-impact exercise can actually lessen the pain and improve other symptoms of osteoarthritis. If you don't have osteoarthritis, exercise can reduce your risk of developing it. Low-impact exercise helps keep the muscles around joints strong and flexible, so they can help stabilize and protect the joints.

Myth: If my mom or dad has osteoarthritis, I will also develop it.

Reality: It is true that you are more likely to develop osteoarthritis if a parent has it, but it isn't a sure thing. There are several things you can do to decrease your risk, such as getting regular exercise and maintaining a healthy weight.

Myth: Bad weather causes osteoarthritis.

Reality: Weather conditions do not cause osteoarthritis, although, in some people who already have osteoarthritis, bad weather seems to make the symptoms worse. It is primarily low barometric pressure that increases osteoarthritis pain, probably because it leads to greater pressure inside the joints relative to the outside air pressure. Some people think their osteoarthritis pain is worse in cold weather, but systematic studies have not found convincing evidence for this.

Myth: Joint pain is unavoidable as you get older, so there is no need to see a doctor for it.

Reality: Many people with osteoarthritis think there is nothing that can be done for the pain of osteoarthritis, or that surgery is the only treatment option. In reality, osteoarthritis symptoms often can be improved with a combination of exercise, weight loss, pain management techniques, and pain medications. If osteoarthritis pain interferes with daily life and lasts more than a few days, you should see your doctor.

Myth: Osteoarthritis is inevitable in seniors.

Reality: Although many people over 65 develop osteoarthritis, there are many people who never develop it, no matter how old they live to be. You can reduce your risk of developing osteoarthritis in later life by protecting your joints throughout life.

REVIEW

1. Name the two most common disorders of the skeletal system.
2. What is osteoporosis? What causes it?
3. How is osteoporosis diagnosed?
4. Why is osteoporosis dangerous?
5. Identify risk factors for osteoporosis.
6. How is osteoporosis treated? What can be done to prevent it?
7. What is OA? What are its chief symptoms?
8. What causes OA?
9. Describe how OA is diagnosed.
10. Identify risk factors for OA.
11. How is OA treated?
12. Why is it important to build sufficient bone mass in your young adult years?
13. Explain the difference in the cause of rheumatoid arthritis and osteoarthritis.
14. *True or False:* Osteoarthritis is caused by physical activity, so people who are equally active are equally susceptible to it.
15. *True or False:* Estrogen generally promotes the production of new bone.

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ATTRIBUTIONS

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8.8: CASE STUDY CONCLUSION- HEELS AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: A PAIN IN THE FOOT

You may have seen signs such as the one in Figure 8.8.1 indicating that high-heeled shoes are not allowed on certain walking surfaces because of the risk of injury. High heels affect a person's balance, and wearers can easily twist their ankle on uneven or slippery surfaces, causing a sprain or even a fracture. Besides twisting an ankle, wearing high heels on a regular basis can cause a variety of other negative health consequences—some of which may be long-lasting.



Figure 8.8.1: No heels

As Amari discovered at the beginning of the chapter, wearing high heels can result in a condition called metatarsalgia. Metatarsalgia is named for the metatarsal bones, which are the five bones that run through the ball of the foot just behind the toes (highlighted in Figure 8.8.2) Wearing high heels causes excessive pressure on the ball of the foot, as described at the beginning of this chapter. Additionally, the toes are forced to pull upwards in high heels, which moves the fleshy padding away from the ball of the foot, adding to the overall pressure placed on this region. Over time, this can cause inflammation and direct stress on the bones, resulting in pain in the ball of the foot known as metatarsalgia. The pain particularly occurs in weight-bearing positions such as standing, walking, or running—which is what Amari was experiencing. There may also be pain, numbness, or tingling in the toes associated with metatarsalgia.

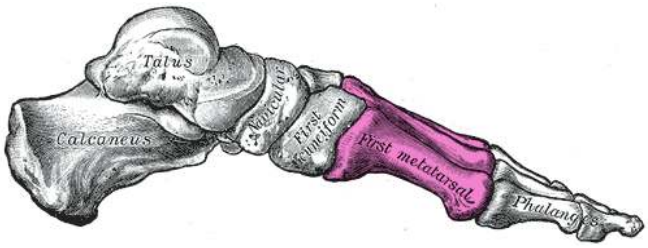


Figure 8.8.2: Illustration of the bones of the foot, with the metatarsal bones highlighted in pink.

Wearing high heels can also cause stress fractures in the feet, which are tiny breaks in the bone that occur due to repeated mechanical stress. This is due to the excessive pressure that high heels put on some of the bones of the feet. These fractures are somewhat similar to what occurs in osteoporosis when the bone mass decreases to the point where bones can fracture easily as people go about their daily activities. In both cases, a major, noticeable injury is not necessary to create tiny fractures. As you have learned, tiny fractures that accrue over time are the cause of dowager's hump, or kyphosis, which is often seen in women with osteoporosis.

Don't think you are immune to stress fractures just because you don't wear high heels! This injury also commonly occurs in people who participate in sports that involve repetitive striking of the foot on the ground, such as running, tennis, basketball, or gymnastics. Stress fractures may be avoided by taking preventative measures such as ramping up any increase in activity slowly, cross-training by engaging in a variety of different sports or activities, resting if you experience pain, and wearing well-cushioned and supportive running shoes.

Amari learned through their online research that wearing high heels can also lead to foot deformities such as bunions and hammertoes. As you saw in the section *Disorders of the Skeletal System*, a bunion is a protrusion on the side of the foot, most often at the base of the big toe. It can be caused by wearing shoes with a narrow, pointed toe box — a common shape for high heels (see Figure 8.8.3). The pressure of the shoes on the side of the foot causes an enlargement of bone or inflammation of other tissues in the region, which pushes the big toe towards the other toes.



Figure 8.8.3: High heels with a narrow, pointed toe box and thin stiletto heels.

Hammertoes are abnormal bend in the middle joint of the second, third, or fourth toe (with the big toe being the first toe), causing the toe to be shaped similar to a hammer as seen in Figure 8.8.4. The narrow, pointed toe box of many high heels, combined with the way the toes are squished into the front of the shoe as a result of the height of the heel, can cause the toes to become deformed in this manner. Treatments for bunions and hammertoe include wearing shoes with a roomy toe box, padding or taping the toes, and toe exercises and stretches. If the bunion or hammertoe does not respond to these treatments, surgery may be necessary to correct the deformity.



Figure **8.8.4**: X-ray of a hammer toe.

Because the bones of the skeleton are connected and work together with other systems to support the body, wearing high heels can also cause physical problems in areas other than the feet. Wearing high heels shifts a person's posture and alignment and can put a strain on tendons, muscles, and other joints in the body. For instance, research from a team at Stanford University published in 2014 suggests that wearing high heels, particularly if the person is overweight or the heels are very high, may increase the risk of osteoarthritis (OA) in the knee due to added stress on the knee joint as the person walks. As you have learned, OA results from the breakdown of cartilage and bone at the joint. Because it can only be treated to minimize symptoms, not cured, OA could be an unfortunate long-term consequence of wearing high heels.

Amari has decided that wearing high heels regularly is not worth the pain and potential long-term damage to their body. After consulting with their doctor, who confirmed they have metatarsalgia, Amari was able to successfully treat it with ice, rest, and wearing comfortable, supportive shoes instead of heels.

High heels are not the only kind of shoes that can cause problems. Flip-flops, worn-out sneakers, and shoes that are too tight can all cause foot issues. To prevent future problems from shoe choices, Amari is following guidelines recommended by medical experts, which include:

- Wearing shoes that fit well, have plenty of room in the toe box, are supportive, and are comfortable right away. There should be no "break-in" period needed for shoes.
- Avoiding shoes that have high heels, especially ones over two inches in height; narrow, pointed toe boxes; or very thin heels. The shoes in Figure **8.8.3** are an example of a type that should be avoided!
- If high heels must be worn, they should be worn for only a limited period of time.

As you have learned in this chapter, your skeletal system carries out a variety of important functions in your body, including physical support. But even though it is strong, your skeletal system can become damaged and deformed—even through such a seemingly innocuous act as wearing a certain type of shoe. Taking good care of your skeletal system is necessary to help it continue to take good care of the rest of you.

CHAPTER SUMMARY

In this chapter, you learned about the skeletal system. Specifically, you learned that:

- The skeletal system is the organ system that provides an internal framework for the human body. In adults, the skeletal system contains 206 bones.
- Bones are organs made of dense connective tissues, mainly the tough protein collagen. Bones also contain blood vessels, nerves, and other tissues. Bones are hard and rigid due to deposits of calcium and other mineral salts within their living tissues. Besides bones, the skeletal system includes cartilage and ligaments.
- The skeletal system has many different functions, including supporting the body and giving it shape, protecting internal organs, providing attachment surfaces for skeletal muscles, allowing body movements, producing blood cells, storing minerals, helping to maintain mineral homeostasis, and producing endocrine hormones.
- The skeleton is traditionally divided into two major parts: the axial skeleton and the appendicular skeleton.
- The axial skeleton consists of a total of 80 bones. It includes the skull, vertebral column, and rib cage. It also includes the three tiny ossicles in the middle ear and the hyoid bone in the throat.
    - The skull provides a bony framework for the head. It consists of 22 different bones: eight in the cranium, which encloses the brain, and 14 in the face, which includes the upper and lower jaw.
    - The vertebral column is a flexible, S-shaped column of 33 vertebrae that connects the trunk with the skull and encloses the spinal cord. The vertebrae are divided into five regions: cervical, thoracic, lumbar, sacral, and coccygeal regions. The S shape of the vertebral column allows it to absorb shocks and distribute the weight of the body.
    - The rib cage holds and protects the organs of the upper part of the trunk, including the heart and lungs. It includes the 12 thoracic vertebrae, the sternum, and 12 pairs of ribs.
- The appendicular skeleton consists of a total of 126 bones. It includes the bones of the four limbs, shoulder girdle, and pelvic girdle. The girdles attach the appendages to the axial skeleton.
    - Each upper limb consists of 30 bones. There is one bone, called the humerus, in the upper arm, and two bones, called the ulna and radius, in the lower arm. The wrist contains eight carpal bones, the hand contains five metacarpals, and the fingers consist of 14 phalanges. The thumb is opposable to the palm and fingers of the same hand.
    - Each lower limb also consists of 30 bones. There is one bone, called the femur, in the upper leg, and two bones, called the tibia and fibula, in the lower leg. The patella covers the knee joint. The ankle contains seven tarsal bones, and the foot contains five metatarsals. The tarsals and metatarsals form the heel and arch of the foot. The bones in the toes consist of 14 phalanges.

  - The shoulder girdle attaches the upper limbs to the trunk of the body. It is connected to the axial skeleton only by muscles, allowing mobility of the upper limbs. Bones of the shoulder girdle include a right and left clavicle and a right and left scapula.
  - The pelvic girdle attaches the legs to the trunk of the body and supports the organs of the abdomen. It is connected to the axial skeleton by ligaments. The pelvic girdle consists of two halves that are fused together in adults. Each half consists of three bones: the ilium, pubis, and ischium.
- Bones are organs that consist mainly of bone, or osseous, tissue. Osseous tissue is a type of connective tissue consisting of a collagen matrix that is mineralized with calcium and phosphorus crystals. The combination of flexible collagen and minerals makes bone hard without making it brittle.
  - There are two types of osseous tissues: cortical bone tissue and spongy bone tissue. Cortical bone tissue is smooth and dense. It forms the outer layer of bones. Spongy bone tissue is porous and light. It is found inside many bones.
- Besides osseous tissues, bones also contain nerves, blood vessels, bone marrow, and periosteum.
- Bone tissue is composed of four different types of bone cells: osteoblasts, osteocytes, osteoclasts, and osteogenic cells. Osteoblasts form new collagen matrix and mineralize it, osteoclasts break down bone, osteocytes regulate the formation and breakdown of bone, and osteogenic cells divide and differentiate to form new osteoblasts. Bone is a very active tissue, constantly being remodeled by the work of osteoblasts and osteoclasts.
- There are six types of bones in the human body: long bones such as the limb bones, short bones such as the wrist bones, sesamoid bones such as the patella, sutural bones in the skull, and irregular bones such as the vertebrae.
- Early in the development of a human fetus, the skeleton is made almost entirely of cartilage. The relatively soft cartilage gradually turns into hard bone. This is called ossification. It begins at a primary ossification center in the middle of the bone and later also occurs at secondary ossification centers in the ends of the bone. The bone can no longer grow in length after the areas of ossification meet and fuse at the time of skeletal maturity.
- Throughout life, bone is constantly being replaced in the process of bone remodeling. In this process, osteoclasts resorb bone and osteoblasts make new bone to replace it. Bone remodeling shapes the skeleton, repairs tiny flaws in bones, and helps maintain mineral homeostasis in the blood.
- Bone repair is the natural process in which a bone repairs itself following a bone fracture. This process may take several weeks. In the process, periosteum produces cells that develop into osteoblasts, and the osteoblasts form a new bone matrix to heal the fracture. Bone repair may be affected by diet, age, pre-existing bone disease, or other factors.
- Joints are locations at which bones of the skeleton connect with one another.
- Joints can be classified structurally or functionally, and there is significant overlap between the two types of classifications.
- The structural classification of joints depends on the type of tissue that binds the bones to each other at the joint. There are three types of joints in the structural classification: fibrous, cartilaginous, and synovial joints.
- The functional classification of joints is based on the type and degree of movement that they allow. There are three types of joints in the functional classification: immovable, partly movable, and movable joints.
  - Movable joints can be classified further according to the type of movement they allow. There are six classes of movable joints: pivot, hinge, saddle, plane, condyloid, and ball-and-socket joints.
- A number of disorders affect the skeletal system, including bone fractures and bone cancers. The two most common disorders of the skeletal system are osteoporosis and osteoarthritis.
- Osteoporosis is an age-related disorder in which bones lose mass, weaken, and break more easily than normal bones. The underlying mechanism in all cases of osteoporosis is an imbalance between bone formation and bone resorption in bone remodeling. Osteoporosis may also occur as a side effect of other disorders or certain medications.
  - Osteoporosis is diagnosed by measuring a patient's bone density and comparing it with the normal level of peak bone density. Fractures are the most dangerous aspect of osteoporosis. Osteoporosis is rarely fatal, but complications of fractures often are.
  - Risk factors for osteoporosis include older age, female sex, European or Asian ancestry, family history of osteoporosis, short stature and small bones, smoking, alcohol consumption, lack of exercise, vitamin D deficiency, poor nutrition, and consumption of soft drinks.
  - Osteoporosis is often treated with medications such as bisphosphonates that may slow or even reverse bone loss. Preventing osteoporosis includes eliminating any risk factors that can be controlled through changes of behavior, such as undertaking weight-bearing exercise.
- Osteoarthritis (OA) is a joint disease that results from the breakdown of joint cartilage and bone. The most common symptoms are joint pain and stiffness. OA is thought to be caused by mechanical stress on the joints with insufficient self-repair of cartilage, coupled with low-grade inflammation of the joints.
  - Diagnosis of OA is typically made on the basis of signs and symptoms, such as joint deformities, pain, and stiffness. X-rays or other tests are sometimes used to either support the diagnosis or rule out other disorders. Age is the chief risk factor for OA. Other risk factors include joint injury, excess body weight, and a family history of OA.

- OA cannot be cured, but the symptoms can often be treated successfully. Treatments may include exercise, efforts to decrease stress on joints, pain medications, and surgery to replace affected hip or knee joints.

As you have learned in this chapter, one of the important functions of the skeletal system is to allow movement of the body. But it doesn't do it alone. Movement is caused by the contraction of muscles, which pull on the bones, causing them to move. Read the next chapter to learn about this and other important functions of the muscular system.

CHAPTER SUMMARY REVIEW

1. Hematopoiesis is carried out by:
   A. spongy bone tissue
   B. periosteum
   C. yellow bone marrow
   D. red bone marrow
2. *True or False.* Osteocalcin is a hormone produced by bone cells.
3. *True or False.* Vertebrae make up part of the rib cage.
4. For each of the following bones, indicate whether they are part of the axial or appendicular skeleton.
   A. The ossicles of the middle ear
   B. The femur
   C. The phalanges
   D. The bones of the cranium
   E. The ilium
5. Why does the rib cage need to be flexible and why is it able to be flexible?
6. In general, what do "girdles" in the skeletal system do?
7. Which protein does bone mainly consist of?
   A. Keratin
   B. Collagen
   C. Cellulose
   D. Elastin
8. For each of the descriptions below, identify which process best fits the description. Use each process only once. Processes: bone growth; bone repair; bone remodeling
   A. New osteoblasts form from the periosteum and produce new bone tissue.
   B. Cartilage grows, and the primary and secondary ossification centers move towards each other.
   C. Osteoclasts break down bone tissue and osteoblasts build new bone tissue.
9. For each of the following processes, describe when it occurs.
   A. Bone growth
   B. Bone repair
   C. Bone remodeling
10. Would swimming likely be more effective as an exercise for preventing osteoporosis or as a treatment for osteoarthritis? Explain your answer.
11. *True or False.* Use of anabolic steroids in the teenage years generally makes people taller.
12. *True or False.* The largest joint in the human body is the knee joint.
13. How much of an adult's skeletal mass is broken down and rebuilt each year?
    A. None
    B. 5 percent
    C. 10 percent
    D. 30 percent
14. Explain why some of the vertebrae become misshapen in the condition called dowager's hump, or kyphosis.
15. Explain why osteoarthritis often involves inflammation in the joints.
16. Osteoporosis can involve both excess bone resorption as well as insufficient production of new bone tissue. What are the two main bone cell types that carry out these processes, respectively?
17. *True or False.* Bone mass does not decrease as men age.
18. *True or False.* Ideally, a person's spine would be perfectly straight and rigid.
19. Compare and contrast a tendon and a ligament.
20. Describe two roles that calcium plays in the bones of the body.
21. How many bones are in the adult human skeleton?
    A. 80
    B. 126
    C. 206
    D. 270

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CHAPTER OVERVIEW

9: MUSCULAR SYSTEM

This chapter describes the structure and functions of the muscular system. It compares and contrasts the three major types of muscle tissue and explains in detail how muscles contract according to the sliding filament theory. The chapter also relates physical exercise to fitness and health and describes several musculoskeletal and neuromuscular disorders.

9.1: Case Study- Muscles and Movement

9.2: Introduction to the Muscular System

9.3: Types of Muscle Tissue

9.4: Muscle Contraction

9.5: Physical Exercise

9.6: Disorders of the Muscular System

9.7: Case Study Conclusion- Needing to Relax and Chapter Summary

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9.1: CASE STUDY- MUSCLES AND MOVEMENT

CASE STUDY: NEEDING TO RELAX

The dog in Figure **9.1.3** is expressing his interest in something—perhaps a piece of food—by using the neck muscles to tilt its head in an adorable fashion. Humans also sometimes tilt their heads to express interest. But imagine how disturbing and painful it would be if your neck tilted involuntarily, without you being able to control it! Forty-three-year-old Nasir, unfortunately, knows just how debilitating this can be. Nasir uses they, them, and their pronouns.



Figure **9.1.1**: Curious dog

Nasir has a rare condition called cervical dystonia, which is also called spasmodic torticollis. In this condition, the muscles in the neck contract involuntarily, often causing the person's head to twist to one side. The illustration in Figure **9.1.2** shows one type of abnormal head positioning that can be caused by cervical dystonia. The muscles may contract in a sustained fashion, holding the head and neck in one position, or they may spasm repeatedly, causing jerky movements of the head and neck.

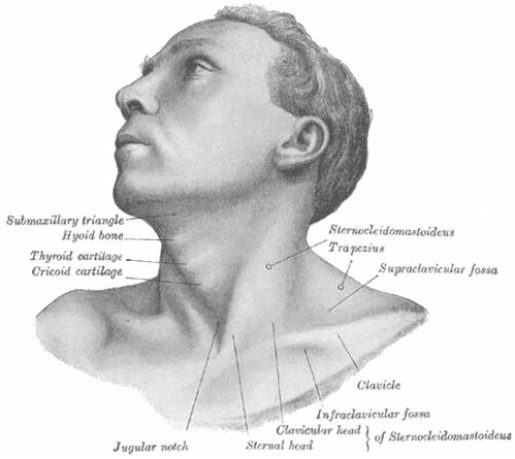


Figure **9.1.2**: Illustration from a medical book written around 1910, showing a person identified as having spasmodic torticollis. The person's neck is permanently tilted to the side.

Cervical dystonia is painful and can significantly interfere with individuals' ability to carry out their usual daily activities. In Nasir's case, they can no longer drive a car, because their uncontrollable head and neck movements and abnormal head positioning prevent them from navigating the road safely. Nasir also has severe neck and shoulder pain much of the time.

Although it can be caused by an injury, there is no known cause of cervical dystonia—and there is also no cure. Fortunately for Nasir and other cervical dystonia sufferers, though, there is a treatment that can significantly reduce symptoms in many people. You may be surprised to learn that this treatment is the same substance that, when injected into the face, is used for cosmetic purposes to reduce wrinkles!

The substance is botulinum toxin, one preparation of which may be familiar to you by its brand name: Botox. It is a neurotoxin produced by the bacterium *Clostridium botulinum*, and can cause a life-threatening illness called botulism. However, when injected in very small amounts by a skilled medical professional, botulinum toxins have some safe and effective uses. In addition to cervical dystonia, botulinum toxins can be used to treat other disorders involving the muscular system, such as strabismus (misalignment of the eyes), eye twitches, excessive muscle contraction due to neurological conditions like cerebral palsy; and even overactive bladder.

Botulinum toxin has its effect on the muscular system by inhibiting muscle contractions. When used to treat wrinkles, it relaxes the muscles of the face, lessening the appearance of wrinkles. When used to treat cervical dystonia and other disorders involving excessive muscle contraction, it reduces abnormal contractions.

In this chapter, you will learn about the muscles of the body, how they contract to produce movements and carry out their functions, and some disorders that affect the muscular system. At the end of the chapter, you will find out if botulinum toxin helped relieve Nasir's cervical dystonia, and how this toxin works to inhibit muscle contraction.

CHAPTER OVERVIEW: MUSCULAR SYSTEM

In this chapter, you will learn about the muscular system, which carries out both voluntary body movements and involuntary contractions of internal organs and structures. Specifically, you will learn about:

- The different types of muscle tissue—skeletal, cardiac, and smooth muscle—and their different characteristics and functions
- How muscle cells are specialized to contract and cause voluntary and involuntary movements
- The ways in which muscle contraction is controlled
- How skeletal muscles can grow or shrink, causing changes in strength
- The structure and organization of skeletal muscles (including the different types of muscle fibers) and how actin and myosin

filaments move across each other, according to the sliding filament theory, to cause muscle contraction
- How cardiac muscle tissue in the heart contracts to pump blood through the body
- Smooth muscle tissue that makes up internal organs and structures, such as the digestive system, blood vessels, and uterus
- The physical and mental health benefits of aerobic and anaerobic exercise, such as running and weight lifting
- How individuals vary in their response to exercise
- Disorders of the muscular system, including musculoskeletal disorders (such as strains and carpal tunnel syndrome) and neuromuscular disorders (such as muscular dystrophy, myasthenia gravis, and Parkinson's disease)

As you read the chapter, think about the following questions:

1. How is the contraction of skeletal muscles controlled?
2. Botulinum toxin works on the cellular and molecular levels to inhibit muscle contraction. Based on what you learn about how muscle contraction works, can you think of some ways it could potentially be inhibited?
3. What is one disorder involving a lack of sufficient muscle contraction? Why does it occur?

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9.2: INTRODUCTION TO THE MUSCULAR SYSTEM

MARVELOUS MUSCLES

Does the word *muscle* make you think of the well-developed muscles of a weightlifter, like a woman in Figure **9.2.1**? Her name is Natalia Zabolotnaya, and she's a Russian Olympian. The muscles that are used to lift weights are easy to feel and see, but they aren't the only muscles in the human body. Many muscles are deep within the body, where they form the walls of internal organs and other structures. You can flex your biceps at will, but you can't control internal muscles like these. It's a good thing that these internal muscles work without any conscious effort on your part because the movement of these muscles is essential for survival. Muscles are the organs of the muscular system.



Figure **9.2.1**: weightlifter lifting weight over her head.

WHAT IS THE MUSCULAR SYSTEM?



Figure **9.2.2**: Many of the skeletal muscles in the human muscular system are shown in this drawing of the human body.

The **muscular system** consists of all the muscles of the body. The largest percentage of muscles in the muscular system consists of skeletal muscles, which are attached to bones and enable voluntary body movements. There are almost 650 skeletal muscles in the human body, many of them shown in Figure **9.2.2**. Besides skeletal muscles, the muscular system also includes cardiac muscle — which makes up the walls of the heart — and smooth muscles, which control movement in other internal organs and structures.

MUSCLE STRUCTURE AND FUNCTION

Muscles are organs composed mainly of muscle cells, which are also called **muscle fibers** (mainly in skeletal and cardiac muscle) or **myocytes** (mainly in smooth muscle). Muscle cells are long and thin cells that are specialized for the function of contracting. They contain protein filaments that slide over one another using energy in ATP. The sliding filaments increase the tension in — or shorten the length of — muscle cells, causing a contraction. Muscle contractions are responsible for virtually *all* the movements of the body, both inside and out.

Skeletal muscles are attached to the bones of the skeleton. When these muscles contract, they move the body. They allow us to use our limbs in a variety of ways, from walking to turning cartwheels. Skeletal muscles also maintain posture and help keep balance.

Smooth muscles in the walls of blood vessels contract to cause vasoconstriction, which may help conserve body heat. Relaxation of these muscles causes vasodilation, which may help the body lose heat. In the organs of the digestive system, smooth muscles squeeze food through the gastrointestinal tract by contracting in sequence to form a wave of muscle contractions called **peristalsis.** Think of squirting toothpaste through a tube by applying pressure in sequence from the bottom of the tube to the top, and you have a good idea of how food is moved by muscles through the digestive system. Peristalsis of smooth muscles also moves urine through the urinary tract.

Cardiac muscle tissue is found only in the walls of the heart. When cardiac muscle contracts, it makes the heartbeat. The pumping action of the beating heart keeps blood flowing through the cardiovascular system.

MUSCLE HYPERTROPHY AND ATROPHY

Muscles can grow larger, or **hypertrophy.** This generally occurs through increased use, although hormonal or other influences can also play a role. The increase in testosterone during puberty, for example, causes a significant increase in muscle size. Physical exercise that involves weight-bearing or resistance training can increase the size of skeletal muscles in virtually everyone. Exercises (such as running) that increase the heart rate may also increase the size and strength of cardiac muscle. The size of a muscle, in turn, is the main determinant of muscle strength, which may be measured by the amount of force a muscle can exert.

Muscles can also grow smaller, or **atrophy**, which can occur through lack of physical activity or from starvation. People who are immobilized for any length of time — for example, because of a broken bone or surgery — lose muscle mass relatively quickly. People in concentration or famine camps may be so malnourished

that they lose much of their muscle mass, becoming almost literally just “skin and bones.” Astronauts on the International Space Station may also lose significant muscle mass because of weightlessness in space (Figure 9.2.3).

Many diseases, including cancer and AIDS, are often associated with muscle atrophy. Atrophy of muscles also happens with age. As people grow older, there is a gradual decrease in the ability to maintain skeletal muscle mass, known as **sarcopenia.** The exact cause of sarcopenia is not known, but one possible cause is a decrease in sensitivity to growth factors that are needed to maintain muscle mass. Because muscle size determines the strength, muscle atrophy causes a corresponding decline in muscle strength.

In both hypertrophy and atrophy, the number of muscle fibers does not change. What changes the size of the muscle fibers? When muscle hypertrophy happens, the individual fibers become wider. When muscle atrophy happens, the fibers become narrower.

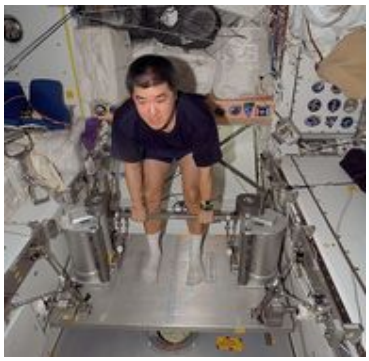


Figure 9.2.3: An astronaut exercising in space. It is important for astronauts to exercise onboard the International Space Station to help counter the loss of muscle mass that occurs because they are weightless without Earth’s gravity.

INTERACTIONS WITH OTHER BODY SYSTEMS

Muscles cannot contract on their own. Skeletal muscles need stimulation from motor neurons in order to contract. The point where a motor neuron attaches to a muscle is called a **neuromuscular junction**. Let’s say you decide to raise your hand in class. Your brain sends electrical messages through motor neurons to your arm and shoulder. The motor neurons, in turn, stimulate muscle fibers in your arm and shoulder to contract, causing your arm to rise.

Involuntary contractions of smooth and cardiac muscles are also controlled by electrical impulses, but in the case of these muscles, the impulses come from the autonomic nervous system (smooth muscle) or specialized cells in the heart (cardiac muscle). Hormones and some other factors also influence involuntary contractions of cardiac and smooth muscles. For example, the fight-or-flight hormone adrenaline increases the rate at which cardiac muscle contracts, thereby speeding up the heartbeat.

Muscles cannot move the body on their own. They need the skeletal system to act upon. The two systems together are often referred to as the **musculoskeletal system**. Skeletal muscles are attached to the skeleton by tough connective tissues called **tendons**. Many skeletal muscles are attached to the ends of bones that meet at a joint. The muscles span the joint and connect the bones. When the muscles contract, they pull on the bones, causing them to move. The skeletal system provides a system of levers that allow body movement. The muscular system provides the force that moves the levers.

REVIEW

1. What is the muscular system?
2. Describe muscle cells and their function.
3. Identify three types of muscle tissue and where each type is found.
4. Define muscle hypertrophy and muscle atrophy.
5. What are the possible causes of muscle hypertrophy?
6. Give three reasons that muscle atrophy may occur.
7. How do muscles change when they increase or decrease in size?
8. How do changes in muscle size affect strength?
9. Explain why astronauts can easily lose muscle mass in space.
10. Describe how the terms *muscle cells*, *muscle fibers*, and *myocytes* relate to each other.
11. Muscle tissue in the stomach is considered _____.

A. cardiac muscle

B. skeletal muscle

C. smooth muscle

D. voluntary muscle

12. Muscle contraction is the _____ of muscle fibers.

A. hypertrophy

B. atrophy

C. lengthening

D. shortening

13. *True or False:* Smooth muscle does not contract.
14. Name two systems in the body that work together with the muscular system to carry out movements.
15. Describe one way in which the muscular system is involved in regulating body temperature.

EXPLORE MORE

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9.3: TYPES OF MUSCLE TISSUE

WORK THOSE EYE MUSCLES!

Turn your eyes—a tiny movement, considering the conspicuously large and strong external eye muscles that control eyeball movements. These muscles have been called the strongest muscles in the human body relative to the work they do. However, the external eye muscles actually do a surprising amount of work. Eye movements occur almost constantly during waking hours, especially when we are scanning faces or reading. Eye muscles are also exercised nightly during the phase of sleep called rapid eye movement sleep. External eye muscles can move the eyes because they are made mainly of muscle tissue.



Figure **9.3.1**: Eyes

WHAT IS MUSCLE TISSUE?

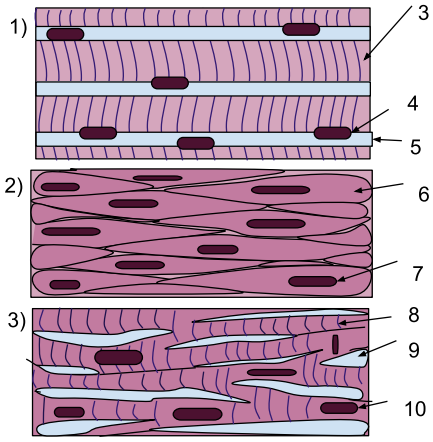


Figure **9.3.2**: Muscle type 1) Skeletal muscle cells are long tubular cells with striations (3) and multiple nuclei (4). The nuclei are embedded in the cell membrane (5) to be just inside the cell. This type of tissue occurs in the muscles that are attached to the skeleton. Skeletal muscles function for the voluntary movements of the body. Muscle type 2) Smooth muscle cells are spindle-shaped (6), and each cell has a single nucleus (7). Unlike skeletal muscle, there are no striations. The smooth muscle acts involuntarily and functions in the movement of substances in the lumens. They are primarily found in blood vessel walls and walls along the digestive tract. Muscle type 3) Cardiac muscle cells branch off from each other, rather than remaining, like the cells in the skeletal and smooth muscle tissues. Because of this, there are junctions between adjacent cells (9). The cells have striations (8), and each cell has a single nucleus (10). This type of tissue occurs in the heart wall, and its primary function is for pumping blood. This is an involuntary action.

Muscle tissue is a soft tissue that makes up most of the tissues in the muscles of the human muscular system. Other tissues in muscles are connective tissues, such as tendons that attach skeletal muscles to bones and sheaths of connective tissues that cover or line muscle tissues. Only muscle tissue per se, however, has cells with the ability to contract.

There are three major types of muscle tissues in the human body: skeletal, smooth, and cardiac muscle tissues. Figure **9.3.2** shows how the three types of muscle tissues appear under a microscope. When you read about each type below, you will learn why the three types appear as they do.

SKELETAL MUSCLE TISSUE

Skeletal muscle is muscle tissue attached to bones by **tendons**, which are bundles of collagen fibers. Whether you are moving your eyes or running a marathon, you are using skeletal muscles. Contractions of skeletal muscles are voluntary or under the conscious control of the central nervous system via the somatic nervous system. Skeletal muscle tissue is the most common type of muscle tissue in the human body. By weight, an average adult male is about 42 percent skeletal muscles, and the average adult female is about 36 percent skeletal muscles. Some of the major skeletal muscles in the human body are labeled in Figures **9.3.3** and Figure **9.3.4** and listed in Table **9.3.1**.

Table **9.3.1**: Skeletal muscles. Some muscles are visible from both anterior and posterior views.

Muscles visible in Figure **9.3.3**	Muscles visible in Figure **9.3.4**
rotator cuff (multiple muscles are part of this group)	levator scapulae
biceps brachii	rhomboids
brachialis	rotator cuff
pronator teres	triceps brachii
brachioradialis	gluteus maximus
adductor muscles	tibialis posterior
tibialis anterior	peroneus longus
deltoid	peroneus brevis
pectoralis major	trapezius
rectus abdominis	deltoid
abdominal external oblique	brachioradialis
iliopsoas	latissimus dorsi
quadriceps femoris	biceps femoris
peroneus longus	semitendinosus
peroneus bravis	semimembranousus
	gastrocnemius
	soleus

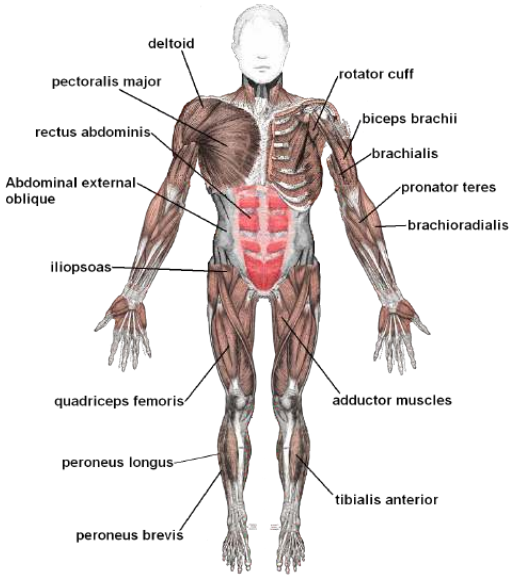


Figure **9.3.3**: This figure shows major skeletal muscles in the front (anterior) of the body.

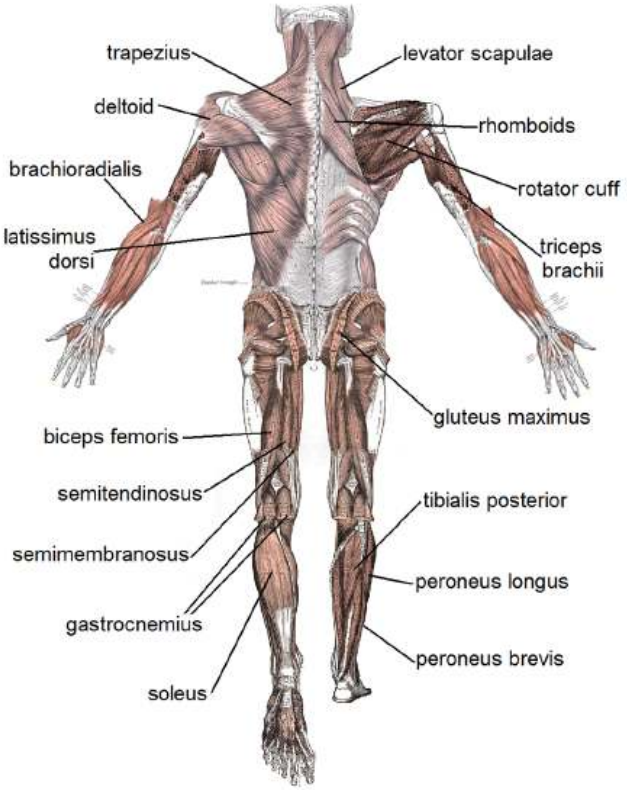


Figure **9.3.4**: This figure shows major skeletal muscles in the back (posterior) of the body.

SKELETAL MUSCLE PAIRS

To move bones in opposite directions, skeletal muscles often consist of muscle pairs that work in opposition to one another. For example, when the biceps muscle (on the front of the upper arm) contracts, it can cause the elbow joint to flex or bend the arm, as shown in Figure **9.3.5**. When the triceps muscle (on the back of the upper arm) contracts, it can cause the elbow to extend or straighten the arm. The biceps and triceps muscles are examples of a muscle pair where the muscles work in opposition to each other.

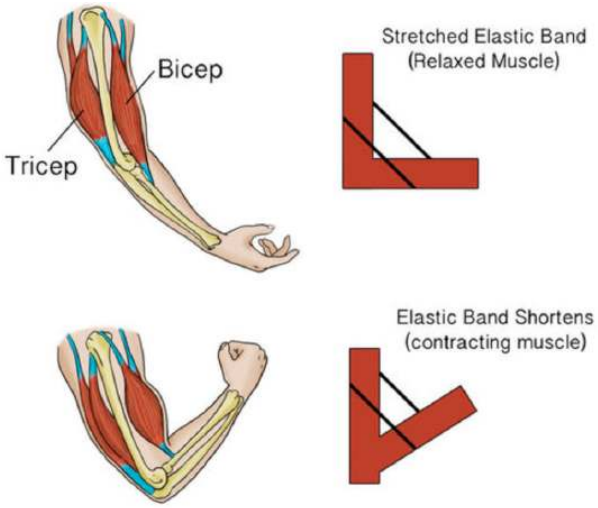


Figure **9.3.5**: Triceps and biceps muscles in the upper arm are opposing muscles that move the arm at the elbow in opposite directions.

SKELETAL MUSCLE STRUCTURE

Each skeletal muscle consists of hundreds — or even *thousands* — of skeletal muscle fibers, which are long, string-like cells. As shown in Figure **9.3.6**, skeletal muscle fibers are individually wrapped in connective tissue called **endomysium**. The skeletal muscle fibers are bundled together in units called **muscle fascicles**, surrounded by sheaths of connective tissue called **perimysium**. Each fascicle contains between ten and 100 (or even more!) skeletal muscle fibers. Fascicles, in turn, are bundled together to form individual skeletal muscles, which are wrapped in connective tissue called **epimysium**. The connective tissues in skeletal muscles have a variety of functions. They support and protect muscle fibers, allowing them to withstand contraction forces by distributing the forces applied to the muscle. They also provide pathways for nerves and blood vessels to reach the muscles. Also, the epimysium anchors the muscles to tendons.

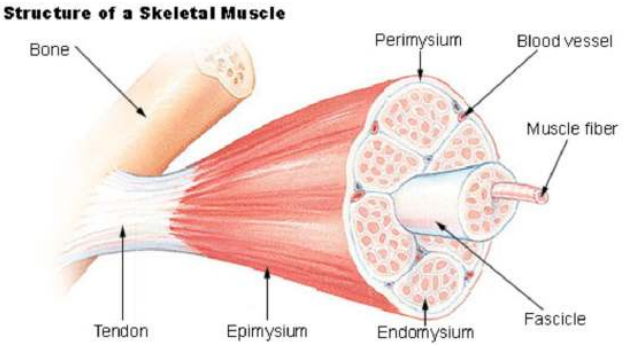


Figure **9.3.6**: Each skeletal muscle has a structure of bundles within bundles. Bundles of muscle fibers make up a muscle fascicle, and fascicles' bundles make up a skeletal muscle. At each level of bundling, a connective tissue membrane surrounds the bundle. The muscle cells, fascicle, and the whole muscle are surrounded by Endomysium, perimysium, and epimysium, respectively. All connective tissues merge together to make a tendon that attaches the muscle to bones.

The same bundles-within-bundles structure is replicated within each muscle fiber. As shown in Figure **9.3.7**, a muscle fiber consists of a bundle of myofibrils, which are themselves bundles of protein filaments. These protein filaments consist of thin filaments of the protein actin, anchored to structures called Z discs — and thick filaments of the protein myosin. The filaments are arranged together within a myofibril in repeating units called **sarcomeres,** which run from one Z disc to the next. The sarcomere is the basic functional unit of skeletal (and cardiac) muscles. It contracts as actin and myosin filaments slide over one another. Skeletal muscle tissue is said to be striated because it appears striped. It has this appearance because of the regular, alternating A (dark) and I (light) bands of filaments arranged in sarcomeres inside the muscle fibers. Other components of a skeletal muscle fiber include multiple nuclei and mitochondria.

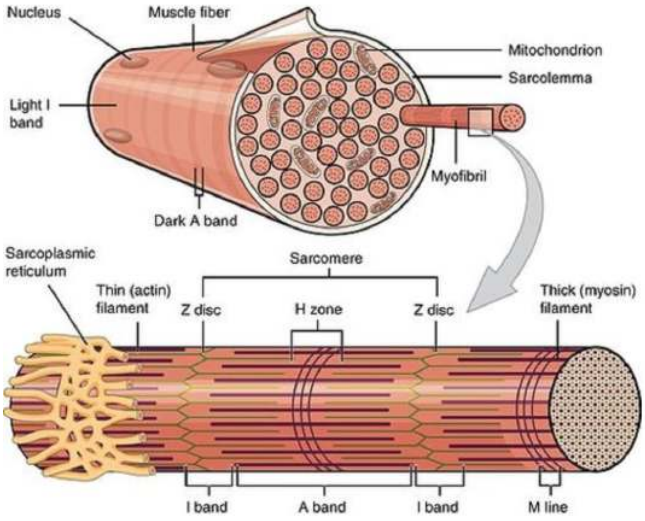


Figure **9.3.7**: Bundles of protein filaments form a myofibril, and bundles of myofibrils make up a single muscle fiber. I and A bands refer to the positioning of myosin and actin fibers in a myofibril. Sarcoplasmic reticulum is a specialized type of endoplasmic reticulum that forms a network around each myofibril. It serves as a reservoir for calcium ions, which are needed for muscle contractions. H zones and Z discs are also involved in muscle contractions, which you can read about in the concept of Muscle Contraction.

SLOW- AND FAST-TWITCH SKELETAL MUSCLE FIBERS

Skeletal muscle fibers can be divided into two types, called slow-twitch (or type I) muscle fibers and fast-twitch (or type II) muscle fibers.

- **Slow-twitch muscle fibers** are dense with capillaries and rich in mitochondria and myoglobin, a protein that stores oxygen until needed for muscle activity. Relative to fast-twitch fibers, slow-twitch fibers can carry more oxygen and sustain aerobic (oxygen-using) activity. Slow-twitch fibers can contract for long periods of time, but not with very much force. They are relied upon primarily in endurance events, such as distance running or cycling.
- **Fast-twitch muscle fibers** contain fewer capillaries and mitochondria and less myoglobin. This type of muscle fiber can contract rapidly and powerfully, but it fatigues very quickly. Fast-twitch fibers can sustain only short, anaerobic (non-oxygen-using) bursts of activity. Relative to slow-twitch fibers, fast-twitch fibers contribute more to muscle strength and have a greater potential for increasing mass. They are relied upon primarily in short, strenuous events, such as sprinting or weight lifting.

Proportions of fiber types vary considerably from muscle to muscle and from person to person. Individuals may be genetically predisposed to have a larger percentage of one type of muscle fiber than the other. Generally, an individual who has more slow-twitch fibers is better suited for activities requiring endurance. In contrast, an individual who has more fast-twitch fibers is better suited for activities requiring short bursts of power.

SMOOTH MUSCLE

Smooth muscle is muscle tissue in the walls of internal organs and other internal structures such as blood vessels. When smooth muscles contract, they help the organs and vessels carry out their functions. When smooth muscles in the stomach wall contract, they squeeze the food inside the stomach, helping to mix and churn the food and break it into smaller pieces. This is an important part of digestion. Contractions of smooth muscles are involuntary, so they are not under conscious control. Instead, they are controlled by the autonomic nervous system, hormones, neurotransmitters, and other physiological factors.

STRUCTURE OF SMOOTH MUSCLE

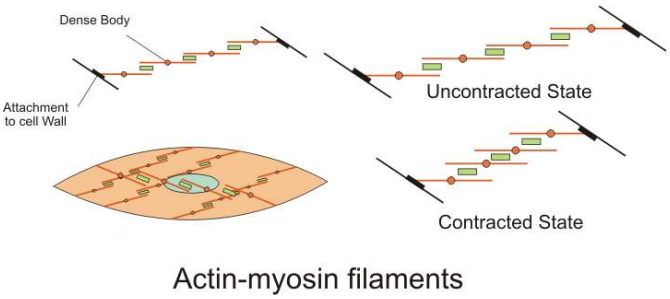


Figure **9.3.8**: The smooth muscle cell is composed of actin and myosin filaments, but they are not arranged in the sarcomere. The arrangement of these filaments is alternate and staggered.

The cells that make up smooth muscle are generally called **myocytes.** Unlike the muscle fibers of striated muscle tissue, the myocytes of smooth muscle tissue do not have their filaments arranged in sarcomeres. Therefore, smooth tissue is not striated. However, the myocytes of smooth muscle contain myofibrils, which contain bundles of myosin and actin filaments. The filaments cause contractions when they slide over each other, as shown in Figure **9.3.8**.

FUNCTIONS OF SMOOTH MUSCLE

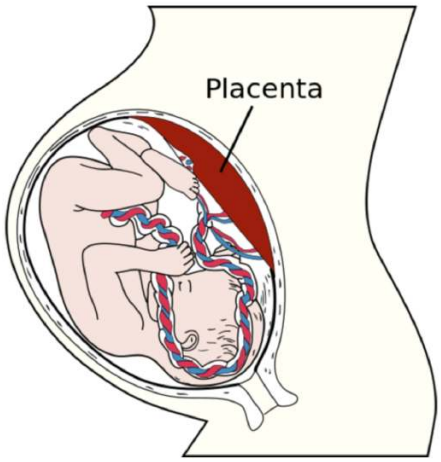


Figure **9.3.9**: The muscular uterine wall stretches to a great extent to accommodate a growing fetus, yet it can still contract with great force during the labor that precedes childbirth. At that time, it can exert up to 100 pounds of force.

Unlike striated muscle, smooth muscle can sustain very long-term contractions. Smooth muscle can also stretch and still maintain its contractile function, which striated muscle cannot. An extracellular matrix secreted by myocytes enhances the elasticity of smooth muscle. The matrix consists of elastin, collagen, and other stretchy fibers. The ability to stretch and still contract is an important attribute of smooth muscle in organs such as the stomach and uterus (Figure **9.3.9**), both of which must stretch considerably as they perform their normal functions.

The following list indicates where many smooth muscles are found, along with some of their specific functions.

- Walls of the gastrointestinal tract (such as the esophagus, stomach, and intestines), moving food through the tract by peristalsis.
- Walls of air passages of the respiratory tract (such as the bronchi), controlling the diameter of the passages and the volume of air that can pass through them
- Walls of organs of the male and female reproductive tracts; in the uterus, for example, pushing a baby out of the uterus and into the birth canal
- Walls of the urinary system structures, including the urinary bladder, allow the bladder to expand so it can hold more urine and then contract as urine is released.
- Walls of blood vessels, controlling the diameter of the vessels and thereby affecting blood flow and blood pressure
- Walls of lymphatic vessels, squeezing the fluid called lymph through the vessels.
- Iris of the eyes, controlling the size of the pupils and thereby the amount of light entering the eyes
- Arrector pili in the skin, raising hairs in hair follicles in the dermis.

CARDIAC MUSCLE

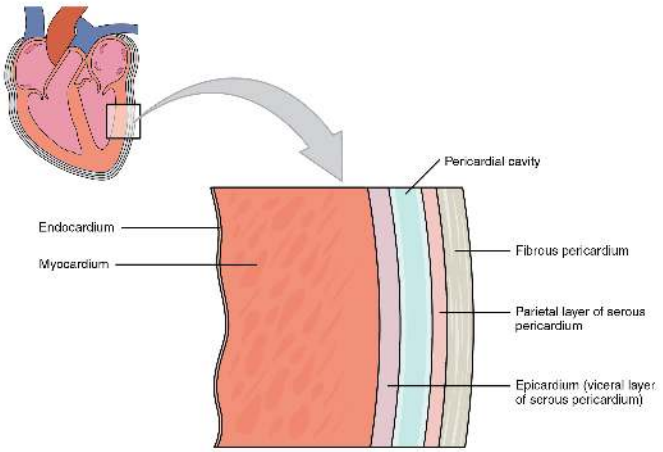


Figure **9.3.10**: The thick wall of the heart consists mainly of cardiac muscle tissue called myocardium. The thin epithelial tissue endocardium covers the chambers of the heart and the epicardium covers the myocardium. The heart is located in the pericardial cavity of the chest. The covering of the pericardial cavity is composed of fibrous and serous layers.

Cardiac muscle is found only in the wall of the heart. It is also called myocardium. As shown in Figure **9.3.10**, the myocardium is enclosed within connective tissues, including the endocardium on

the inside of the heart and pericardium on the outside of the heart. When cardiac muscle contracts, the heart beats and pumps blood. Contractions of cardiac muscle are involuntary, like those of smooth muscles. They are controlled by electrical impulses from specialized cardiac muscle cells in the heart muscle area called the sinoatrial node.

Like skeletal muscle, cardiac muscle is striated because its filaments are arranged in sarcomeres inside the muscle fibers. However, in cardiac muscle, the myofibrils are branched at irregular angles rather than arranged in parallel rows (as they are in skeletal muscle). This explains why cardiac and skeletal muscle tissues look different from one another.

The cells of cardiac muscle tissue are arranged in interconnected networks. This arrangement allows rapid transmission of electrical impulses, which stimulate virtually simultaneous contractions of the cells. This enables the cells to coordinate contractions of the heart muscle.

The heart is the muscle that performs the greatest amount of physical work in a lifetime. Although the heart's power output is much less than the maximum power output of some other muscles in the human body, the heart does its work continuously over an entire lifetime without rest. The cardiac muscle contains many mitochondria, which produce ATP for energy and help the heart resist fatigue.

FEATURE: HUMAN BODY IN THE NEWS

The human heart develops in a sequence of events that are controlled by communication among different types of cells, including cells that will become myocardium (the cardiac muscle that forms the wall of the heart) and cells that will become endocardium (the connective tissue that covers the inside surface of the myocardium). If communication among the cells is abnormal, it can lead to various heart defects, such as cardiac hypertrophy or abnormal enlargement of the heart muscle. Cardiac hypertrophy causes the heart to thicken and weaken over time, so it is less able to pump blood. Eventually, heart failure may develop, causing fluid to build up in the lungs and extremities.

Abnormal cell communication is the mechanism by which a mutation called PTPN11 leads to cardiac hypertrophy in disorder referred to as NSML (Noonan Syndrome with Multiple Lentigines). New research by scientists at Beth Israel Deaconess Medical Center in Boston has determined which type of cell abnormalities occur that lead to NSML. In the research, the scientists engineered mouse models to express the PTPN11 mutation as they developed. The researchers manipulated the mouse models so that the mutation was expressed only in cells that would develop into the myocardium in some of the mice. In contrast, in other mice, the mutation was expressed only in cells that would develop into endocardium. Unexpectedly, the heart's hypertrophy occurred only in the mice that expressed the mutation in endocardial cells, not in myocardial cells, which had long been assumed to be the cells affected. The results of the research suggest potential targets for the treatment of NSML. They may also help scientists understand the causes of other cardiac disorders that are much more common than NSML.

REVIEW

1. What is muscle tissue?
2. Where is the skeletal muscle found, and what is its general function?
3. Why do many skeletal muscles work in pairs?
4. Describe the structure of a skeletal muscle.
5. Relate muscle fiber structure to the functional units of muscles.
6. Why is skeletal muscle tissue striated?
7. Compare and contrast slow-twitch and fast-twitch skeletal muscle fibers.
8. Where is the smooth muscle found? What controls the contraction of smooth muscle?
9. Compare and contrast smooth muscle and striated muscle (such as skeletal muscle).
10. Where is the cardiac muscle found? What controls its contractions?
11. Both cardiac and skeletal muscle tissues are striated, but they look different from one another. Why?
12. The heart muscle is smaller and less powerful than some other muscles in the body. Why is the heart the muscle that performs the greatest amount of physical work in a lifetime? How does the heart resist fatigue?
13. Arrange the following units within a skeletal muscle in order, from smallest to largest: *fascicle; sarcomere; muscle fiber; myofibril*
14. Give one example of connective tissue that is found in muscles. Describe one of its functions.
15. *True or False:* skeletal muscle fibers are cells with multiple nuclei.

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9.4: MUSCLE CONTRACTION

ARM WRESTLING

A sport like arm-wrestling depends on muscle contractions. Arm wrestlers must contract muscles in their hands and arms and *keep* them contracted to resist their opponent's opposing force. The wrestler whose muscles can contract with greater force wins the match.



Figure **9.4.1**: Arm wrestling

MUSCLE CONTRACTION

HOW A SKELETAL MUSCLE CONTRACTION BEGINS

Excluding reflexes, all skeletal muscle contractions occur as a result of conscious effort originating in the brain. The brain sends electrochemical signals through the somatic nervous system to motor neurons that innervate muscle fibers (to review how the brain and neurons function, see the chapter *Nervous System*). A single motor neuron with multiple axon terminals can innervate multiple muscle fibers, thereby causing them to contract at the same time. The connection between a motor neuron axon terminal and a muscle fiber occurs at a neuromuscular junction site**.** This is a chemical synapse where a motor neuron transmits a signal to muscle fiber to initiate a muscle contraction.

The process by which a signal is transmitted at a neuromuscular junction is illustrated in Figure **9.4.2**. The sequence of events begins when an action potential is initiated in the cell body of a motor neuron, and the action potential is propagated along the neuron's axon to the neuromuscular junction. Once the action potential reaches the end of the axon terminal, it causes the neurotransmitter acetylcholine (ACh) from synaptic vesicles in the axon terminal. The ACh molecules diffuse across the synaptic cleft and bind to the muscle fiber receptors, thereby initiating a muscle contraction. Muscle contraction is initiated with the depolarization of the sarcolemma caused by the sodium ions' entrance through the sodium channels associated with the ACh receptors.

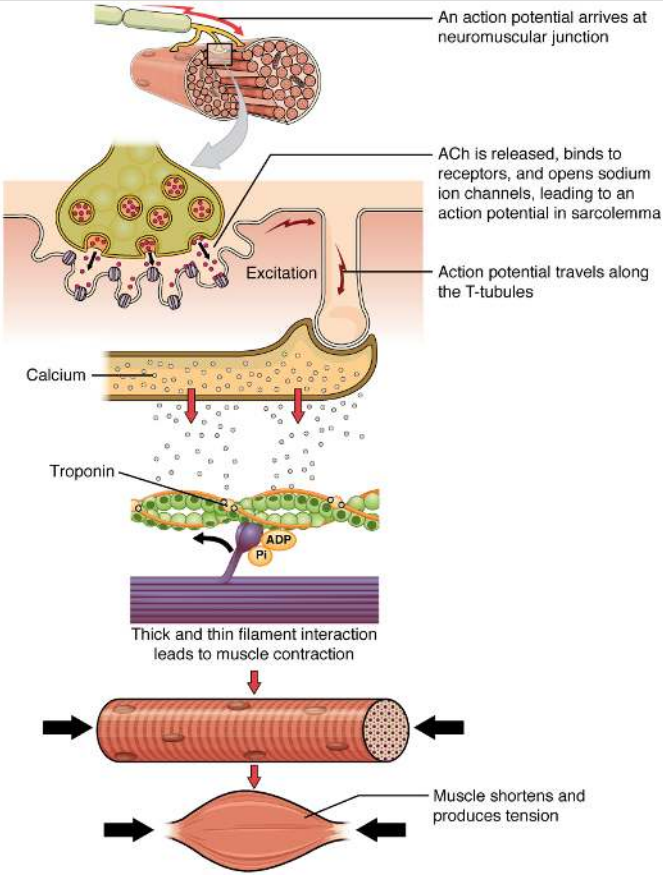


Figure **9.4.2**: This diagram represents the sequence of events that occurs when a motor neuron stimulates a muscle fiber to contract. The action potential travels down the t-tubules and excites the sarcoplasmic reticulum which releases calcium. Calcium when bound to troponin causes conformational changes in the sarcomere. Consequently, the interaction of thick and thin filaments of the sarcomere leads to muscle contraction.

Things happen very quickly in the world of excitable membranes (think about how quickly you can snap your fingers as soon as you decide to do it). Immediately following depolarization of the membrane, it repolarizes, re-establishing the negative membrane potential. Meanwhile, the ACh in the synaptic cleft is degraded by the enzyme acetylcholinesterase (AChE). The ACh cannot rebind to a receptor and reopen its channel, which would cause unwanted extended muscle excitation and contraction.

Propagation of an action potential along the sarcolemma enters the **T-tubules**. For the action potential to reach the membrane of the Sarcoplasmic Reticulum (SR), there are periodic invaginations in the sarcolemma, called **T-tubules** ("T" stands for "transverse"). The arrangement of a T-tubule with the membranes of SR on either side is called a **triad** (Figure **9.4.3**). The triad surrounds the cylindrical structure called a **myofibril**, which contains actin and myosin. The T-tubules carry the action potential into the interior of the cell, which triggers the opening of calcium channels in the membrane of the adjacent SR, causing Ca^{++} to diffuse out of the SR and into the sarcoplasm. It is the arrival of Ca^{++} in the sarcoplasm that initiates

contraction of the muscle fiber by its contractile units, or sarcomeres.

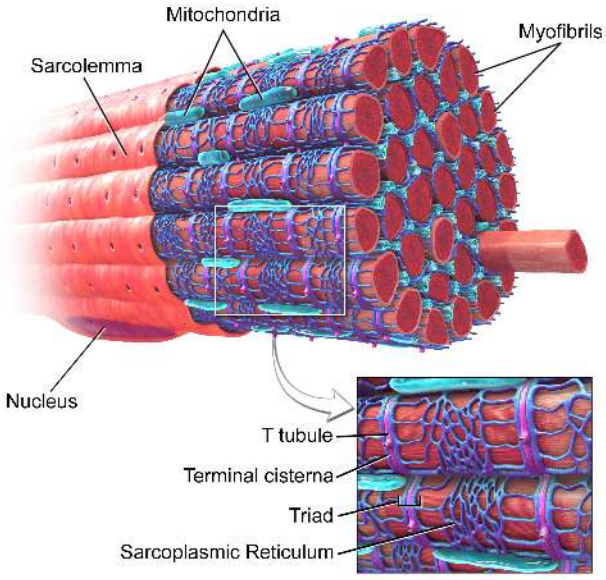


Figure **9.4.3**: Narrow T-tubules permit the conduction of electrical impulses. The SR functions to regulate intracellular levels of calcium. Two terminal cisternae (where enlarged SR connects to the T-tubule) and one T-tubule comprise a triad—a "threesome" of membranes, with those of SR on two sides and the T-tubule sandwiched between them.

EXCITATION-CONTRACTION COUPLING

Although the term **excitation-contraction coupling** confuses or scares some students, it comes down to this: for a skeletal muscle fiber to contract, its membrane must first be "excited"—in other words, it must be stimulated to fire an action potential. The muscle fiber action potential, which sweeps along the sarcolemma as a wave, is "coupled" to the actual contraction through the release of calcium ions (Ca^{++}) from the SR. Once released, the Ca^{++} interacts with the shielding proteins, troponin and tropomyosin complex, forcing them to move aside so that the actin-binding sites are available for attachment by myosin heads. The myosin then pulls the actin filaments toward the center, shortening the muscle fiber.

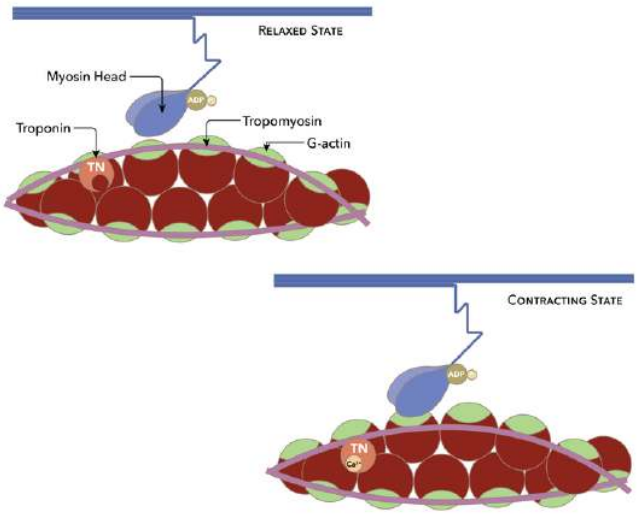


Figure **9.4.4**: Tropomyosin Troponin complex shields the cross-bridge sites on actin. Myosin can only bind with actin when this complex is removed with the help of Calcium ions.

In skeletal muscle, this sequence begins with signals from the somatic motor division of the nervous system. In other words, the "excitation" step in skeletal muscles is always triggered by signaling from the nervous system.

SLIDING FILAMENT THEORY OF MUSCLE CONTRACTION

Once the muscle fiber is stimulated by the motor neuron, actin, and myosin protein filaments within the skeletal muscle fiber slide past each other to produce a contraction. The **sliding filament theory** is the most widely accepted explanation for how this occurs. According to this theory, muscle contraction is a cycle of molecular events in which thick myosin filaments repeatedly attach to and pull on thin actin filaments, so they slide over one another. The actin filaments are attached to Z discs, each of which marks the end of a sarcomere. The sliding of the filaments pulls the Z discs of a sarcomere closer together, thus shortening the sarcomere. As this occurs, the muscle contracts.

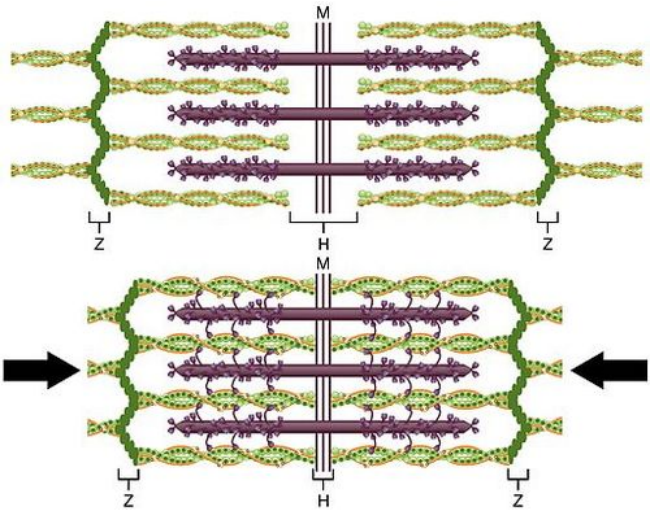


Figure **9.4.5**: The top diagram shows a relaxed sarcomere, and the bottom diagram shows a contracted sarcomere. Please note the z discs, h zone, and M line. In a contracted sarcomere the H zone reduces as compared to relaxed sarcomere because actin fibers (greenish-yellow double helix) move towards the M line.

CROSSBRIDGE CYCLING

Crossbridge cycling is a sequence of molecular events that underlies the sliding filament theory. There are many projections from the thick myosin filaments, each of which consists of two myosin heads (you can see the projections and heads in Figures **9.4.5** and **9.4.3**). Each myosin head has binding sites for ATP (or ATP hydrolysis products: ADP and P_i) and actin. The thin actin filaments also have binding sites for the myosin heads—a cross-bridge forms when a myosin head binds with an actin filament.

The process of cross-bridge cycling is shown in Figure **9.4.6**. A cross-bridge cycle begins when the myosin head binds to an actin filament. ADP and P_i are also bound to the myosin head at this stage. Next, a power stroke moves the actin filament inward toward the sarcomere center, thereby shortening the sarcomere. At the end of the power stroke, ADP and P_i are released from the myosin head, leaving the myosin head attached to the thin filament until another ATP binds to the myosin head. When ATP binds to the myosin head, it causes the myosin head to detach from the actin filament. ATP is again split into ADP and P_i and the energy released is used to move the myosin head into a "cocked" position. Once in this position, the myosin head can bind to the actin filament again, and another cross-bridge cycle begins.

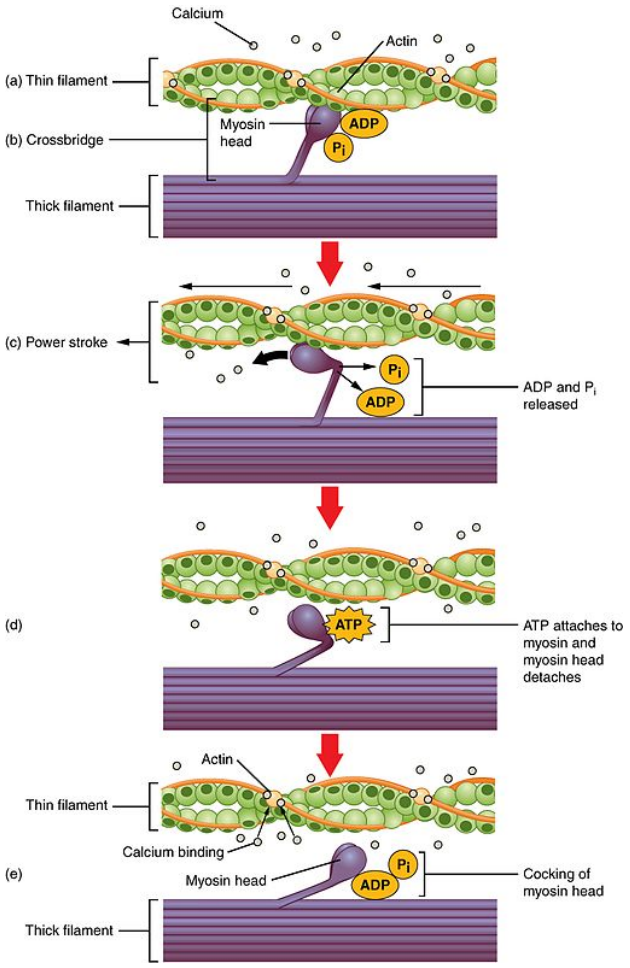


Figure **9.4.6**: Crossbridge cycling

FEATURE: HUMAN BIOLOGY IN THE NEWS

Interesting and hopeful basic research on muscle contraction is often in the news because muscle contractions are involved in so many different body processes and disorders, including heart failure and stroke.

- **Heart failure** is a chronic condition in which cardiac muscle cells cannot contract forcefully enough to keep body cells adequately supplied with oxygen. In 2016, researchers at the University of Texas Southwestern Medical Center identified a potential new target for developing drugs to increase the strength of cardiac muscle contractions in patients with heart failure. The UT researchers found a previously unidentified protein involved in muscle contraction. The minimal protein turns off the “brake” on the heart, so it pumps blood more vigorously. At the molecular level, the protein affects the calcium-ion pump that controls muscle contraction. This result is likely to lead to searches for additional such proteins.
- A **stroke** occurs when a blood clot lodges in an artery in the brain and cuts off blood flow to part of the brain. Damage from the clot would be reduced if the smooth muscles lining brain arteries relaxed following a stroke because the arteries

would dilate and allow greater blood flow to the brain. In a recent study undertaken at the Yale University School of Medicine, researchers determined that the muscles lining blood vessels in the brain actually contract after a stroke. This constricts the vessels, reduces blood flow to the brain, and appears to contribute to permanent brain damage. The hopeful takeaway of this finding is that it suggests a new target for stroke therapy.

REVIEW

1. What is skeletal muscle contraction?
2. Distinguish between isometric and isotonic contractions of skeletal muscle.
3. How does a motor neuron stimulate a skeletal muscle contraction?
4. What is the sliding filament theory?
5. Describe cross-bridge cycling.
6. Where does the ATP needed for a muscle contraction come from?
7. Explain why an action potential in a single motor neuron can cause multiple muscle fibers to contract.
8. The name of the synapse between a motor neuron and a muscle fiber is the _____ _____.
9. If a drug blocks the acetylcholine receptors on muscle fibers, what do you think this would do to muscle contraction? Explain your answer.
10. *True or False:* According to the sliding filament theory, actin filaments actively attach to and pull on myosin filaments.
11. *True or False:* When a motor neuron produces an action potential, the sarcomeres in the muscle fiber that it innervates become shorter as a result.
12. Explain how cross-bridge cycling and sliding filament theory are related to each other.
13. When does anaerobic respiration typically occur in human muscle cells?
14. If there were no ATP available in a muscle, how would this affect cross-bridge cycling? What would this do to muscle contraction?

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9.5: PHYSICAL EXERCISE

STROLLERS

These caregivers are setting a great example for their children by engaging in physical exercise. Adopting a regular physical exercise habit is one of the most important ways to maintain fitness and good health. From higher self-esteem to a healthier heart, physical exercise can positively affect virtually all aspects of health, including physical, mental, and emotional health.



Figure **9.5.1**: Jogging with strollers

WHAT IS PHYSICAL EXERCISE?

Physical exercise is any bodily activity that enhances or maintains physical fitness and overall health and wellness. We generally think of physical exercise as activities that are undertaken for the main purpose of improving physical fitness and health. However, physical activities that are undertaken for other purposes may also count as physical exercise. Scrubbing a floor, raking a lawn, or playing active games with young children or a dog are all activities that can have fitness and health benefits, even though they generally are not done mainly for this purpose.

How much physical exercise should people get? In the United States, both the Centers for Disease Control and Prevention and the Surgeon General have recommended that every adult participates in moderate exercise for a minimum of 30 minutes a day. This might include walking, swimming, and/or household or yard work.

TYPES OF PHYSICAL EXERCISE

Physical exercise can be classified into three types, depending on the effects it has on the body: aerobic exercise, anaerobic exercise, and flexibility exercise. Many specific physical exercise examples (including playing soccer and rock climbing) can be classified as more than one type.

AEROBIC EXERCISE

Aerobic exercise is any physical activity in which muscles are used below their maximum contraction strength, but for long periods of time. Aerobic exercise uses a relatively high percentage of slow-twitch muscle fibers that consume a large amount of oxygen. The main goal of aerobic exercise is to increase cardiovascular endurance, although it can have many other benefits, including muscle toning. Examples of aerobic exercise include cycling, swimming, brisk walking, jumping rope, rowing, hiking, and tennis.

ANAEROBIC EXERCISE

Anaerobic exercise is any physical activity in which muscles are used close to their maximum contraction strength but for relatively short periods of time. Anaerobic exercise uses a relatively high percentage of fast-twitch muscle fibers that consume a small amount of oxygen. The goals of anaerobic exercise include building and strengthening muscles and improving bone strength, balance, and coordination. Examples of anaerobic exercise include push-ups, lunges, sprinting, interval training, resistance training, and weight training (such as biceps curls with a dumbbell, as pictured Figure **9.5.2**).



Figure **9.5.2**: Pitting the biceps muscle in the upper arm against a heavyweight helps build and strengthen this muscle.

FLEXIBILITY EXERCISE

Flexibility exercise is any physical activity that stretches and lengthens muscles. The goals of flexibility exercise include increasing joint flexibility, keeping muscles limber, and improving the range of motion, all of which can reduce the risk of injury. Examples of flexibility exercises include stretching, yoga, and tai chi.

HEALTH BENEFITS OF PHYSICAL EXERCISE

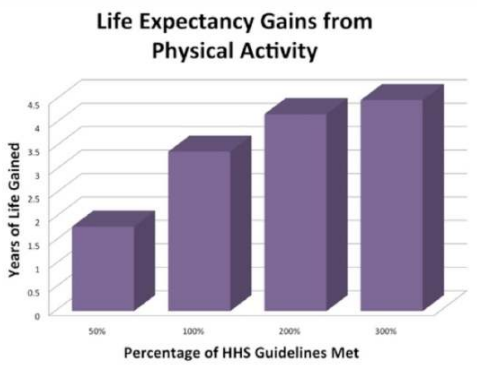


Figure 9.5.3: The U.S. Department of Health and Human Services (HHS) recommends that adults aged 18 to 64 engage in regular aerobic physical activity for 2.5 hours at moderate intensity (1.25 hours at vigorous intensity) each week. Moderate activities are those during which a person could talk but not sing. Vigorous activities are those during which a person could say only a few words without stopping to breathe. When people exercise at 50 percent of the HHS guidelines, they gain an average of 1.5 years of life. Exercising at 100 percent of the HHS guidelines results in a gain of almost four years of life. The gain in life expectancy starts to level off at about 300 percent of the HHS guidelines.

Many studies have shown that physical exercise is positively correlated with a diversity of health benefits. Some of these benefits include maintaining physical fitness, losing weight and maintaining a healthy weight, regulating digestive health, building and maintaining healthy bone density, increasing muscle strength, improving joint mobility, strengthening the immune system, boosting cognitive ability, and promoting psychological well-being. Some studies have also found a significant positive correlation between exercise and quality of life and life expectancy. People who participate in moderate to high levels of physical activity have been shown to have lower mortality rates than people of the same ages who are not physically active. The years of life gained with different amounts of physical activity are shown in the graph in Figure 9.5.3.

The underlying physiological mechanisms explaining why exercise has these positive health benefits are not completely understood. However, developing research suggests that many of the benefits of exercise may come about because of skeletal muscles' role as endocrine organs. Contracting muscles release hormones called **myokines**, which promote tissue repair and the growth of new tissue. Myokines also have anti-inflammatory effects, which, in turn, reduce the risk of developing inflammatory diseases. Exercise also reduces cortisol levels, the adrenal cortex stress hormone that may cause many health problems — both physical and mental — at sustained high levels.

CARDIOVASCULAR BENEFITS OF PHYSICAL EXERCISE

The beneficial effects of exercise on the cardiovascular system are well documented. Physical inactivity has been identified as a risk factor for the development of coronary artery disease. There is also a direct correlation between physical inactivity and cardiovascular disease mortality. Physical exercise, in contrast, has been demonstrated to reduce several risk factors for cardiovascular disease, including hypertension (high blood pressure), "bad" cholesterol (low-density lipoproteins), high total cholesterol, and excess body weight. Physical exercise has also been shown to increase "good" cholesterol (high-density lipoproteins), insulin sensitivity, the mechanical efficiency of the heart, and exercise tolerance, which can perform physical activity without undue stress and fatigue.

COGNITIVE BENEFITS OF PHYSICAL EXERCISE

Physical exercise has been shown to help protect people from developing neurodegenerative disorders, such as dementia. A 30-year study of almost 2,400 men found that those who exercised regularly had a 59 percent reduction in dementia when compared with those who did not exercise. Similarly, a review of cognitive enrichment therapies for the elderly found that physical activity — in particular, aerobic exercise — can enhance the cognitive function of older adults. Anecdotal evidence suggests that frequent exercise may even help reverse alcohol-induced brain damage. There are several possible reasons why exercise is so beneficial for the brain. Physical exercise:

- increases blood flow and oxygen availability to the brain
- increases growth factors that promote new brain cells and new neuronal pathways in the brain
- increases levels of neurotransmitters (such as serotonin), which increase memory retention, information processing, and cognition

MENTAL HEALTH BENEFITS OF PHYSICAL EXERCISE

Numerous studies suggest that regular aerobic exercise works as well as pharmaceutical antidepressants in treating mild-to-moderate depression. A possible reason for this effect is that exercise increases the biosynthesis of at least three neurochemicals that may act as euphoriants. The euphoric effect of exercise is well known. Distance runners may refer to it as "runner's high," and people who participate in the crew (Figure 9.5.4) may refer to it as "rower's high." Because of these effects, health care providers often promote aerobic exercise as a treatment for depression.



Figure 9.5.4: This crew team is competing for the U.S. Army in the lightweight division of the world championships in 2003. They are clearly exerting themselves — and no doubt increasing their euphoriant neurochemicals in the process.

Additional mental health benefits of physical exercise include reducing stress, improving body image, and promoting positive self-esteem. Conversely, there is evidence to suggest that being sedentary is associated with an increased risk of anxiety.

SLEEP BENEFITS OF PHYSICAL EXERCISE

A recent review of published scientific research suggests that exercise generally improves sleep for most people and helps sleep disorders, such as insomnia. Exercise is the most recommended alternative to sleeping pills for people with insomnia. For sleep benefits, the optimum time to exercise is four to eight hours before bedtime, although exercise at any time of day seems to be beneficial. The only possible exception is a heavy exercise undertaken shortly before bedtime, which may actually interfere with sleep.

OTHER BENEFITS OF PHYSICAL EXERCISE

Some studies suggest that physical activity may benefit the immune system. For example, moderate excise is associated with a decreased incidence of upper respiratory tract infections. Evidence from many studies has found a correlation between physical exercise and reduced death rates from cancer, specifically breast cancer and colon cancer. Physical exercise has also been shown to reduce the risk of type 2 diabetes and obesity.

VARIATION IN RESPONSES TO PHYSICAL EXERCISE

Not everyone benefits equally from physical exercise. When participating in aerobic exercise, most people will have a moderate increase in their endurance, but some will double their endurance. On the other hand, some people will show little or no increase in endurance from aerobic exercise. Genetic differences in slow-twitch and fast-twitch skeletal muscle fibers may play a role in these different results. People with more slow-twitch fibers may develop greater endurance because these muscle fibers have more capillaries, mitochondria, and myoglobin than fast-twitch fibers. As a result, slow-twitch fibers can carry more oxygen and sustain aerobic activity for a longer period of time than fast-twitch fibers. Studies show that endurance athletes (like the marathoner in Figure **9.5.5**) generally tend to have a higher proportion of slow-twitch fibers than other people.



Figure **9.5.5**: This winning marathoner is likely to have a relatively high proportion of slow-twitch muscle fibers that increase his endurance.

There is also great variation in individual responses to muscle building as a result of anaerobic exercise. Some people have a much greater capacity to increase muscle size and strength, whereas other people never develop large muscles, no matter how much they exercise them. People who have more fast-twitch than slow-twitch muscle fibers may develop bigger, stronger muscles because fast-twitch muscle fibers contribute more to muscle strength and have greater potential to increase in mass. Evidence suggests that athletes who excel at power activities (such as throwing and jumping) tend to have a higher proportion of fast-twitch fibers than endurance athletes.

CAN YOU "OVERDOSE" ON PHYSICAL EXERCISE?



Figure **9.5.6**: New military recruits may suffer muscle damage from overexertion of unconditioned muscles. The drill instructor pictured here (in an orange shirt) is doing his best to encourage these marine recruits to expend their maximum effort.

Is it possible to exercise too much? Can too much exercise be harmful? Evidence suggests that some adverse effects may occur if exercise is extremely intense and the body is not given proper rest between exercise sessions. Athletes who train for multiple marathons have been shown to develop scarring of the heart and heart rhythm abnormalities. Doing too much exercise without prior conditioning also increases the risk of injuries to muscles and joints. Damage to muscles due to overexertion is often seen in new military recruits (Figure **9.5.6**). Too much exercise in females may cause amenorrhea, which is a cessation of menstrual periods. When this occurs, it generally indicates that a woman is pushing her body too hard.

Many people develop delayed onset muscle soreness (DOMS), which is pain or discomfort in muscles felt one to three days after exercising and generally subsides two or three days later. DOMS was once thought to be caused by the buildup of lactic acid in the muscles. Lactic acid is a product of anaerobic respiration in muscle tissues. However, lactic acid disperses fairly rapidly, so it is unlikely to explain pain experienced several days after exercise. The current theory is that DOMS is caused by tiny tears in muscle fibers, which occur when muscles are used at too high a level of intensity.

FEATURE: MY HUMAN BODY

Most people know that exercise is important for good health, and it's easy to find endless advice about exercise programs and fitness plans. What is not so easy to find is the motivation to start exercising and stick with it. This is the main reason why so many people fail to get regular exercise. Practical concerns like a busy schedule and bad weather can certainly make exercising more of a challenge, but the biggest barriers to adopting a

regular exercise routine are mental. If you want to exercise but find yourself making excuses or getting discouraged and giving up, here are some tips that may help you get started and stay moving:

- **Avoid an all-or-nothing point of view.** Don't think you need to spend hours sweating at the gym or training for a marathon to get healthy. Even a little bit of exercise is better than nothing at all. Start with ten or 15 minutes of moderate activity each day. Taking a walk around your neighborhood is a great way to begin! From there, gradually increase the amount of time until you exercise to at least 30 minutes a day, five days a week.
- **Be kind to yourself, and reinforce positive behaviors with rewards.** Don't be down on yourself because you are overweight or out of shape. Don't beat yourself up because of a supposed lack of willpower. Instead, look at any past failures as opportunities to learn and do better. When you do achieve even small exercise goals, treat yourself to something special. Did you complete your first workout? Reward yourself with a relaxing bath or other treats.
- **Don't make excuses for not exercising.** Common complaints include being too busy or tired or not athletic enough. Such excuses are not valid reasons to avoid exercising, and they will sabotage any plans to improve your fitness. If you can't find a 30-minute period to work out, try to find ten minutes, three times a day. If you're feeling tired, know that exercise can actually reduce fatigue and boost your energy level. If you feel clumsy and uncoordinated, remind yourself that you don't need to be athletic to take a walk or engage in vigorous house or yard work.
- **Find an activity that you truly enjoy doing.** Don't think you have to lift weights or run on a treadmill to exercise your muscles. If you find such activities boring or unpleasant, you won't stick with them. Any activity that increases your heart rate and uses large muscles can provide a workout, especially if you're not in the habit of exercising, so find something you like to do. Do you like to dance? Put on some music and dance up a sweat! Do you enjoy gardening? Get out in the yard and dig up some dirt! Still not interested? Try an activity-based video game, such as Wii or Kinect. You may find it so much fun that it doesn't seem like exercise until you realize you've worked up a sweat.
- **Make yourself accountable.** Tell friends and family members that you're going to start exercising. You'll be letting them — as well as yourself — down if you don't follow through. Some people find that keeping an exercise log to track their progress is a good way to be accountable and stick to an exercise program. Perhaps the best way to keep at it is to find an exercise partner. If you've got someone waiting to exercise with you, you will be less likely to make excuses for not exercising.
- **Add more physical activity to your daily life.** You don't need to follow a structured exercise program to increase your activity level. Do your house or yard work briskly for a workout. Park your car further than necessary from work or the mall, and walk the extra distance. If you live close enough, leave the car at home and walk to and from your destination. Rather than taking elevators or escalators, walk up and downstairs. When you take breaks at work, take a walk instead of sitting. Every time a commercial comes on while you're watching TV, take a quick exercise break — run in place or do some curls with hand weights.

REVIEW

1. How is physical exercise defined?
2. What are the current recommendations for physical exercise for adults?
3. Describe aerobic exercise, and give examples of aerobic exercises.
4. How does anaerobic exercise differ from aerobic exercise, and what are some examples of anaerobic exercises?
5. Define flexibility exercise, and state its benefits. What are two examples of flexibility exercises?
6. In general, how does physical exercise affect health, quality of life, and longevity?
7. What mechanism may underlie many of the general health benefits of physical exercise?
8. Relate physical exercise to cardiovascular disease risk.
9. What may explain the positive benefits of physical exercise on cognition?
10. How does physical exercise compare with antidepressant drugs in the treatment of depression?
11. Identify several other health benefits of physical exercise.
12. Explain how genetics may influence the way individuals respond to physical exercise.
13. Can too much physical exercise be harmful?
14. Lifting hefty weights for a short period of time is likely to:

    A. use a relatively high percentage of fast-twitch muscle fibers

    B. use a relatively high percentage of slow-twitch muscle fibers

    C. be an aerobic exercise

    D. use a large amount of oxygen

15. Walking quickly for an extended period of time is likely to:

    A. use a relatively high percentage of fast-twitch muscle fibers

    B. use a relatively high percentage of slow-twitch muscle fibers

    C. use muscles at close to their maximum contraction

    D. cause the muscles to use only a small amount of oxygen

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9.6: DISORDERS OF THE MUSCULAR SYSTEM

PAIN IN THE NECK

Spending hours each day looking down at hand-held devices is a pain in the neck — literally. The weight of the head bending forward can put a lot of strain on neck muscles, and muscle injuries can be excruciating. Neck pain is one of the most common complaints that bring people to the doctor's office. In any given year, about one in five adults will suffer from neck pain. That's a lot of pain in the neck! Not all of them are due to muscular disorders, but many of them are. Muscular disorders, in turn, generally fall into two general categories: musculoskeletal disorders and neuromuscular disorders.



Figure **9.6.1**: On the phone

MUSCULOSKELETAL DISORDERS

Musculoskeletal disorders are injuries in muscles or associated tissues (such as tendons) because of biomechanical stresses. They may be caused by sudden exertion, over-exertion, repetitive motions, or long periods of maintaining awkward positions. Musculoskeletal disorders often work- or sports-related, and generally, just one or a few muscles are affected. They can often be treated successfully, and full recovery can be very likely. The disorders include muscle strains, tendonitis, and carpal tunnel syndrome.

MUSCLE STRAIN

A **muscle strain** is an injury in which muscle fibers tear as a result of overstretching. A muscle strain is also commonly called a pulled muscle or torn muscle. (Strains are often confused with sprains, which are similar injuries to ligaments.) Depending on the degree of injury to muscle fibers, a muscle strain can range from mildly to extremely painful. Besides pain, typical symptoms include stiffness and bruising in the area of the strained muscle. Figure **9.6.2** shows a large bruise caused by a hamstring muscle strain. Hamstring strains are prevalent in track and field athletes. In sprinters, for example, about one-third of injuries are hamstring injuries. Having a previous hamstring injury puts an athlete at increased risk of having another one.



Figure **9.6.2**: Bleeding in muscle tissue may cause a muscle strain to produce a bruise over the affected muscle, as in this hamstring bruise. The photos show two images of the same leg, both taken four days after the injury occurred.

Proper first aid for a muscle strain includes five steps, which are represented by the acronym PRICE. The PRICE steps should be followed for several days after the injury. The five steps are:

1. **Protection:** Apply soft padding to the strained muscle to minimize impact with objects that might cause further damage.
2. **Rest:** Rest the muscle to accelerate healing and reduce the potential for re-injury.
3. **Ice:** Apply ice for 20 minutes at a time every two hours to reduce swelling and pain.
4. **Compression:** Apply a stretchy bandage to the strained muscle to reduce swelling.
5. **Elevation:** Keep the strained muscle elevated to reduce the chance of blood pooling in the muscle.

Non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen) can help reduce inflammation and relieve pain. However, because such drugs interfere with blood clotting, they should be taken only after bleeding in the muscle has stopped — not immediately after the injury occurs. For severe muscle strains, professional medical care may be needed.

TENDINITIS

Tendinitis is inflammation of a tendon that occurs when it is over-extended or worked too hard without rest. Tendons that are commonly affected include those in the ankle, knee, shoulder, and elbow. The affected tendon depends on the type of use that causes inflammation. Rock climbers tend to develop tendinitis in their fingers, while basketball players are more likely to develop tendonitis in the knees, to name a few examples.

Symptoms of tendinitis may include aching, sharp pain, a burning sensation, or joint stiffness. In some cases, swelling occurs around the inflamed tendon, and the area feels hot and looks red. Treatment includes the PRICE guidelines listed above and the use of NSAIDs to reduce inflammation and pain further. Although symptoms should show improvement within a few days of treatment, full recovery may take several months. A gradual return to exercise or other use of the affected tendon is recommended. Physical or occupational therapy may speed the return to normal activity levels.

CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome is a common biomechanical problem in the wrist when the median nerve becomes compressed between carpal bones (Figure **9.6.3**). This may occur due to repetitive use of the wrist, a tumor, or trauma to the wrist. Two-thirds of the cases are work-related. Computer work, work with vibrating tools and work requiring a strong grip all increase one's risk of developing this problem. Carpal tunnel syndrome occurs more often in women than in men. Other risk factors include obesity, pregnancy, and arthritis. Genetics may also play a role.

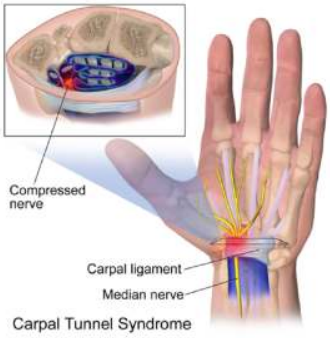


Figure **9.6.3**: Carpal tunnel syndrome occurs when the median nerve in the wrist becomes compressed.

Compression of the median nerve results in the muscles' inadequate nervous stimulation in the thumb and first two fingers of the hand. The main symptoms are pain, numbness, and tingling in these digits. Sometimes, symptoms can be improved by wearing a wrist splint or receiving corticosteroid injections. Surgery to cut the carpal ligament reduces pressure on the median nerve and is generally more effective than nonsurgical treatment. Recurrence of carpal tunnel syndrome after surgery is rare. On the other hand, without treatment, the lack of nervous stimulation by the median nerve may eventually cause the affected muscles of the hand to weaken and waste away.

NEUROMUSCULAR DISORDERS

Neuromuscular disorders are systemic disorders that occur because of problems with the nervous control of muscle contractions or muscle cells themselves. These disorders are often due to faulty genes and not due to biomechanical stresses. Other system-wide problems, such as abnormal immune system responses, may also be involved in neuromuscular disorders.

Unlike musculoskeletal disorders, neuromuscular disorders generally affect most or all of the muscles in the body. The disorders also tend to be progressive and incurable. However, in most cases, treatment is available to slow the disease progression or lessen symptoms. Examples of neuromuscular disorders include muscular dystrophy, myasthenia gravis, and Parkinson's disease.

MUSCULAR DYSTROPHY

Muscular dystrophy is a genetic disorder caused by defective proteins in muscle cells. It is characterized by progressive skeletal muscle weakness and death of muscle cells and tissues. Muscles become increasingly unable to contract in response to nervous stimulation.

There are at least nine major types of muscular dystrophy caused by different gene mutations. Some of the mutations cause autosomal recessive or autosomal dominant disorders, and some cause X-linked disorders. The most common type of childhood muscular dystrophy is Duchenne muscular dystrophy (DMD) due to a mutation in a recessive gene on the X chromosome. As an X-linked recessive disorder, Duchenne muscular dystrophy occurs almost exclusively in males.

Different types of muscular dystrophy affect different major muscle groups. In Duchenne muscular dystrophy, the lower limbs are affected. Signs of the disorder usually first become apparent when a child starts walking. Difficulty walking becomes progressively worse through childhood. By the time a child is ten, braces may be needed for walking — and walking may no longer even be possible by age 12. The lifespan of someone with muscular dystrophy is likely to be shorter than normal because of the disease, ranging from 15 to 45 years.

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.

In some cases, physical therapy, drug therapy, or orthopedic surgery may improve muscular dystrophy signs and symptoms. However, at present, there is no known cure for the disorder. Research is ongoing to find a cure, with financial support from such sources as the Muscular Dystrophy Association (MDA) (see photo below). MDA is a non-profit organization dedicated to curing muscular dystrophy by funding worldwide research.



Figure **9.6.4**: A firefighters from Camp Pendleton, California, who collected donations during their off hours for the Muscular Dystrophy Association (MDA) in 2010.

MYASTHENIA GRAVIS

Myasthenia gravis is an autoimmune disorder in which circulating antibodies block the nicotinic acetylcholine receptors on the neuromuscular junction's motor endplate. This blockage of acetylcholine receptors causes muscle weakness, often first exhibiting drooping eyelids and expanding to include overall muscle

weakness and fatigue. It occurs more commonly in women and generally begins between the ages of 20 and 40. The initial symptom of myasthenia gravis is painless muscle weakness, generally in muscles around the eye (Figure 9.6.5). The disease then progresses to muscles elsewhere in the body, eventually involving most of the muscles. Swallowing and chewing may become difficult as the disease progresses, and speech may become slow and slur. In more advanced cases, myasthenia crises may occur, during which the muscles that control breathing may be affected. Emergency medical care to provide assisted ventilation is required to sustain life. A myasthenia gravis crisis may be triggered by various stressors, such as infection, fever, or stress. Treatment of myasthenia gravis may include medications to counter the mutant gene's effects or suppress the immune system.



Figure 9.6.5: The photograph on the left shows a myasthenia gravis patient with a drooping eyelid. The photo on the right shows the same patient after administering a drug that blocks the breakdown of acetylcholine.

PARKINSON'S DISEASE



Figure 9.6.6: The awkward, stooped gait of this person is typical of people with advanced Parkinson's disease.

Parkinson's disease is a degenerative disorder of the central nervous system that mainly affects the muscular system and movement. Four motor signs and symptoms are considered defining Parkinson's disease: muscle tremor (shaking), muscle rigidity, slowness of movement, and postural instability. Tremor is the most common and obvious symptom, and it most often occurs in a limb at rest, so it disappears during sleep or when the patient moves the limb voluntarily. Difficulty walking eventually develops, and dementia is common in the advanced stages of the disease. Depression is common, as well.

Parkinson's disease is more common in older people, with most cases being diagnosed after 50. Often, the disease occurs for no known reason. Cases like this are called primary Parkinson's disease. Sometimes, the disease has a known or suspected cause, such as exposure to toxins in pesticides or repeated head trauma. In this case, it is called secondary Parkinson's disease. Regardless of the cause, the disease's motor symptoms result from the death of neurons in the midbrain. The cause of cell death is not fully understood, but it appears to involve the buildup in the brain of protein structures called Lewy bodies. Early in the course of the illness, medications can be prescribed to help reduce the motor disturbances. As the disease progresses, however, the medications become ineffective. They also cause a negative side effect of involuntary writhing movements.

FEATURE: HUMAN BIOLOGY IN THE NEWS

On June 3, 2016, media worldwide exploded with news of the death of Muhammad Ali at the age of 74. The world champion boxer and Olympic gold medalist died that day of a respiratory infection complication, but the underlying cause was Parkinson's disease. Ali was diagnosed with Parkinson's in 1984 when he was only 42 years old. Doctors attributed his disease to repeated head trauma from boxing.

In the days following Ali's death, the news was full of stories and images from milestones in the athlete's life, both before and after his diagnosis with Parkinson's disease. Sadly, the news coverage also provided an overview of his gradual decline as the disease progressed. Ali was pictured in 1996, lighting the flame at the Summer Olympics in Atlanta. In 2012, Ali had to be helped to his feet by his wife to stand before the flag he was supposed to carry into the stadium. He was unable to carry it because of the ravages of Parkinson's disease.

Muhammad Ali retired from boxing in 1981 at 39, but he didn't retire from fighting. Until the final year of his life, Ali was a passionate activist for peace and justice and against war and racism. In 1998, he joined Michael J. Fox, who also has Parkinson's disease, to raise awareness and fund research on Parkinson's disease. In 2002, Fox and Ali made a joint appearance before Congress to present their case. In 2005, Ali received the Presidential Medal of Freedom from George W. Bush (Figure 9.6.7) for the many achievements and contributions he made throughout his amazing life, despite Parkinson's disease.



Figure 9.6.7: President George W. Bush gives a congratulatory hug to Muhammad Ali after awarding him a Presidential Medal of Freedom in 2005 as Ali's wife, Lonnie Ali, looks on.

REVIEW

1. What are musculoskeletal disorders? What causes them?
2. How does a muscle strain occur?
3. Define tendinitis. Why does it occur?
4. Identify first-aid steps for treating musculoskeletal disorders such as muscle strains and tendinitis.
5. Describe carpal tunnel syndrome and how it may be treated.
6. Define neuromuscular disorders.
7. Identify the cause and symptoms of muscular dystrophy.

8. Outline the cause and progression of myasthenia gravis.
9. What is Parkinson's disease? List four characteristic signs of the disorder.
10. What are the main differences between musculoskeletal disorders and neuromuscular disorders?
11. Why is the padding of a strained muscle part of the typical treatment?
12. Which disorder would be the most likely to be caused by repeated use of a jackhammer?

    A. Parkinson's disease

    B. Muscular dystrophy

    C. Carpal tunnel syndrome

    D. A neuromuscular disorder

13. *True or False.* Participation in some sports may cause Parkinson's disease.
14. *True or False.* Myasthenia gravis occurs because the body stops making acetylcholine.
15. What are two tissues, other than muscle tissue, that can experience problems that result in muscular system disorders?

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9.7: CASE STUDY CONCLUSION- NEEDING TO RELAX AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: NEEDING TO RELAX

As you learned at the beginning of this chapter, botulinum toxin—one form sold under the brand name Botox—does much more than smooth out wrinkles. It can be used to treat several disorders involving excessive muscle contraction, including cervical dystonia. You also learned that cervical dystonia, from which Nasir suffers, causes abnormal, involuntary muscle contractions of the neck. This results in the head and neck's jerky movements and/or a sustained abnormal tilt to the head. It is often painful and can significantly interfere with a person's life.

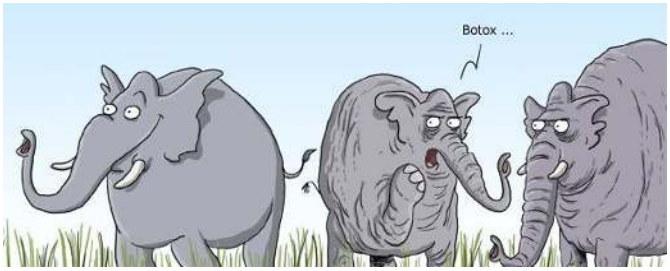


Figure **9.7.1**: Botox, he whispered.

How could a toxin actually *help* treat a muscular disorder? The soil bacterium *Clostridium botulinum* produces the botulinum toxin, and it is the cause of the potentially deadly disease called botulism. Botulism is often a foodborne illness, commonly caused by improperly canned foods. Other forms of botulism are caused by wound infections or occur when infants consume the bacteria's spores from soil or honey.

Botulism can be life-threatening because it paralyzes muscles throughout the body, including those involved in breathing. When a minimal amount of botulinum toxin is injected carefully into specific muscles by a trained medical professional, however, it can inhibit unwanted muscle contractions.



Figure **9.7.2**: These pickles are jokingly labeled "botulism," but actual botulism is really no joke.

For cosmetic purposes, botulinum toxin injected into the facial muscles relaxes them to reduce wrinkles' appearance. When used to treat cervical dystonia, it is injected into the neck muscles to inhibit excessive muscle contractions. For many patients, this helps relieve the abnormal positioning, movements, and pain associated with the disorder. The effect is temporary, so the injections must be repeated every three to four months to keep the symptoms under control.

How does botulinum toxin inhibit muscle contraction? First, recall how skeletal muscle contraction works. A motor neuron instructs skeletal muscle fibers to contract at a synapse between them called the neuromuscular junction. A nerve impulse called an action potential travels down to the motor neuron's axon terminal, where it causes the release of the neurotransmitter acetylcholine (ACh) from synaptic vesicles. The ACh travels across the synaptic cleft and binds to ACh receptors on the muscle fiber, signaling the muscle fiber to contract. According to the sliding filament theory, muscle fibers' contraction occurs due to the sliding of myosin and actin filaments across each other. This causes the Z discs of the sarcomeres to close together, shortening the sarcomeres and causing the muscle fiber to contract.

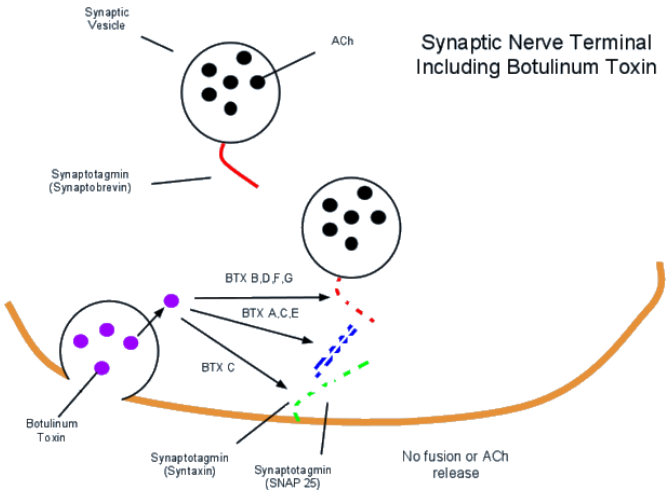


Figure **9.7.3**: Botulinum toxins cleave (break down) proteins (depicted here as red, blue, and green lines) that normally allow synaptic vesicles to bind to the membrane of the motor neuron's axon terminal to release the neurotransmitter ACh. Cleavage of these proteins prevents the synaptic vesicles from fusing to the membrane, and therefore ACh release is inhibited. In this illustration, BTX A-G refers to different subtypes of botulinum toxins.

If you wanted to inhibit muscle contraction, at what points could you theoretically interfere with this process? Inhibiting the action potential in the motor neuron, the release of ACh, the activity of ACh receptors, or the sliding filament process in the muscle fiber would all theoretically impair this process and inhibit muscle contraction. For example, in the disease myasthenia gravis, the ACh receptors' function is impaired, causing a lack of sufficient muscle contraction. As you have learned, this results in muscle weakness that can eventually become life-threatening. Botulinum toxin works by inhibiting the release of ACh from the motor neurons, thereby removing the signal instructing the muscles to contract (Figure **9.7.3**).

Fortunately, Nasir's excessive muscle contractions and associated pain improved significantly, thanks to botulinum toxin injections.

Although cervical dystonia cannot currently be cured, botulinum toxin injections have improved many patients' quality of life with this and other disorders involving excessive involuntary muscle contractions.

As you have learned in this chapter, our muscular system allows us to make voluntary movements, digest our food, and pump blood through our bodies. Whether in your arm, heart, stomach, or blood vessels, muscle tissue works by contracting. But as you have seen here, too much contraction can be a terrible thing. Fortunately, scientists and physicians have found a way to put a potentially deadly toxin—and wrinkle-reducing treatment—to excellent use as a medical treatment for some muscular system disorders.

CHAPTER SUMMARY

In this chapter, you learned about the muscular system. Specifically, you learned that:

- The muscular system consists of all the muscles of the body. There are three types of muscle: skeletal muscle (which is attached to bones by tendons and enables voluntary body movements), cardiac muscle (which makes up the walls of the heart and makes it beat), and smooth muscle (which is found in the walls of internal organs and other internal structures and controls their movements).
- Muscles are organs composed mainly of muscle cells, which may also be called muscle fibers or myocytes. Muscle cells are specialized for contracting, which occurs when protein filaments inside the cells slide over one another using energy from ATP. Muscle tissue is the only type of tissue that has cells with the ability to contract.
- Muscles can grow larger or hypertrophy. This generally occurs through increased use, although hormonal or other influences can also play a role. Muscles can also grow smaller or atrophy. This may occur through lack of use, starvation, certain diseases, or aging. In both hypertrophy and atrophy, the size—but not the number—of muscle fibers changes. The size of the muscles is the main determinant of muscle strength.
- Skeletal muscles need the stimulus of motor neurons to contract and to move the body; they need the skeletal system to act upon.
- Skeletal muscle is the most common type of muscle tissue in the human body. To move bones in opposite directions, skeletal muscles often consist of pairs of muscles that work in opposition to move bones in different directions at joints.
- Skeletal muscle fibers are bundled together in muscle fascicles, which are bundled together to form individual skeletal muscles. Skeletal muscles also have connective tissue supporting and protecting the muscle tissue.
    - Each skeletal muscle fiber consists of a bundle of myofibrils, which are bundles of protein filaments. The filaments are arranged in repeating units called sarcomeres, which are the skeletal muscles' basic functional units. Skeletal muscle tissue is striated because of the pattern of sarcomeres in its fibers.
    - Skeletal muscle fibers can be divided into two types, called slow-twitch and fast-twitch fibers. Slow-twitch fibers are used mainly in aerobic endurance activities (such as long-distance running). Fast-twitch fibers are used mainly for non-aerobic, strenuous activities (such as sprinting). Proportions of the two types of fibers vary from muscle to muscle and person to person.
- Smooth muscle tissue is found in the walls of internal organs and vessels. When smooth muscles contract, they help the organs and vessels carry out their functions. Contractions of smooth muscles are involuntary and controlled by the autonomic nervous system, hormones, and other substances.
    - Cells of smooth muscle tissue are not striated because they lack sarcomeres, but the cells contract in the same basic way as striated muscle cells. Unlike striated muscle, smooth muscle can sustain very long-term contractions and maintain its contractile function, even when stretched.
- Cardiac muscle tissue is found only in the wall of the heart. When cardiac muscle contracts, the heart beats and pumps blood. Contractions of cardiac muscle are involuntary, like those of smooth muscles. Electrical impulses from specialized cardiac cells control them.
    - Like skeletal muscle, cardiac muscle is striated because its filaments are arranged in sarcomeres. However, the exact arrangement differs, making cardiac and skeletal muscle tissues look different from one another.
    - The heart is the muscle that performs the greatest amount of physical work in a lifetime. Its cells contain many mitochondria to produce ATP for energy and help the heart resist fatigue.
- A muscle contraction is an increase in tension or a decrease in the length of a muscle. A muscle contraction is isometric if muscle tension changes, but muscle length remains the same. It is isotonic if muscle length changes, but muscle tension remains the same.
    - A skeletal muscle contraction begins with the electrochemical stimulation of a muscle fiber by a motor neuron. This occurs at a chemical synapse called a neuromuscular junction. The neurotransmitter acetylcholine diffuses across the synaptic cleft and binds to receptors on the muscle fiber. This initiates a muscle contraction.
    - Once stimulated, the skeletal muscle fibers' protein filaments slide past each other to produce a contraction. The sliding filament theory is the most widely accepted explanation for how this occurs. According to this theory, thick myosin filaments repeatedly attach to and pull on thin actin filaments, thus shortening sarcomeres.
    - Crossbridge cycling is a cycle of molecular events that underlies the sliding filament theory. Using energy in ATP, myosin heads repeatedly bind with and pull on actin filaments. This moves the actin filaments toward the center of

a sarcomere, shortening the sarcomere and causing a muscle contraction.
    - The ATP needed for a muscle contraction comes first from ATP already available in the cell, and more is generated from creatine phosphate. These sources are quickly used up. Glucose and glycogen can be broken down to form ATP and pyruvate. Pyruvate can then be used to produce ATP in aerobic respiration if oxygen is available or used in anaerobic respiration if oxygen is not available.
- Physical exercise is defined as any bodily activity that enhances or maintains physical fitness and overall health. Activities such as household chores may even count as physical exercise! Current recommendations for adults are 30 minutes of moderate exercise a day.
- Aerobic exercise is any physical activity that uses muscles at less than their maximum contraction strength but for long periods of time. This type of exercise uses a relatively high percentage of slow-twitch muscle fibers that consume large amounts of oxygen. Aerobic exercises increase cardiovascular endurance and include cycling and brisk walking.
- Anaerobic exercise is any physical activity that uses muscles at close to their maximum contraction strength, but for short periods of time. This type of exercise uses a relatively high percentage of fast-twitch muscle fibers that consume small amounts of oxygen. Anaerobic exercises increase muscle and bone mass and strength, and they include push-ups and sprinting.
- Flexibility exercise is any physical activity that stretches and lengthens muscles, thereby improving the range of motion and reducing injury risk. Examples include stretching and yoga.
- Many studies have shown that physical exercise is positively correlated with a diversity of physical, mental, and emotional health benefits. Physical exercise also increases the quality of life and life expectancy.
    - Many of the exercise benefits may come about because contracting muscles release hormones called myokines, which promote tissue repair and growth and have anti-inflammatory effects.
    - Physical exercise can reduce risk factors for cardiovascular disease, including hypertension and excess body weight. Physical exercise can also increase cardiovascular health factors, such as the mechanical efficiency of the heart.
    - Physical exercise has been shown to offer protection from dementia and other cognitive problems, perhaps because it increases blood flow or neurotransmitters in the brain, among other potential effects.
    - Numerous studies suggest that regular aerobic exercise works and pharmaceutical antidepressants in treating mild-to-moderate depression, possibly because it increases the synthesis of natural euphoriants in the brain.
    - Research shows that physical exercise generally improves sleep for most people and helps sleep disorders, such as insomnia. Other health benefits of physical exercise include better immune system function and reduced risk of type 2 diabetes and obesity.
- There is great variation in individual responses to exercise, partly due to genetic differences in proportions of slow-twitch and fast-twitch muscle fibers. People with more slow-twitch fibers may be able to develop greater endurance from aerobic exercise. In contrast, people with more fast-twitch fibers may develop greater muscle size and strength from anaerobic exercise.
- Some adverse effects may occur if exercise is extremely intense, and the body is not given proper rest between exercise sessions. Many people who overwork their muscles develop delayed onset muscle soreness (DOMS), caused by tiny tears in muscle fibers.
- Musculoskeletal disorders are injuries in muscles or associated tissues (such as tendons) because of biomechanical stresses. The disorders may be caused by sudden exertion, over-exertion, repetitive motions, and similar stresses.
    - A muscle strain is an injury in which muscle fibers tear as a result of overstretching. First aid for a muscle strain includes the five steps represented by the acronym PRICE (protection, rest, ice, compression, and elevation). Medications for inflammation and pain (such as NSAIDs) may also be used.
    - Tendinitis is inflammation of a tendon that occurs when it is over-extended or worked too hard without rest. Tendinitis may also be treated with PRICE and NSAIDs.
    - Carpal tunnel syndrome is a biomechanical problem in the wrist when the median nerve becomes compressed between carpal bones. It may occur with repetitive use, a tumor, or trauma to the wrist. It may cause pain, numbness, and eventually—if untreated—muscle wasting in the thumb and first two fingers of the hand.
- Neuromuscular disorders are systemic disorders that occur because of problems with the nervous control of muscle contractions or muscle cells themselves.
    - Muscular dystrophy is a genetic disorder caused by defective proteins in muscle cells. It is characterized by progressive skeletal muscle weakness and death of muscle tissues.
    - Myasthenia gravis is a genetic neuromuscular disorder characterized by fluctuating muscle weakness and fatigue. More muscles are affected, and muscles become increasingly weakened, as the disorder progresses. Myasthenia gravis most often occurs because immune system antibodies block acetylcholine receptors on muscle cells because of the actual loss of acetylcholine receptors.
    - Parkinson's disease is a degenerative disorder of the central nervous system that mainly affects the muscular system and movement. It occurs because of the death of neurons in the midbrain. Characteristic signs of the disorder are muscle tremor, muscle rigidity, slowness of movement, and postural instability. Dementia and depression also often characterize advanced stages of the disease.

As you saw in this chapter, muscles need oxygen to provide enough ATP for most of their activities. In fact, all of the body's systems

require oxygen and remove waste products, such as carbon dioxide. In the next chapter, you will learn about how the respiratory system obtains and distributes oxygen throughout the body and how it removes wastes, such as carbon dioxide.

CHAPTER SUMMARY REVIEW

1. *True or False.* Each motor neuron controls one muscle fiber.
2. *True or False.* Peristalsis is a pattern of muscle contraction in smooth muscle tissue.
3. When muscles atrophy:
   A. muscle fibers become narrower
   B. muscle fibers turn into fat cells
   C. muscle fibers are lost
   D. muscle fibers become shorter
4. What are tendons?
5. What is a muscular system disorder involving tendons?
6. Which of the main types of muscle tissue is used when you make a voluntary movement of one of your limbs?
7. Which main types of muscle tissue function independently of conscious control by the brain?
8. Describe the relationship between muscles, muscle fibers, and fascicles.
9. *Choose one.* The (autonomic; somatic) nervous system controls the skeletal muscles.
10. *True or False.* Sarcomeres are the cells of the muscular system.
11. *True or False.* Muscles contain connective tissue as well as muscle tissue.
12. The biceps and triceps muscles are shown in Figure **9.7.4**. Answer the following questions about these arm muscles.
    A. When the biceps contract and become shorter, as in the illustration, what kind of motion does this produce in the arm?
    B. Is the situation described in part more likely to be an isometric or isotonic contraction? Explain your answer.
    C. If the triceps were to then contract, which way would help the arm move?

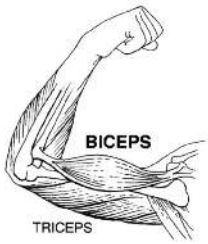


Figure **9.7.4**: biceps

13. Put the following events in order of when they occur during the process of skeletal muscle contraction, from earliest to latest:
    A. Acetylcholine binds to receptors on the muscle fiber
    B. Actin filaments slide, shortening the sarcomere
    C. An action potential is initiated in a motor neuron
    D. Acetylcholine is released from synaptic vesicles
14. What are Z discs, and what happens to them during muscle contraction?
15. *True or False.* Synapses only exist between neurons.
16. *True or False.* Muscles can produce hormones.
17. Which have been called the strongest muscles in the human body, relative to their work?
    A. The heart muscles
    B. The hamstring muscles
    C. The external eye muscles
    D. The stomach muscles
18. What is the function of mitochondria in muscle cells? Which type of muscle fiber has more mitochondria—slow-twitch or fast-twitch?
19. Fast-twitch and slow-twitch are types of which kind of muscle fibers?
    A. skeletal
    B. smooth
    C. cardiac
    D. B and C
20. Myoglobin:
    A. Stores oxygen for anaerobic respiration
    B. Stores oxygen for aerobic respiration
    C. Is present in higher amounts in fast-twitch fibers than slow-twitch fibers
    D. Is where ATP is produced
21. *True or False.* All people have the same proportion of slow-twitch to fast-twitch muscle fibers.
22. *True or False.* A sprain is a tear in the muscle fibers.
23. Which condition directly damages neurons, not muscles?
    A. Myasthenia gravis
    B. Muscular dystrophy
    C. Musculoskeletal disorder
    D. Parkinson's disease
24. What is the difference between primary and secondary Parkinson's disease?
25. Why can carpal tunnel syndrome cause muscle weakness in the hands?
26. *True or False.* The heart consists of smooth muscle tissue.
27. *True or False.* Sprinting is considered an anaerobic exercise

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CHAPTER OVERVIEW

10: RESPIRATORY SYSTEM

This chapter describes the structure and function of the respiratory system, including how breathing occurs and what controls it, as well as how the process of gas exchange takes place in the lungs. The chapter also describes several disorders of the respiratory system and details the adverse health effects of smoking.

10.1: Case Study- Respiratory System and Gas Exchange

10.2: Structure and Function of the Respiratory System

10.3: Breathing

10.4: Disorders of the Respiratory System

10.5: Smoking and Health

10.6: Case Study Conclusion- Bronchitis and Chapter Summary

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10.1: CASE STUDY- RESPIRATORY SYSTEM AND GAS EXCHANGE

CASE STUDY: COUGH THAT WON'T QUIT

Three weeks ago, 20-year-old Sacheen came down with symptoms typical of the common cold. She had a runny nose, fatigue, and a mild cough. Her symptoms had been starting to improve, but recently her cough has been getting worse. She coughs up a lot of thick mucus, her throat is sore from frequent coughing, and her chest feels very congested. According to her wife, Sacheen has a "chest cold." Sacheen is a smoker and wonders if her habit is making her cough worse. She decides that it is time to see a doctor.



Figure **10.1.1**: Coughing

Dr. Tsosie examines Sacheen and asks about her symptoms and health history. She checks the level of oxygen in Sacheen's blood by attaching a device called a pulse oximeter to Sacheen's finger (Figure **10.1.2**). Dr. Tsosie concludes that Sacheen has bronchitis, an infection that commonly occurs after a person has a cold or flu. Bronchitis is sometimes referred to as a "chest cold," so Sacheen's wife was right! Bronchitis causes inflammation and a build-up of mucus in the bronchial tubes in the chest.



Figure **10.1.2**: A pulse oximeter, used to measure blood oxygen levels.

Because viruses, and not bacteria, usually cause bronchitis, Dr. Tsosie tells Sacheen that antibiotics are not likely to help. Instead, she recommends that Sacheen try to thin and remove the mucus by drinking plenty of fluids and using a humidifier, or spending time in a steamy shower. She also recommends that Sacheen get plenty of rest.

Dr. Tsosie also tells Sacheen some things *not* to do—most importantly, not to smoke while she is sick and to try to quit smoking in the long term. She explains that smoking can make people more susceptible to bronchitis and can hinder recovery. She also advises Sacheen not to take over-the-counter cough suppressant medication.

As you read this chapter on the respiratory system, you will better understand what bronchitis is and why Dr. Tsosie made the treatment recommendations that she did. At the end of the chapter, you will learn more about acute bronchitis, which is the type that Sacheen has. This information may come in handy to you personally because the chances are high that you will get this common infection at some point in your life—there are millions of bronchitis cases every year!

CHAPTER OVERVIEW: RESPIRATORY SYSTEM

In this chapter, you will learn about the respiratory system, the system that exchanges gases such as oxygen and carbon dioxide between the body and the outside air. Specifically, you will learn about:

- The process of respiration, in which oxygen moves from the outside air into the body and carbon dioxide and other waste gases move from inside the body into the outside air.
- The organs of the respiratory system, including the lungs, bronchial tubes, and the rest of the respiratory tract.
- How the respiratory tract protects itself from pathogens and other potentially harmful substances in the air.
- How the rate of breathing is regulated to maintain homeostasis of blood gases and pH.
- How ventilation, or breathing, allows us to inhale air into the body and exhale air out of the body.
- The conscious and unconscious control of breathing.
- Nasal breathing compared to mouth breathing.
- What happens when a person is drowning.
- How gas exchange occurs between the air and blood in the alveoli of the lungs, and between the blood and cells throughout the body.
- Disorders of the respiratory system, including asthma, pneumonia, chronic obstructive pulmonary disease (COPD), and lung cancer.
- The negative health effects of smoking.

As you read the chapter, think about the following questions:

1. Where are the bronchial tubes, and what is their function?
2. What is the function of mucus, and why can too much mucus be a bad thing?
3. Why did Dr. Tsosie check Sacheen's blood oxygen level?
4. Why do you think Dr. Tsosie warned Sacheen not to take cough suppressant medications?
5. How does acute bronchitis compare to chronic bronchitis, and how do they both relate to smoking?

ATTRIBUTIONS

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10.2: STRUCTURE AND FUNCTION OF THE RESPIRATORY SYSTEM

SEEING YOUR BREATH

Why can you "see your breath" on a cold day? The air you exhale through your nose and mouth is warm, like the inside of your body. Exhaled air also contains a lot of water vapor because it passes over moist surfaces from the lungs to the nose or mouth. The water vapor in your breath cools suddenly when it reaches the much colder outside air. This causes the water vapor to condense into a fog of tiny droplets of liquid water. You release water vapor and other gases from your body through the process of respiration.



Figure **10.2.1**: Breath on a cold day

WHAT IS RESPIRATION?

Respiration is the life-sustaining process in which gases are exchanged between the body and the outside atmosphere. Specifically, oxygen moves from the outside air into the body; and water vapor, carbon dioxide, and other waste gases move from inside the body into the outside air. Respiration is carried out mainly by the **respiratory system.** It is important to note that respiration by the respiratory system is not the same process as cellular respiration that occurs inside cells, although the two processes are closely connected. Cellular respiration is the metabolic process in which cells obtain energy, usually by "burning" glucose in the presence of oxygen. When cellular respiration is aerobic, it uses oxygen and releases carbon dioxide as a waste product. Respiration by the respiratory system supplies the oxygen needed by cells for aerobic cellular respiration and removes the carbon dioxide produced by cells during cellular respiration.

Respiration by the respiratory system actually involves two subsidiary processes. One process is ventilation or breathing. This is the physical process of conducting air to and from the lungs. The other process is gas exchange. This is the biochemical process in which oxygen diffuses out of the air and into the blood while carbon dioxide and other waste gases diffuse out of the blood and into the air. All of the organs of the respiratory system are involved in breathing, but only the lungs are involved in gas exchange.

RESPIRATORY ORGANS

The organs of the respiratory system form a continuous system of passages called the **respiratory tract,** through which air flows into and out of the body. The respiratory tract has two major divisions: the upper respiratory tract and the lower respiratory tract. The organs in each division are shown in Figure **10.2.2**. In addition to these organs, certain muscles of the thorax (the body cavity that fills the chest) are also involved in respiration by enabling breathing. Most important is a large muscle called the diaphragm, which lies below the lungs and separates the thorax from the abdomen. Smaller muscles between the ribs also play a role in breathing. You can learn more about breathing muscles in the concept of *Breathing*.

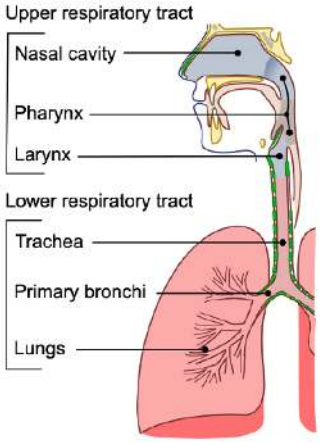


Figure **10.2.2**: During breathing, inhaled air enters the body through the nose and passes through the pharynx, larynx, trachea, bronchi, and then enters the lungs. Exhaled air travels from the lungs in the opposite direction.

UPPER RESPIRATORY TRACT

All of the organs and other structures of the upper respiratory tract are involved in the conduction or the movement of air into and out of the body. Upper respiratory tract organs provide a route for air to move between the outside atmosphere and the lungs. They also clean, humidity, and warm the incoming air. However, no gas exchange occurs in these organs.

NASAL CAVITY

The **nasal cavity** is a large, air-filled space in the skull above and behind the nose in the middle of the face. It is a continuation of the two nostrils. As inhaled air flows through the nasal cavity, it is warmed and humidified. Hairs in the nose help trap larger foreign particles in the air before they go deeper into the respiratory tract. In addition to its respiratory functions, the nasal cavity also contains chemoreceptors that are needed for the sense of smell and that contribute importantly to the sense of taste.

PHARYNX

The **pharynx** is a tube-like structure that connects the nasal cavity and the back of the mouth to other structures lower in the throat, including the larynx. The pharynx has dual functions: both air and

food (or other swallowed substances) pass through it, so it is part of both the respiratory and digestive systems. Air passes from the nasal cavity through the pharynx to the larynx (as well as in the opposite direction). Food passes from the mouth through the pharynx to the esophagus.

LARYNX

The **larynx** connects the pharynx and trachea and helps to conduct air through the respiratory tract. The larynx is also called the voice box because it contains the vocal cords, which vibrate when air flows over them, thereby producing sound. You can see the vocal cords in the larynx in Figure **10.2.3**. Certain muscles in the larynx move the vocal cords apart to allow breathing. Other muscles in the larynx move the vocal cords together to allow the production of vocal sounds. The latter muscles also control the pitch of sounds and help control their volume.

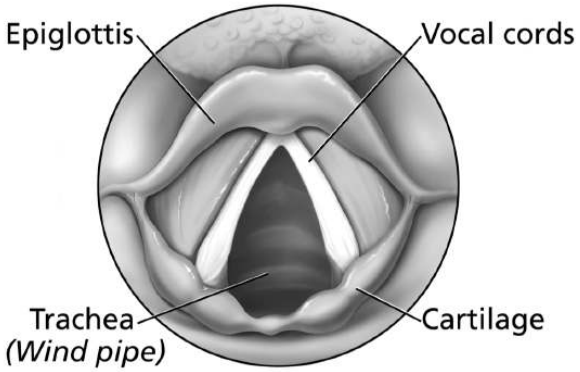


Figure **10.2.3**: The larynx is viewed from the top. opening to the trachea is closed by epiglottis during swallowing. Cartilage and vocal cords are also visible.

A very important function of the larynx is protecting the trachea from aspirated food. When swallowing occurs, the backward motion of the tongue forces a flap called the epiglottis to close over the entrance to the larynx. You can see the epiglottis in Figure **10.2.3**. This prevents swallowed material from entering the larynx and moving deeper into the respiratory tract. If swallowed material does start to enter the larynx, it irritates the larynx and stimulates a strong cough reflex. This generally expels the material out of the larynx and into the throat.

LOWER RESPIRATORY TRACT

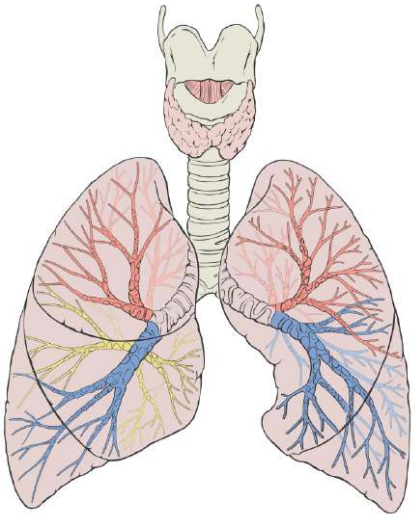


Figure **10.2.4**: This diagram illustrates the tree-like branching of the passages of the lower respiratory tract within the lungs.

The trachea and other passages of the lower respiratory tract conduct air between the upper respiratory tract and the lungs. These passages form an inverted tree-like shape (Figure **10.2.4**), with repeated branching as they move deeper into the lungs. All told, there are an astonishing 1,500 miles of airways conducting air through the human respiratory tract! It is only in the lungs, however, that gas exchange occurs between the air and the bloodstream.

TRACHEA

The **trachea,** or windpipe, is the widest passageway in the respiratory tract. It is about 2.5 cm (1 in.) wide and 10-15 cm (4-6 in.) long. It is formed by rings of cartilage, which make it relatively strong and resilient. The trachea connects the larynx to the lungs for the passage of air through the respiratory tract. The trachea branches at the bottom to form two bronchial tubes.

BRONCHI AND BRONCHIOLES

There are two main bronchial tubes, or **bronchi (singular, bronchus)**, called the right and left bronchi. The bronchi carry air between the trachea and lungs. Each bronchus branches into smaller, secondary bronchi; and secondary bronchi branch into still smaller tertiary bronchi. The smallest bronchi branch into very small tubules called bronchioles. The tiniest bronchioles end in alveolar ducts, which terminate in clusters of minuscule air sacs, called alveoli (singular, alveolus), in the lungs.

LUNGS

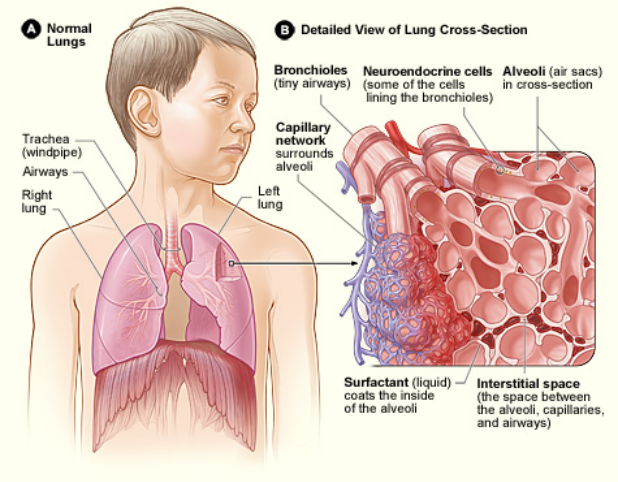


Figure **10.2.5**: The cross-section of lung tissue on the right shows the alveoli in which gas exchange takes place with the capillary network that surrounds them. Neuroendocrine cells lining the bronchioles control their diameter and the flow of air through them. A surfactant is a liquid that covers the inside of the alveoli and prevents them from collapsing and sticking together when air empties out of them during exhalation.

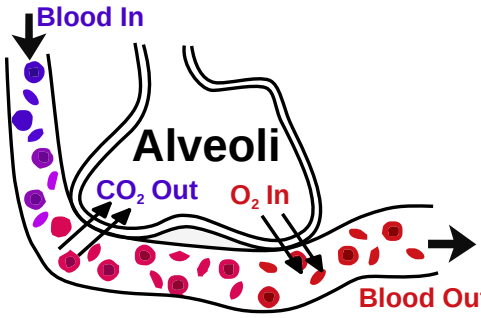


Figure **10.2.6**: The gaseous exchange between blood and outside air inside the lung alveoli.

The **lungs** are the largest organs of the respiratory tract. They are suspended within the pleural cavity of the thorax. In Figure **10.2.5**, you can see that each of the two lungs is divided into sections. These are called lobes, and they are separated from each other by connective tissues. The right lung is larger and contains three lobes. The left lung is smaller and contains only two lobes. The smaller left lung allows room for the heart, which is just left of the center of the chest.

Lung tissue consists mainly of alveoli (Figure **10.2.6**). These tiny air sacs are the functional units of the lungs where gas exchange takes place. The two lungs may contain as many as 700 million alveoli, providing a huge total surface area for gas exchange to take place. In fact, alveoli in the two lungs provide as much surface area as half a tennis court! Each time you breathe in, the alveoli fill with air, making the lungs expand. Oxygen in the air inside the alveoli is absorbed by the blood in the mesh-like network of tiny capillaries that surrounds each alveolus. The blood in these capillaries also releases carbon dioxide into the air inside the alveoli. Each time you breathe out, air leaves the alveoli and rushes into the outside atmosphere, carrying waste gases with it.

The lungs receive blood from two major sources. They receive deoxygenated blood from the heart. This blood absorbs oxygen in the lungs and carries it back to the heart to be pumped to cells throughout the body. The lungs also receive oxygenated blood from the heart that provides oxygen to the cells of the lungs for cellular respiration.

PROTECTING THE RESPIRATORY SYSTEM

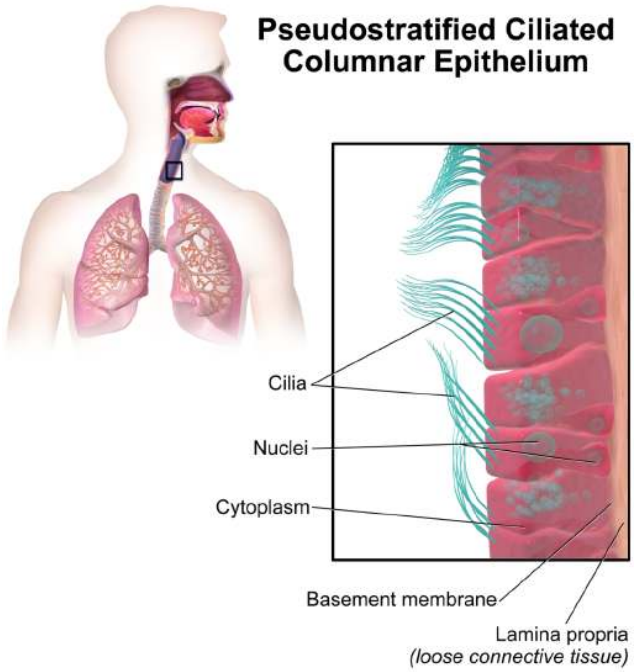


Figure **10.2.7**: The upward sweeping motion of cilia lining the respiratory tract helps keep it free from dust, pathogens, and other harmful substances.

You may be able to survive for weeks without food and for days without water, but you can survive without oxygen for only a matter of minutes except under exceptional circumstances. Therefore, protecting the respiratory system is vital. That's why making sure a patient has an open airway is the first step in treating many medical emergencies. Fortunately, the respiratory system is well protected by the ribcage of the skeletal system. However, the extensive surface area of the respiratory system is directly exposed to the outside world and all its potential dangers in inhaled air. Therefore, it should come as no surprise that the respiratory system has a variety of ways to protect itself from harmful substances such as dust and pathogens in the air.

The main way the respiratory system protects itself is called the mucociliary escalator. From the nose through the bronchi, the respiratory tract is covered in the epithelium that contains mucus-secreting goblet cells. The mucus traps particles and pathogens in the incoming air. The epithelium of the respiratory tract is also covered with tiny cell projections called cilia (singular, cilium), as shown in Figure **10.2.7**. The cilia constantly move in a sweeping motion upward toward the throat, moving the mucus and trapped particles and pathogens away from the lungs and toward the outside of the body.

What happens to the material that moves up the mucociliary escalator to the throat? It is generally removed from the respiratory tract by clearing the throat or coughing. Coughing is a largely involuntary response of the respiratory system that occurs when nerves lining the airways are irritated. The response causes air to be expelled forcefully from the trachea, helping to remove mucus and any debris it contains (called phlegm) from the upper respiratory tract to the mouth. The phlegm may spit out (expectorated), or it may be swallowed and destroyed by stomach acids.

Sneezing is a similar involuntary response that occurs when nerves lining the nasal passage are irritated. It results in forceful expulsion of air from the mouth, which sprays millions of tiny droplets of mucus and other debris out of the mouth and into the air, as shown in Figure **10.2.8**. This explains why it is so important to sneeze into a sleeve rather than the air to help prevent the transmission of respiratory pathogens.



Figure **10.2.8**: Sneezing results in tiny particles from the mouth being forcefully ejected into the air.

HOW THE RESPIRATORY SYSTEM WORKS WITH OTHER ORGAN SYSTEMS

The amount of oxygen and carbon dioxide in the blood must be maintained within a limited range for the survival of the organism. Cells cannot survive for long without oxygen, and if there is too much carbon dioxide in the blood, the blood becomes dangerously acidic (pH is too low). Conversely, if there is too little carbon dioxide in the blood, the blood becomes too basic (pH is too high). The respiratory system works hand-in-hand with the nervous and cardiovascular systems to maintain homeostasis in blood gases and pH.

It is the level of carbon dioxide rather than the level of oxygen that is most closely monitored to maintain blood gas and pH homeostasis. The level of carbon dioxide in the blood is detected by cells in the brain, which speed up or slow down the rate of breathing through the autonomic nervous system as needed to bring the carbon dioxide level within the normal range. Faster breathing lowers the carbon dioxide level (and raises the oxygen level and pH); slower breathing has the opposite effects. In this way, the levels of carbon dioxide and oxygen, as well as pH, are maintained within normal limits.

The respiratory system also works closely with the cardiovascular system to maintain homeostasis. The respiratory system exchanges gases between the blood and the outside air, but it needs the cardiovascular system to carry them to and from body cells. Oxygen is absorbed by the blood in the lungs and then transported through a vast network of blood vessels to cells throughout the body where it is needed for aerobic cellular respiration. The same system absorbs carbon dioxide from cells and carries it to the respiratory system for removal from the body.

FEATURE: MY HUMAN BODY

Choking is the mechanical obstruction of the flow of air from the atmosphere into the lungs. It prevents breathing and may be partial or complete. Partial choking allows some though inadequate airflow into the lung—prolonged or complete choking results in asphyxia, or suffocation, which is potentially fatal.

Obstruction of the airway typically occurs in the pharynx or trachea. Young children are more prone to choking than are older people, in part because they often put small objects in their mouths and do not appreciate the risk of choking that they pose. Young children may choke on small toys or parts of toys or on household objects in addition to food. Foods that can adapt their shape to that of the pharynx, such as bananas and marshmallows, are especially dangerous and may cause choking in adults as well as children.

How can you tell if a loved one is choking? The person cannot speak or cry out or has great difficulty doing so. Breathing, if possible, is labored, producing gasping or wheezing. The person may desperately clutch at his or her throat or mouth. If breathing is not soon restored, the person's face will start to turn blue from lack of oxygen. This will be followed by unconsciousness if oxygen deprivation continues beyond a few minutes.

If an infant is choking, turning the baby upside down and slapping on the back may dislodge the obstructing object. To help an older person who is choking, first, encourage the person to cough. Give them a few hardback slaps to help force the lodged object out of the airway. If these steps fail, perform the Heimlich maneuver on the person. You can easily find instructional videos online to learn how to do it. If the Heimlich maneuver also fails, call for emergency medical care immediately.



Figure **10.2.9**: The Heimlich maneuver may be needed to help force an aspirated object out of the respiratory tract.

REVIEW

1. What is respiration, as carried out by the respiratory system? Name the two subsidiary processes it involves.
2. Describe the respiratory tract.
3. Identify the organs of the upper respiratory tract, and state their functions.
4. List the organs of the lower respiratory tract. Which organs are involved only in conduction?
5. Where does gas exchange take place?
6. How does the respiratory system protect itself from potentially harmful substances in the air?
7. Explain how the rate of breathing is controlled.
8. Why does the respiratory system need the cardiovascular system to help it perform its main function of gas exchange?
9. Place the following organs or structures of the respiratory system in order of when they are encountered by air entering the body — from earliest to latest.

   trachea; nasal cavity; alveoli; bronchioles; larynx; bronchi; pharynx
10. Which organ is part of both the digestive and respiratory systems?

    A. Larynx

    B. Trachea

    C. Pharynx

    D. Bronchus
11. Describe two ways in which the body prevents food from entering the lungs.
12. *True or False.* The lungs receive some oxygenated blood.
13. *True or False.* Gas exchange occurs in both the upper and lower respiratory tracts.
14. Coughing can expel _____ from the body.

    A. mucus

    B. food particles

    C. phlegm

    D. All of the above
15. What is the relationship between respiration and cellular respiration?

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10.3: BREATHING

DOING THE 'FLY

The swimmer in this photo is doing the butterfly stroke. This swimming style requires the swimmer to carefully control his breathing so it is coordinated with his swimming movements. Breathing is the process of moving air into and out of the lungs, which are the organs in which gas exchange takes place between the atmosphere and the body. Breathing is also called **ventilation,** and it is one of two parts of the life-sustaining process of respiration, the other part being gas exchange. Before you can understand how breathing is controlled, you need to know how breathing occurs.



Figure **10.3.1**: Butterfly stroke

HOW BREATHING OCCURS

Breathing is a two-step process that includes drawing air into the lungs, or inhaling, and letting the air out of the lungs, or exhaling. Both processes are illustrated in Figure **10.3.2**.

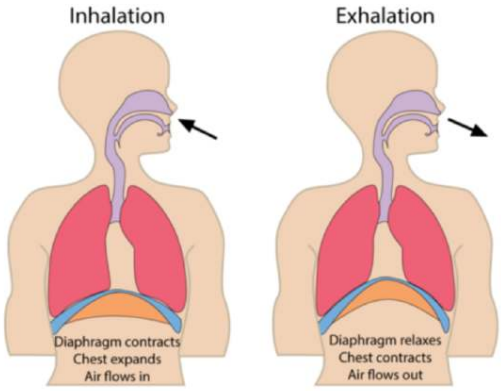


Figure **10.3.2**: Inhalation and exhalation during breathing depend mainly on repeated contractions of the diaphragm.

INHALING

Inhaling is an active process that results mainly from the contraction of a muscle called the diaphragm, shown in Figure **10.3.2**. The **diaphragm** is a large, dome-shaped muscle below the lungs that separates the thoracic (chest) and abdominal cavities. When the diaphragm contracts, the thoracic cavity expands and the contents of the abdomen are pushed downward. Other muscles, such as external intercostal muscles between the ribs, also contribute to the process of inhalation, especially when inhalation is forced, as when taking a deep breath. These muscles help increase thoracic volume by expanding the ribs outward. With the chest expanded, there is lower air pressure inside the lungs than outside the body, so outside air flows into the lungs via the respiratory tract.

EXHALING

Exhaling involves the opposite series of events. The diaphragm relaxes, so it moves upward and decreases the volume of the thorax (Figure **10.3.2**. Air pressure inside the lungs increases so it is higher than the air pressure outside the lungs. Exhaling, unlike inhaling, is typically a passive process that occurs mainly due to the elasticity of the lungs. With the change in air pressure, the lungs contract to their pre-inflated size, forcing out the air they contain in the process. Air flows out of the lungs, similar to the way air rushes out of a balloon when it is released. If exhalation is forced, internal intercostal and abdominal muscles may help move the air out of the lungs.

CONTROL OF BREATHING

Breathing is one of the few vital bodily functions that can be controlled consciously as well as unconsciously. Think about using your breath to blow up a balloon. You take a long, deep breath, and then you exhale the air as forcibly as you can into the balloon. Both the inhalation and exhalation are consciously controlled.

CONSCIOUS CONTROL OF BREATHING

You can control your breathing by holding your breath, slowing your breathing, or **hyperventilating,** which is breathing more quickly and shallowly than necessary. You can also exhale or inhale more forcefully or deeply than usual. Conscious control of breathing is common in many activities besides blowing up balloons, including swimming, speech training, singing, playing many different musical instruments (Figure **10.3.3**), and doing yoga, to name just a few.



Figure **10.3.3**: Playing the oboe is hard work. Exhaled air must be forced through a tiny opening between two very small wooden reeds.

There are limits on the conscious control of breathing. For example, it is not possible for a healthy person to voluntarily stop breathing indefinitely. Before long, there is an irrepressible urge to breathe. If you were able to stop breathing for a long enough time, you would lose consciousness. The same thing would happen if you were to

hyperventilate for too long. Once you lose consciousness so you can no longer exert conscious control over your breathing, involuntary control of breathing takes over.

UNCONSCIOUS CONTROL OF BREATHING

Unconscious breathing is controlled by **respiratory centers** in the medulla and pons of the brainstem (Figure **10.3.4**). The respiratory centers automatically and continuously regulate the rate of breathing depending on the body's needs. These are determined mainly by blood acidity or pH. When you exercise, for example, carbon dioxide levels increase in the blood because of increased cellular respiration by muscle cells. The carbon dioxide reacts with water in the blood to produce carbonic acid, making the blood more acidic, so pH falls. The drop in pH is detected by chemoreceptors in the medulla. Blood levels of oxygen and carbon dioxide, in addition to pH, are also detected by chemoreceptors in major arteries, which send the "data" to the respiratory centers. The respiratory center responds by sending nerve impulses to the diaphragm, "telling" it to contract more quickly so the rate of breathing speeds up. With faster breathing, more carbon dioxide is released into the air from the blood, and blood pH returns to the normal range.

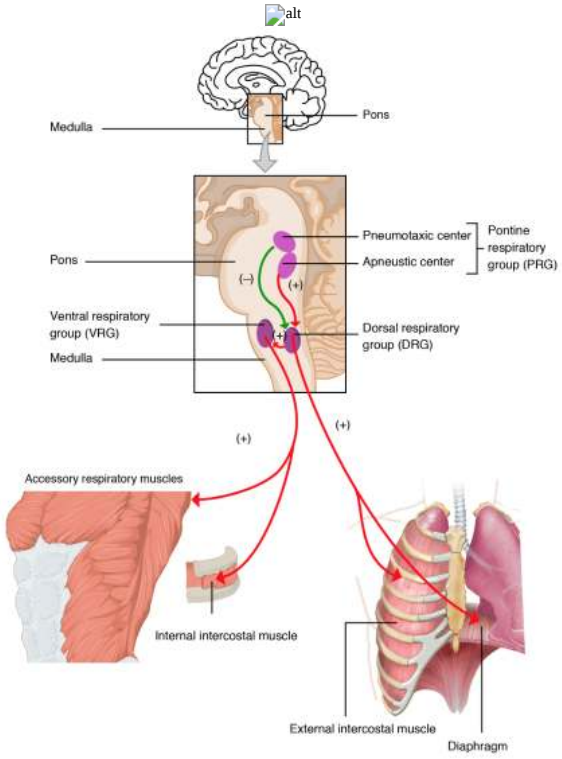


Figure **10.3.4**: Clusters of cells in the pons and medulla of the brain stem are the respiratory centers of the brain that have involuntary control over breathing muscles, such as the diaphragm and external and internal intercostal.

The opposite events occur when the level of carbon dioxide in the blood becomes too low and blood pH rises. This may occur with involuntary hyperventilation, which can happen in panic attacks, episodes of severe pain, asthma attacks, and many other situations. When you hyperventilate, you blow off a lot of carbon dioxide, leading to a drop in blood levels of carbon dioxide. The blood becomes more basic (alkaline), causing its pH to rise.

NASAL VS. MOUTH BREATHING

Nasal breathing is breathing through the nose rather than the mouth, and it is generally considered to be superior to mouth breathing. The hair-lined nasal passages do a better job of filtering particles out of the air before it moves deeper into the respiratory tract. The nasal passages are also better at warning and moistening the air, so nasal breathing is especially advantageous in the winter when the air is cold and dry. In addition, the smaller diameter of the nasal passages creates greater pressure in the lungs during exhalation. This slows the emptying of the lungs, giving them more time to extract oxygen from the air.

FEATURE: MYTH VS. REALITY

Drowning is defined as respiratory impairment from being in or under a liquid. It is further classified according to its outcome into death, ongoing health problems, or no ongoing health problems (full recovery). In the United States, accidental drowning is the second leading cause of death (after motor vehicle crashes) in children aged 12 years and younger. There are some potentially dangerous myths about drowning. Knowing what they are might save your life or the life of a loved one, especially a child.

Myth: People drown when they aspirate water into their lungs.

Reality: Generally, in the early stages of drowning, very little water enters the lungs. A small amount of water entering the trachea causes a muscular spasm in the larynx that seals the airway and prevents the passage of water into the lungs. This spasm is likely to last until unconsciousness occurs.

Myth: You can tell when someone is drowning because they will shout for help and wave their arms to attract attention.

Reality: The muscular spasm that seals the airway prevents the passage of air as well as water, so a person who is drowning is unable to shout or call for help. In addition, instinctive reactions that occur in the final minute or so before a drowning person sinks under the water may look similar to calm, safe behavior. The head is likely to be low in the water, tilted back with the mouth open. The person may have uncontrolled movements of the arms and legs, but they are unlikely to be visible above the water.

Myth: It is too late to save a person who is unconscious in the water.

Reality: An unconscious person rescued with an airway still sealed from the muscular spasm of the larynx stands a good chance of full recovery if they start receiving CPR within minutes. Without water in the lungs, CPR is much more effective. Even if the cardiac arrest has occurred so the heart is no longer beating, there is still a chance of recovery. However, the longer the brain goes without oxygen, the more likely brain

cells will die. Brain death is likely after about six minutes without oxygen, except in exceptional circumstances, such as young people drowning in very cold water. There are examples of children surviving, apparently without lasting ill effects, for as long as an hour in cold water (see Explore More below for an example). Therefore, rescuers retrieving a child from cold water should attempt resuscitation even after a protracted period of immersion.

Myth: If someone is drowning, you should start administering CPR immediately, even before you try to get the person out of the water.

Reality: Removing a drowning person from the water is the first priority because CPR is ineffective in the water. The goal should be to bring the person to stable ground as quickly as possible and then to start CPR.

Myth: You are unlikely to drown unless you are in water over your head.

Reality: Depending on circumstances, people have drowned in as little as 30 mm (about 1 ½ in.) of water. For example, inebriated people or those under the influence of drugs have been known to have drowned in puddles. Hundreds of children have drowned in the water in toilets, bathtubs, basins, showers, pails, and buckets (see figure below).



Figure **10.3.5**: Young children should never be left unattended around sources of water that pose a risk of drowning, including water in toilets, bathtubs, and buckets.

REVIEW

1. Define breathing.
2. What is another term for the process of breathing?
3. What is the main difference between the processes of inhaling and exhaling?
4. Give examples of activities in which breathing is consciously controlled.
5. Young children sometimes threaten to hold their breath until they get something they want. Why is this an idle threat?
6. Explain how unconscious breathing is controlled.
7. Why is nasal breathing generally considered to be superior to mouth breathing?
8. For each of the following, indicate whether it occurs during the process of inhalation (I) or exhalation (E).
   A. The diaphragm moves downward.
   B. The diaphragm relaxes.
   C. The thoracic cavity becomes smaller.
   D. The air pressure in the lungs is lower than outside the body.
9. Give one example of a situation that would cause blood pH to rise excessively and explain why this occurs.
10. Blood levels of oxygen and carbon dioxide and pH are detected by which of these:
    A. Mechanoreceptors
    B. Chemoreceptors
    C. Lung receptors
    D. Carbon receptors
11. True or False. The diaphragm can contract due to conscious control.
12. True or False. Hypoventilating is breathing that is fast and shallow.

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10.4: DISORDERS OF THE RESPIRATORY SYSTEM

A "MITEY" MONSTER

The scary beast in Figure **10.4.1** is likely to be lurking in your own home, where it feeds on organic debris, including human skin. What is it? It's the common dust mite, a close relative of spiders. The dust mite is so small that it is barely visible with the unaided eye, so it's obviously shown above greatly enlarged. If you think you can get rid of dust mites in your home by frequent and thorough cleaning, think again. There may be thousands of dust mites in just one gram of dust! Regardless of how clean you keep your house, you can't eliminate dust mites entirely. So why even bother trying? The feces of dust mites contain proteins that are a common trigger of asthma attacks.



Figure **10.4.1**: Dust mite

ASTHMA

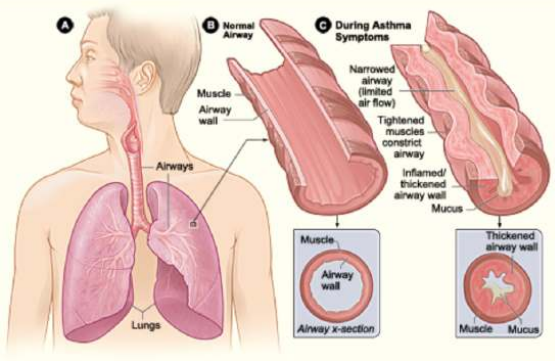


Figure **10.4.2**: During an asthma attack, airways narrow and may become clogged with mucus, making breathing difficult.

Asthma is a chronic inflammatory disease of the airways in the lungs, in which the airways periodically become inflamed. As you can see in Figure **10.4.2**, this causes swelling and narrowing of the airways, often accompanied by excessive mucus production. Symptoms of asthma include difficulty breathing, coughing, wheezing, shortness of breath, and chest tightness. Some people with asthma rarely experience symptoms, and then usually only in response to certain triggers in the environment. Other people may have symptoms almost all of the time.

Asthma is thought to be caused by a combination of genetic and environmental factors. A person with a family history of asthma is more likely to develop the disease. Dozens of genes have been found to be associated with asthma, many of which are related to the immune system. Additional risk factors include obesity and sleep apnea (see the feature My Human Body below). Environmental factors trigger asthma attacks in people who have a genetic predisposition to the disease. Besides dust mite feces, triggers may include other allergens (such as pet dander, cockroaches, and mold), certain medications including aspirin, air pollution, and stress, among other possible factors. Symptoms tend to be worse at night and early in the morning. They may also worsen during upper respiratory tract infections, strenuous exercise, or when the airways are exposed to cold air.

There is no cure for asthma at present, but the symptoms of asthma attacks usually can be reversed with the use of inhaled medications called bronchodilators. These medications soothe the constricted air passages and help to re-expand them, making breathing easier. The medications usually start to take effect almost immediately. Other medications can be taken for long-term control of the disease. These medications help prevent asthma attacks from occurring. Corticosteroids are generally considered the most effective treatment for long-term control. Another way to prevent asthma attacks is by avoiding triggers whenever possible.

PNEUMONIA

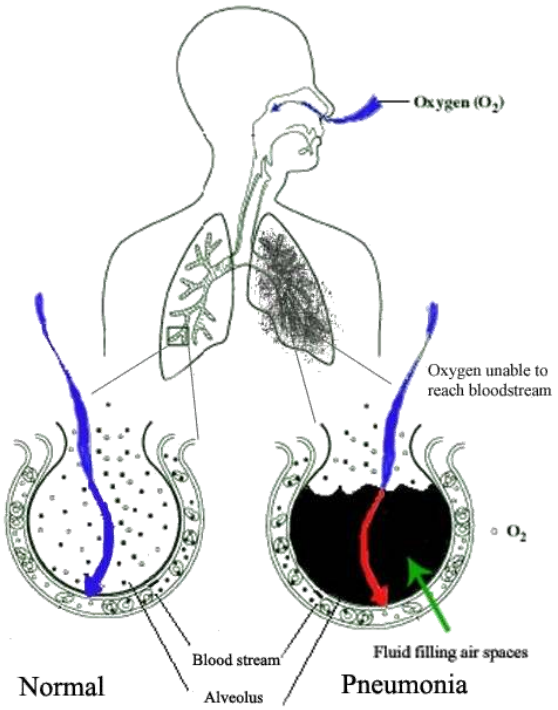


Figure **10.4.3**: Fluid-filled alveoli characteristic of pneumonia inhibit normal gas exchange with the blood.

Another common inflammatory disease of the respiratory tract is **pneumonia.** In pneumonia, the inflammation affects primarily the alveoli, which are the tiny air sacs of the lungs. Inflammation causes some of the alveoli to become filled with fluid so that gas exchange cannot occur. This is illustrated in Figure **10.4.3**. Symptoms of pneumonia typically include coughing, chest pain, difficulty breathing, and fever.

Pneumonia often develops as a consequence of an upper respiratory tract infection such as the common cold or flu, especially in the very young and the elderly. It is usually caused by bacteria or viruses, although some cases may be caused by other microorganisms such as fungi. The majority of cases are caused by just a few pathogens, the most common being the bacterium *Streptococcus pneumoniae.* Pneumonia is more likely to develop in people who have other lung diseases such as asthma, a history of smoking, heart failure, or a weakened immune system.

Vaccines are available to prevent certain types of bacterial and viral pneumonia, including pneumonia caused by *Streptococcus pneumoniae.* Treatment of pneumonia depends on the cause. For example, if it is caused by bacteria, antibiotics are generally prescribed. In cases of severe pneumonia, hospitalization and supplemental oxygen may be required.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic poor airflow. The main symptoms include shortness of breath and a cough that produces phlegm. These symptoms are usually present for a long period of time and typically become worse over time. Eventually, walking upstairs and similar activities become difficult because of shortness of breath.

COPD formerly was referred to as chronic bronchitis or emphysema. Now, the term *chronic bronchitis* is used to refer to the symptoms of COPD, and the term *emphysema* is used to refer to the lung changes that occur with COPD. Some of these lung changes are shown in Figure **10.4.4**. They include a breakdown of connective tissues that reduces the number and elasticity of alveoli. As a result, the patient can no longer fully exhale air from the lungs, so the air becomes trapped in the lungs. Gas exchange is hampered and may lead to low oxygen levels and too much carbon dioxide in the blood.

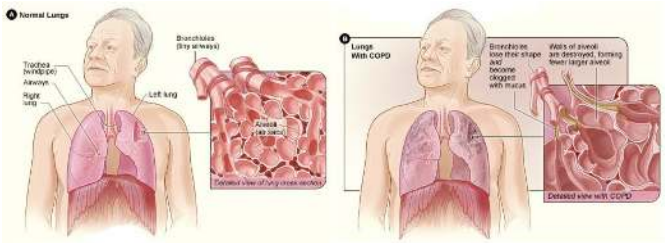


Figure **10.4.4**: The physiological changes that occur with COPD include a breakdown of alveolar walls, reducing the surface area for gas exchange.

Tobacco smoking is the major cause of COPD, with a number of other factors such as air pollution and genetics playing smaller roles. Of people who are life-long smokers, about half will eventually develop COPD. Exposure to secondhand smoke in nonsmokers also increases the risk of COPD and accounts for about 20 percent of cases. Most cases of COPD could have been prevented by never smoking. In people who have already been diagnosed with COPD, cessation of smoking can slow down the rate at which COPD worsens. People with COPD may be treated with supplemental oxygen and inhaled bronchodilators. These treatments may reduce the symptoms but there is no cure for COPD except, in very severe cases, lung transplantation (see the Explore More video below).

LUNG CANCER

Lung cancer is a malignant tumor characterized by uncontrolled cell growth in tissues of the lung. The tumor may arise directly from lung tissue (primary lung cancer) or as a result of metastasis from cancer in another part of the body (secondary lung cancer). Primary lung cancer may also metastasize and spread to other parts of the body. Lung cancer develops following genetic damage to DNA that affects the normal functions of the cell. As more damage accumulates, the risk of cancer increases. The most common symptoms of lung cancer include coughing (especially coughing up blood), wheezing, shortness of breath, chest pain, and weight loss.

The major cause of primary lung cancer is tobacco smoking, which accounts for about 85 percent of cases. Cigarette smoke contains numerous cancer-causing chemicals. Besides smoking, other potential causes of lung cancer include exposure to radon gas, asbestos, secondhand smoke, or other air pollutants. When tobacco smoking is combined with other risk factors such as exposure to radon or asbestos, the risk of lung cancer is heightened. People who have close biological relatives with lung cancer are also at increased risk of developing the disease.

Most cases of lung cancer cannot be cured. In many people, cancer has already spread beyond the original site by the time they have symptoms and seek medical attention. About 10 percent of people with lung cancer do not have symptoms when they are diagnosed, and the cancers are found when they have a chest X-ray for another problem. In part because of its typically late diagnosis, lung cancer is the most common cause of cancer-related death in men and the second most common cause in women (after breast cancer). Common treatments for lung cancer include surgical removal of the tumor, radiation therapy, chemotherapy, or some combination of these three types of treatment.

FEATURE: MY HUMAN BODY

Do you — or someone you love — snore? Snoring may be more than just an annoyance. It may also be a sign of a potentially dangerous and common disorder known as sleep apnea. **Sleep apnea** is characterized by pauses in breathing that occur most often because of physical blockage to airflow during sleep. When breathing is paused, carbon dioxide builds up in the bloodstream. The higher-than-normal level of carbon dioxide in the blood causes the respiratory centers in the brain to wake the person enough to start breathing normally. This reduces the carbon dioxide level, and the person falls back asleep. This occurs repeatedly throughout the night, causing serious disruption in sleep. Most people with sleep apnea are unaware that they have the disorder because they don't awake fully enough to remember the repeated awakenings throughout the night. Instead, sleep apnea is more commonly recognized by other people who witness the episodes.

Figure 10.4.5shows how sleep apnea typically occurs. The muscle tone of the body normally relaxes during sleep, allowing the soft tissues in the throat to collapse and block the airway. The relaxation of muscles may be exacerbated by the use of alcohol, tranquilizers, or muscle relaxants. The risk of sleep apnea is greater in people who are overweight, smoke tobacco, or have diabetes. The disorder is also more likely to occur in older people and males. Common symptoms of sleep apnea include loud snoring, restless sleep, and daytime sleepiness and fatigue. Daytime sleepiness, in turn, increases the risk of driving and work-related accidents. Continued sleep deprivation may cause moodiness and belligerence. Lack of adequate oxygen to the body because of sleep apnea may also lead to other health problems including fatty liver diseases and high blood pressure. Symptoms of sleep apnea may be present for years or even decades until (and if) a diagnosis is finally made.

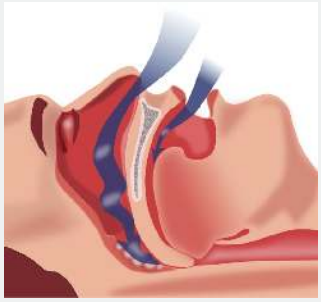


Figure 10.4.5: Sleeping on one's back may increase the risk of the airway becoming temporarily blocked during sleep, resulting in sleep apnea.

Treatment of sleep apnea may include avoiding alcohol, quitting smoking, or losing weight. Elevating the upper body during sleep or sleeping on one's side may help prevent airway collapse in many people with sleep apnea. Another type of treatment is the use of an oral device during sleep that shifts the lower jaw forward to help keep the airway open. The most common treatment for moderate to severe sleep apnea is the use during sleep of CPAP (continuous positive airway pressure), which keeps the airway open by means of pressurized air. In this treatment, the person typically wears a plastic facial mask that is connected by a flexible tube to a small bedside CPAP machine. Although CPAP is effective, long-term compliance is often poor because patients find the mask uncomfortable or they experience unpleasant side effects such as dry mouth and nose. A more extreme form of treatment is surgery to remove some of the tissues — such as the tonsils or part of the soft palate — that tend to collapse and block the airway in people with sleep apnea.

REVIEW

1. What is asthma, and what are its symptoms and causes?
2. Identify common risk factors and triggers of asthma attacks.
3. How can asthma attacks be prevented or controlled?
4. What are the causes and symptoms of pneumonia?
5. How can pneumonia be prevented? How is it treated?
6. Define COPD. How is it related to chronic bronchitis and emphysema?
7. Relate COPD to tobacco smoking.
8. What is the difference between primary and secondary lung cancer?
9. What is the major cause of primary lung cancer?
10. Discuss lung cancer as a cause of death.
11. How is lung cancer treated?
12. Define sleep apnea.
13. What is the difference between how COPD and pneumonia affect the alveoli?

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10.5: SMOKING AND HEALTH

SURE DEATH

The anti-smoking cartoon in Figure **10.5.1** clearly makes the point that smoking causes death. The cartoon is not using hyperbole, because smoking actually is deadly. It causes about six million deaths each year and is the single greatest cause of preventable death worldwide. As many as half of all people who smoke tobacco die from it. As a result of smoking's deadly effects, the life expectancy of long-term smokers is significantly less than that of non-smokers. In fact, long-term smokers can expect their lifespan to be reduced by as much as 18 years, and they are three times as likely to die before the age of 70 as non-smokers.



Figure **10.5.1**: Have another! Sure death

WHY IS SMOKING DEADLY?

As shown in Figure **10.5.2**, tobacco smoking has adverse effects on just about every bodily system and organ. The detrimental health effects of smoking depend on the number of years that a person smokes and how much the person smokes. Contrary to popular belief, all forms of tobacco smoke — including smoke from cigars and tobacco pipes — have similar health risks as those of cigarette smoke. Smokeless tobacco may be less of a danger to the lungs and heart, but it too has serious health effects. It significantly increases the risk of cancers of the mouth and throat, among other health problems.

Even non-smokers may not be spared the deadly risks of tobacco smoke. If you spend time around smokers either at home or on the job, then you are at risk of the dangers of secondhand smoke. **Secondhand smoke** enters the air directly from burning cigarettes (and cigars and pipes) and indirectly from the lungs of smokers. This smoke may linger in indoor air for hours and increase the risk of a wide range of adverse health effects. For example, non-smokers who are exposed to secondhand smoke may have as much as a 30 percent increase in their risk of lung cancer and heart disease. The 2014 U.S. Surgeon General's Report concluded that there is no established risk-free level of exposure to secondhand smoke.

Tobacco contains **nicotine,** which is a psychoactive drug. Although nicotine in tobacco smoke does not directly cause cancer or most of the other health risks of smoking, it is a highly addictive drug. In fact, nicotine is even more addictive than cocaine or heroin. The addictive nature of nicotine explains why it is so difficult for smokers to quit the habit even when they know the health risks and really want to stop smoking. The good news is that if someone does stop smoking, his or her risks of smoking-related diseases and death soon start to fall. For example, by one year after quitting, the risk of heart disease drops to only half of that of a continuing smoker.

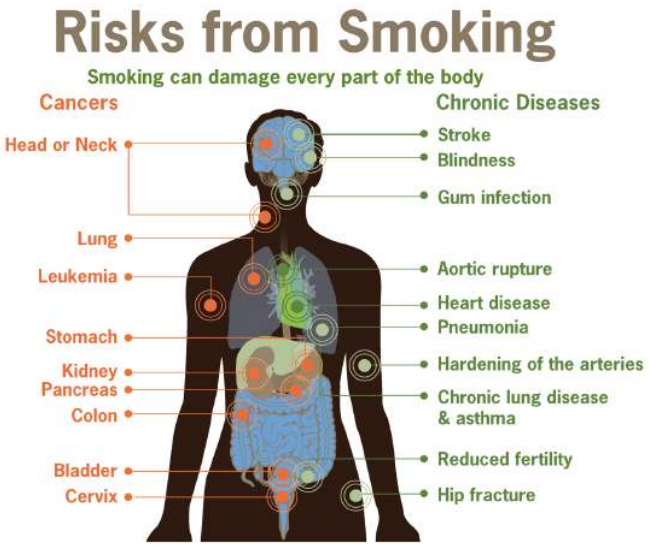


Figure **10.5.2**: Smoking is known to cause many different cancers and chronic diseases such as stroke, blindness, gum infection, aortic rupture, heart disease, pneumonia, hardening of the arteries, chronic lung diseases, reduced fertility, and hip fracture.

SMOKING AND CANCER

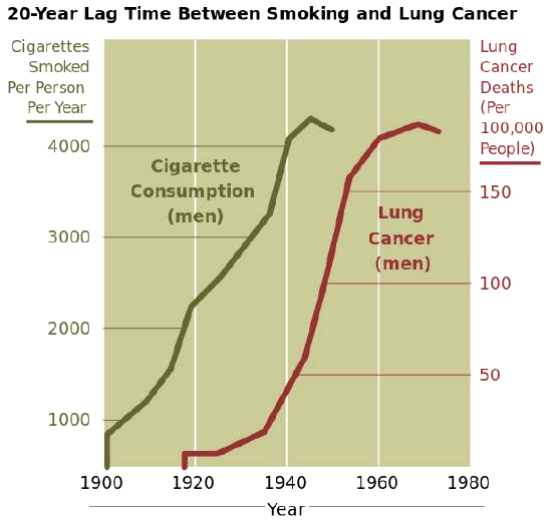


Figure **10.5.3**: Cigarette smoking by men in the U.S. began to decline in the 1950s, but it wasn't until the 1970s — roughly 20 years later — that this was reflected by a concomitant decline in lung cancer deaths in men.

One of the main health risks of smoking is cancer, particularly cancer of the lung. Because of the increased risk of lung cancer with

smoking, the risk of dying from lung cancer before age 85 is more than 20 times higher for a male smoker than for a male non-smoker. As the rate of smoking increases, so does the rate of lung cancer deaths, although the effects of smoking on lung cancer deaths can take up to 20 years to manifest themselves, as shown in Figure **10.5.3**.

Besides lung cancer, several other forms of cancer are also significantly more likely in smokers than non-smokers, including cancers of the kidney, larynx, mouth, lip, tongue, throat, bladder, esophagus, pancreas, and stomach. Unfortunately, many of these cancers have extremely low cure rates.

When you consider the composition of tobacco smoke, it's not surprising that it increases the risk of cancer. Tobacco smoke contains dozens of chemicals that have been proven to be carcinogens or causes of cancer. Many of these chemicals bind to DNA in a smoker's cells and may either kill the cells or cause mutations. If the mutations inhibit programmed cell death, the cells can survive to become cancer cells. Some of the most potent carcinogens in tobacco smoke include benzopyrene, acrolein, and nitrosamines. Other carcinogens in tobacco smoke are radioactive isotopes, including lead-210 and polonium-210.

RESPIRATORY EFFECTS OF SMOKING

Long-term exposure to the compounds found in cigarette smoke, such as carbon monoxide and cyanide, is thought to be responsible for much of the lung damage caused by smoking. These chemicals reduce the elasticity of alveoli, leading to chronic obstructive pulmonary disease (COPD). COPD is a permanent, incurable, and often fatal reduction in the capacity of the lungs, reducing the ability of the lungs to fully exhale air. The chronic inflammation that is also present in COPD is exacerbated by the tobacco smoke carcinogen acrolein and its derivatives. COPD is almost completely preventable simply by not smoking and by also avoiding secondhand smoke.

CARDIOVASCULAR EFFECTS OF SMOKING

Inhalation of tobacco smoke causes several immediate responses in the heart and blood vessels. Within one minute of inhalation of smoke, the heart rate begins to rise, increasing by as much as 30 percent during the first 10 minutes of smoking. Carbon monoxide in tobacco smoke binds with hemoglobin in red blood cells, thereby reducing the blood's ability to carry oxygen. Hemoglobin bound to carbon monoxide forms such a stable complex that it may result in a permanent loss of red blood cell function. Several other chemicals in tobacco smoke lead to the narrowing and weakening of blood vessels and an increase in substances that contribute to blood clotting. These changes increase blood pressure and the chances of a blood clot forming and blocking a vessel, thereby elevating the risk of heart attack and stroke. A recent study found that smokers are five times more likely than non-smokers to have a heart attack before the age of 40.

Smoking has also been shown to have a negative impact on the levels of blood lipids. Total cholesterol levels tend to be higher in smokers than non-smokers. Ratios of "good" cholesterol to "bad" cholesterol tend to be lower in smokers than in non-smokers.

ADDITIONAL ADVERSE HEALTH EFFECTS OF SMOKING

A wide diversity of additional adverse health effects are attributable to smoking. Here are just a few of them:

- Smokers are at a significantly increased risk of developing chronic kidney disease (in addition to kidney cancer). For example, smoking hastens the progression of kidney damage in people with diabetes.
- People who smoke, especially the elderly, have a greater risk of influenza and other infectious diseases than non-smokers. Smoking more than 20 cigarettes a day has been found to increase the risk of infectious diseases by as much as four times the risk in non-smokers. These effects occur because of damage to both the respiratory system and the immune system.
- In addition to oral cancer, smoking causes other oral problems including periodontitis (gum disease). Roughly half of the cases of gum inflammation are attributable to current or former smoking. Such inflammation increases the risk of tooth loss, which is also higher in smokers than non-smokers. In addition, smoking stains the teeth and causes halitosis (bad breath).
- Smoking is a key cause of erectile dysfunction (ED), probably because it leads to narrowing of arteries in the penis as it does elsewhere in the body. The incidence of ED is about 85 percent higher in males who smoke than it is in non-smokers.
- Smoking also has adverse effects on the female reproductive system, potentially causing infertility, in part because it interferes with the body's ability to produce estrogen. Female smokers are about 60 percent more likely to be infertile than non-smokers. Pregnant women who smoke or are exposed to secondhand smoke have a higher risk of miscarriages and low-birth-weight infants.
- Certain therapeutic drugs, including some antidepressants and anticonvulsants, are less effective in smokers than in non-smokers. This occurs because smoking increases levels of liver enzymes that break down the drugs.
- Smoking causes an estimated 10 percent of all deaths due to fires worldwide. Smokers are also at greater risk of dying in motor vehicle crashes and other accidents.
- Smoking leads to an increased risk of bone fractures, especially of the hip. It also leads to slower wound healing after surgery and an increased rate of postoperative complications.

FEATURE: HUMAN BIOLOGY IN THE NEWS

The item in Figure **10.5.4** looks like a regular cigarette, but it's actually an electronic cigarette or e-cigarette. E-cigarettes are battery-powered devices that change flavored liquids and nicotine into a vapor that is inhaled by the user. E-cigarettes are often promoted as being safer than traditional tobacco products and their use is touted as a good way to quit smoking. They are

often not banned in smoke-free areas where it is illegal to smoke tobacco cigarettes.



Figure **10.5.4**: e-cigarette

A study completed in 2015 by researchers at the Harvard School of Public Health and widely reported in the mass media found that e-cigarettes may in fact be very harmful to the user's health. E-cigarettes contain nicotine and cancer-causing chemicals such as formaldehyde. According to the study, about three-quarters of flavored e-cigarettes also contain a chemical named diacetyl that causes an incurable and potentially fatal disorder of the lungs, commonly called "popcorn lung" (bronchiolitis obliterans). In this disorder, the bronchioles compress and narrow due to the formation of scar tissue. This greatly diminishes the breathing capacity of people with the disorder. Popcorn lung gained its common name in 2004 when it was diagnosed in workers at popcorn factories. The buttery flavoring used in the factories contained diacetyl.

Some manufacturers of e-cigarettes and flavorings advertise that their products are now free of diacetyl. However, because e-cigarettes are not currently regulated by the FDA, there is no way of knowing for sure whether the products are actually safe. Equally disturbing is the appeal of flavored e-cigarettes to teens and the attempts of producers to specifically market their products to this age group. Flavors such as "cotton candy," "Katy Perry's cherry," and "alien blood" are obviously marketed to youth. Not surprisingly, the use of e-cigarettes is on the rise in middle and high school students, who are more likely to use them than regular cigarettes. Public health officials fear that e-cigarettes will be a gateway for teens to move on to smoking tobacco cigarettes. Some states have recently passed laws prohibiting minors from buying e-cigarettes. As more questions are raised about their potential negative health effects, it is likely that more laws will be passed to regulate them. Watch the news for updates on this issue.

REVIEW

1. What percentage of people who smoke are likely to die from it?
2. Contrast the life expectancy of long-term smokers and non-smokers.
3. What factors related to smoking determine how smoking affects a smoker's health?
4. What are the two sources of secondhand cigarette smoke? How does exposure to secondhand smoke affect non-smokers?
5. Why is it so difficult for smokers to quit the habit? How is their health likely to be affected by quitting?
6. List five types of cancer that are significantly more likely in smokers than non-smokers.
7. Why does smoking cause cancer?
8. Explain how smoking causes COPD.
9. Identify some of the adverse effects of smoking on the cardiovascular system.
10. Give three examples of additional adverse health effects that are more likely with smoking.
11. Do you think e-cigarettes can be addictive? Explain your reasoning.
12. People who smoke are more likely to get which of these than people who do not smoke.

    A. lung cancer
    B. influenza
    C. kidney disease
    D. All of the above

13. Name three toxic chemicals present in tobacco smoke.
14. *True or False.* Nicotine is more addictive than heroin.
15. *True or False.* Smoking has many negative effects on the respiratory and cardiovascular systems, but not on other systems of the body.

EXPLORE MORE

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10.6: CASE STUDY CONCLUSION- BRONCHITIS AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: COUGH THAT WON'T QUIT

The little child shown in Figure **10.6.1** seems to be enjoying the air coming out of a humidifier. Inhaling the moist air from a humidifier or steamy shower can feel particularly good if you have a respiratory system infection, such as bronchitis. The moist air helps to loosen and thin mucus in the respiratory system, allowing you to breathe easier.



Figure **10.6.1**: Enjoying the Humidifier

At the beginning of this chapter, you learned about Sacheen, who developed acute bronchitis after getting a cold. She had a worsening cough, sore throat due to coughing, and chest congestion. She was also coughing up thick mucus.

Acute bronchitis usually occurs after a cold or flu, usually due to the same viruses that cause cold or flu. Because bronchitis is not usually caused by bacteria (although it can be), antibiotics are not an effective treatment in most cases.

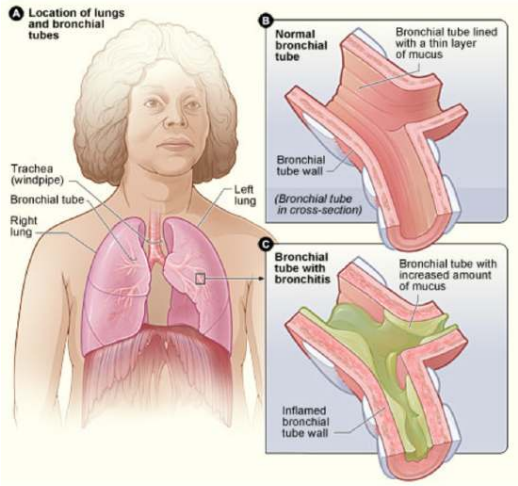


Figure **10.6.2**: Acute Bronchitis

Bronchitis affects the bronchial tubes, which, as you have learned, are air passages in the lower respiratory tract. The main bronchi branch off of the trachea and then branch into smaller bronchi and then bronchioles. In bronchitis, the walls of the bronchi become inflamed, which makes them narrower. Also, there is excessive production of mucus in the bronchi, which further narrows the pathway through which can flow. Figure **10.6.2** shows how bronchitis affects the bronchial tubes.

The function of mucus is to trap pathogens and other potentially dangerous particles that enter the respiratory system from the air. However, when too much mucus is produced in response to an infection (as in the case of bronchitis), it can interfere with normal airflow. The body responds by coughing as it tries to rid itself of the pathogen-laden mucus.

The treatment for most cases of bronchitis involves thinning and loosening the mucus so that it can be effectively coughed out of the airways. This can be done by drinking plenty of fluids, using humidifiers or steam, and in some cases, using over-the-counter medications such as expectorants that are found in some cough medicines. This is why Dr. Tsosie recommended some of these treatments to Sacheen and also warned against using cough suppressants. Cough suppressants work on the nervous system to suppress the cough reflex. When a patient has a “productive” cough —i.e. they are coughing up mucus—doctors generally advise them to not take cough suppressants so that they can cough the mucus out of their bodies.

When Dr. Tsosie was examining Sacheen, she used a pulse oximeter to measure the oxygen level in her blood. Why did she do this? As you have learned, the bronchial tubes branch into bronchioles, which ultimately branch into the alveoli of the lungs. The alveoli are where gas exchange occurs between the air and the blood to take in oxygen and remove carbon dioxide and other wastes. By checking Sacheen’s blood oxygen level, Dr. Tsosie was making sure that her clogged airways were not impacting her level of much-needed oxygen.

Sacheen has acute bronchitis, but you may recall that *chronic* bronchitis was discussed earlier in this chapter as a term that describes the symptoms of chronic obstructive pulmonary disease (COPD). COPD is often due to tobacco smoking and causes damage to the walls of the alveoli, whereas acute bronchitis typically occurs after a cold or flu and involves inflammation and mucus build-up in the bronchial tubes. As implied by the difference in their names, chronic bronchitis is an ongoing, long-term condition, while acute bronchitis is likely to resolve relatively quickly with proper rest and treatment.

However, Sacheen smokes cigarettes, so she is more likely to develop chronic respiratory conditions such as COPD. As you have learned, smoking damages the respiratory system as well as many other systems of the body. Smoking increases the risk of respiratory infections, including bronchitis and flu, due to its damaging effects on the respiratory and immune systems. Dr. Tsosie strongly encouraged Sacheen to quit smoking, not only so that her acute bronchitis resolves, but so that she can avoid future infections and other negative health outcomes associated with smoking, including COPD and lung cancer.

As you have learned in this chapter, the respiratory system is critical to carry out the gas exchange necessary for life’s functions and to

protect the body from pathogens and other potentially harmful substances in the air. But this ability to interface with the outside air has a cost. The respiratory system is prone to infections, as well as damage and other negative effects from allergens, mold, air pollution, and cigarette smoke. Although exposure to most of these things cannot be avoided, not smoking is an important step you can take to protect this organ system—as well as many other systems of your body.

CHAPTER SUMMARY

In this chapter, you learned about the respiratory system. Specifically, you learned that:

- Respiration is the process in which oxygen moves from the outside air into the body and carbon dioxide and other waste gases move from inside the body into the outside air. It involves two subsidiary processes: ventilation and gas exchange.
- The organs of the respiratory system form a continuous system of passages called the respiratory tract. It has two major divisions: the upper respiratory tract and the lower respiratory tract.
    - The upper respiratory tract includes the nasal cavity, pharynx, and larynx. All of these organs are involved in conduction or the movement of air into and out of the body. Incoming air is also cleaned, humidified, and warmed as it passes through the upper respiratory tract. The larynx is also called the voice box because it contains the vocal cords, which are needed to produce vocal sounds.
    - The lower respiratory tract includes the trachea, bronchi and bronchioles, and the lungs. The trachea, bronchi, and bronchioles are involved in conduction. Gas exchange takes place only in the lungs, which are the largest organs of the respiratory tract. Lung tissue consists mainly of tiny air sacs called alveoli, which is where gas exchange takes place between the air in the alveoli and the blood in capillaries surrounding them.
- The respiratory system protects itself from potentially harmful substances in the air by the mucociliary escalator. This includes mucus-producing cells, which trap particles and pathogens in the incoming air. It also includes tiny hair-like cilia that continually move to sweep the mucus and trapped debris away from the lungs and toward the outside of the body.
- The level of carbon dioxide in the blood is monitored by cells in the brain. If the level becomes too high, it triggers a faster rate of breathing, which lowers the level to the normal range. The opposite occurs if the level becomes too low. The respiratory system exchanges gases with the outside air, but it needs the cardiovascular system to carry the gases to and from cells throughout the body.
- Breathing, or ventilation, is the two-step process of drawing air into the lungs (inhaling) and letting the air out of the lungs (exhaling). Inhaling is an active process that results mainly from the contraction of a muscle called the diaphragm. Exhaling is typically a passive process that occurs mainly due to the elasticity of the lungs when the diaphragm relaxes.
    - Breathing is one of the few vital bodily functions that can be controlled consciously as well as unconsciously. Conscious control of breathing is common in many activities, including swimming and singing. However, there are limits on the conscious control of breathing. If you try to hold your breath, for example, you will soon have an irrepressible urge to breathe.
    - Unconscious breathing is controlled by respiratory centers in the medulla and pons of the brainstem. They respond to variations in blood pH by either increasing or decreasing the rate of breathing as needed to return the pH level to the normal range.
    - Nasal breathing is generally considered to be superior to mouth breathing because it does a better job of filtering, warming, and moistening incoming air. It also results in slower emptying of the lungs, which allows more oxygen to be extracted from the air.
- Gas exchange is the biological process through which gases are transferred across cell membranes to either enter or leave the blood. Gas exchange takes place continuously between the blood and cells throughout the body and also between the blood and the air inside the lungs.
    - Gas exchange in the lungs takes place in alveoli. The pulmonary artery carries deoxygenated blood from the heart to the lungs, where it travels through pulmonary capillaries, picking up oxygen, and releasing carbon dioxide. The oxygenated blood then leaves the lungs through pulmonary veins.
    - Gas exchange occurs by diffusion across cell membranes. Gas molecules naturally move down a concentration gradient from an area of higher concentration to an area of lower concentration. This is a passive process that requires no energy.
    - Gas exchange by diffusion depends on the large surface area provided by the hundreds of millions of alveoli in the lungs. It also depends on a steep concentration gradient for oxygen and carbon dioxide. This gradient is maintained by continuous blood flow and constant breathing.
- Asthma is a chronic inflammatory disease of the airways in the lungs, in which the airways periodically become inflamed. This causes swelling and narrowing of the airways, often with excessive mucus production, leading to difficulty breathing and other symptoms. Asthma is thought to be caused by a combination of genetic and environmental factors. Asthma attacks are triggered by allergens, air pollution, or other factors.
- Pneumonia is a common inflammatory disease of the respiratory tract in which inflammation affects primarily the alveoli, which become filled with fluid that inhibits gas exchange. Most cases of pneumonia are caused by viral or bacterial infections.

Vaccines are available to prevent pneumonia; treatment often includes prescription antibiotics.

- Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic poor airflow, which causes shortness of breath and a productive cough. It is caused most often by tobacco smoking, which leads to the breakdown of connective tissues in the lungs. Alveoli are reduced in number and elasticity, making it impossible to fully exhale air from the lungs. There is no cure for COPD, but stopping smoking may reduce the rate at which COPD worsens.
- Lung cancer is a malignant tumor characterized by uncontrolled cell growth in tissues of the lung. It results from accumulated DNA damage, most often caused by tobacco smoking. Lung cancer is typically diagnosed late, so most cases cannot be cured. It may be treated with surgery, chemotherapy, and/or radiation therapy.
- Smoking is the single greatest cause of preventable death worldwide. It has adverse effects on just about every body system and organ. Tobacco smoke affects not only smokers but also non-smokers who are exposed to secondhand smoke. The nicotine in tobacco is highly addictive, making it very difficult to quit smoking.
    - The major health risk of smoking is cancer of the lungs. Smoking also increases the risk of many other types of cancer. Tobacco smoke contains dozens of chemicals that are known carcinogens.
    - Smoking is the primary cause of COPD. Chemicals such as carbon monoxide and cyanide in tobacco smoke reduce the elasticity of alveoli so the lungs can no longer fully exhale air.
    - Smoking damages the cardiovascular system and increases the risk of high blood pressure, blood clots, heart attack, and stroke. Smoking also has a negative impact on levels of blood lipids.
    - A wide diversity of additional adverse health effects are attributable to smoking, such as erectile dysfunction, female infertility, and slow wound healing.

CHAPTER SUMMARY REVIEW

1. Describe the relationship between the bronchi, secondary bronchi, tertiary bronchi, and bronchioles.
2. What is the uppermost structure in the lower respiratory tract?
    A. Bronchus
    B. Lung
    C. Alveolus
    D. Trachea
3. Deoxygenated and oxygenated blood both travel to the lungs. Describe what happens to each there.
4. *True or False.* There are radioactive isotopes in cigarette smoke.
5. *True or False.* The right and left lungs are identical in structure.
6. Explain the difference between ventilation and gas exchange.
7. Which way do oxygen and carbon dioxide flow during a gas exchange in the lungs?
    A. Why does this happen?
    B. Which way do oxygen and carbon dioxide flow during the gas exchange between the blood and the body's cells?
    C. Why does this happen?
8. Why does the body require oxygen and give off carbon dioxide as a waste product?
9. *True or False.* Conduction refers to the movement of gases across cell membranes.
10. *True or False.* Gas exchange does not require energy.
11. What do coughing and sneezing have in common?
12. What is the name of the escalator that protects the respiratory system?
    A. phlegmociliary
    B. mucociliary
    C. mucoflagellar
    D. surfactociliary
13. COPD can lead to too much carbon dioxide in the blood. Answer the following questions about this.
    A. Why can COPD cause there to be too much carbon dioxide in the blood?
    B. What does this do to the blood pH?
    C. How does the body respond to this change in blood pH?
14. From the following list of diseases, choose which one best fits each description. Each disease is used only once. Diseases: asthma, pneumonia, COPD, lung cancer
    A. Alveoli become inflamed and fill with fluid
    B. Can be caused by exposure to inhaled carcinogens
    C. There is a reduction in the number of alveoli
    D. Airways periodically narrow and fill with mucus
15. *True or False.* Pneumonia can be caused by fungi.
16. *True or False.* The diaphragm contracts during exhalation.
17. What are three different types of things that can enter the respiratory system and cause illness or injury? Describe the negative health effects of each in your answer.
18. Where are the respiratory centers of the brain located? What is the main function of the respiratory centers of the brain?
19. Smoking increases the risk of getting influenza, commonly known as the flu. Explain why this could lead to a greater risk of getting pneumonia.
20. If people had a gene that caused them to get asthma, could changes to their environment (such as more frequent cleaning) help their asthma? Why or why not?
21. What does the term *bronchodilator* refer to?
    A. The largest bronchial tube
    B. An area of the brain that increases breathing rate
    C. A medication that opens constricted airways
    D. A medication that clears the nasal cavity
22. Explain why nasal breathing generally stops particles from entering the body at an earlier stage than mouth breathing.

ATTRIBUTIONS

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CHAPTER OVERVIEW

11: CARDIOVASCULAR SYSTEM

This chapter provides a detailed description of the heart, blood vessels, and blood. It explains how they function together to transport substances throughout the body and maintain homeostasis. The chapter also describes several diseases of the cardiovascular system and lifestyle choices that can help prevent most of them.

11.1: Case Study- Your Body's Transportation System

11.2: Introduction to the Cardiovascular System

11.3: Heart

11.4: Blood Vessels

11.5: Blood

11.6: Blood Types

11.7: Cardiovascular Disease

11.8: Case Study Conclusion- Flight and Chapter Summary

Thumbnail: Flow of blood through the cardiac chambers. (Public Domain; Josinho8).

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11.1: CASE STUDY- YOUR BODY'S TRANSPORTATION SYSTEM

CASE STUDY: FLIGHT RISK

Nineteen-year-old Antônio is about to take his first plane flight. Shortly after he boards the plane and sits down, a man in his late sixties sits next to him in the aisle seat. About half an hour after the plane takes off, the pilot announces that she is turning the seat belt light off and that "it is now safe to move about the cabin."



Figure **11.1.1**: Airplane aisle

The man in the aisle seat, who has introduced himself to Antônio as Ahaya, immediately unbuckles his seat belt and paces up and down the aisle a few times before returning to his seat. After about forty-five minutes, Ahaya gets up again, walks some more, then sits back down and does some foot and leg exercises. After the third time, Ahaya gets up and paces the aisles, Antônio asks him whether he is walking so much to accumulate steps on a pedometer or fitness tracking device. Ahaya laughs and says no, he is trying to do something even more important for his health—prevent a blood clot from forming in his legs.

Ahaya explains that he has a chronic condition called heart failure. Although it sounds scary, his condition is currently well-managed and he is able to lead a relatively normal lifestyle. However, it does put him at risk of developing other serious health conditions such as deep vein thrombosis (DVT), which is when a blood clot occurs in the deep veins, usually in the legs. Air travel, or other situations where a person has to sit for a long period of time, increases the risk of DVT. Ahaya's doctor said that he was healthy enough to fly, but that he should walk frequently and do leg exercises to help avoid a blood clot.

As you read this chapter, you will learn about the heart, blood vessels, and blood that make up the cardiovascular system, as well as disorders of the cardiovascular system such as heart failure. At the end of the chapter, you will learn more about why DVT occurs, why Ahaya has to take extra precautions when he flies, and what can be done to lower the risk of DVT and its potentially deadly consequences.

CHAPTER OVERVIEW: CARDIOVASCULAR SYSTEM

In this chapter, you will learn about the cardiovascular system, which transports substances throughout the body. Specifically, you will learn about:

- The major components of the cardiovascular system: the heart, blood vessels, and blood.
- The functions of the cardiovascular system, including transporting needed substances such as oxygen and nutrients to the cells of the body and picking up waste products.
- How blood is oxygenated through the pulmonary circulation, which transports blood between the heart and lungs.
- How blood is circulated throughout the body through the systemic circulation.
- The components of blood, including plasma, red blood cells, white blood cells, and platelets, and their specific functions.
- Types of blood vessels, including arteries, veins, and capillaries, and their functions, similarities, and differences.
- The structure of the heart, how it pumps blood, and how contractions of the heart are controlled.
- What blood pressure is and how it is regulated.
- Blood types: A, B, AB, and O
- Blood disorders, including anemia, HIV, and leukemia.
- Cardiovascular diseases including heart attack, stroke, and angina, and the risk factors and precursors, such as high blood pressure and atherosclerosis, which contribute to them.

As you read the chapter, think about the following questions:

1. What is heart failure? How do you think it increases the risk of DVT?
2. What is a blood clot? What are the possible health consequences of blood clots?
3. Why do you think sitting for long periods of time increases the risk of DVT and why does walking and exercising the legs help reduce this risk?

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11.2: INTRODUCTION TO THE CARDIOVASCULAR SYSTEM

ANT HILL OR PLUMBING SYSTEM?

What do you think Figure **11.2.1** shows? Does it show a maze of underground passageways in an anthill? A network of interconnected pipes in a complex plumbing system? The picture actually shows something that, like ant tunnels and plumbing pipes, functions as a transportation system. It shows a network of blood vessels. Blood vessels are part of the cardiovascular system.

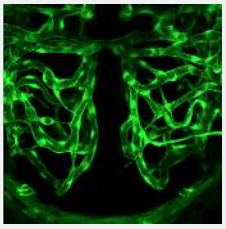


Figure **11.2.1**: Blood Vessels

WHAT IS THE CARDIOVASCULAR SYSTEM?

The **cardiovascular system**, also called the circulatory system, is the organ system that transports materials to and from all the cells of the body. The materials carried by the cardiovascular system include oxygen from the lungs, nutrients from the digestive system, hormones from glands of the endocrine system, and waste materials from cells throughout the body. Transport of these and many other materials is necessary to maintain homeostasis of the body. The main components of the cardiovascular system are the heart, blood vessels, and blood. Each of these components is shown in Figure **11.2.2** and introduced in the text.

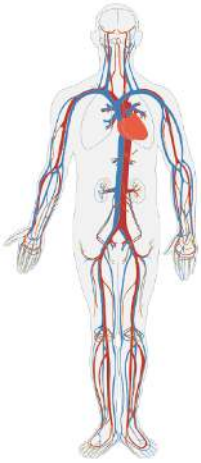


Figure **11.2.2**: This simplified drawing of the cardiovascular system shows its main structures. The heart is shown in the chest in red. Blood vessels called arteries are also shown in red, and blood vessels called veins are shown in blue.

HEART

The heart is a muscular organ in the chest. It consists mainly of cardiac muscle tissue and pumps blood through blood vessels by repeated, rhythmic contractions. As shown in Figure **11.2.3**, the heart has four inner chambers: a right atrium and ventricle and a left atrium and ventricle. On each side of the heart, blood is pumped from the atrium to the ventricle below it and from the ventricle out of the heart. The heart also contains several valves that allow blood to flow only in the proper direction through the heart.

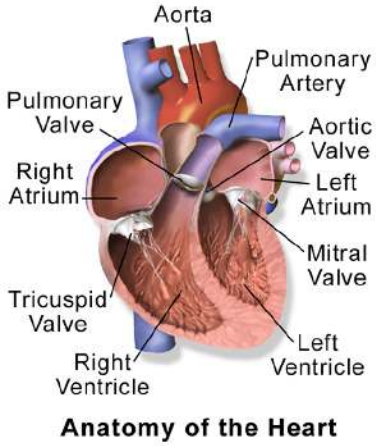


Figure **11.2.3**: The right side of the heart includes the right atrium and right ventricle. The left side includes the left atrium and left ventricle. The valves between the chambers and the major vessels are also visible

Unlike skeletal muscle, cardiac muscle routinely contracts without stimulation by the nervous system. Specialized cardiac muscle cells send out electrical impulses that stimulate the contractions. As a result, the atria and ventricles normally contract with just the right timing to keep blood pumping efficiently through the heart.

BLOOD VESSELS

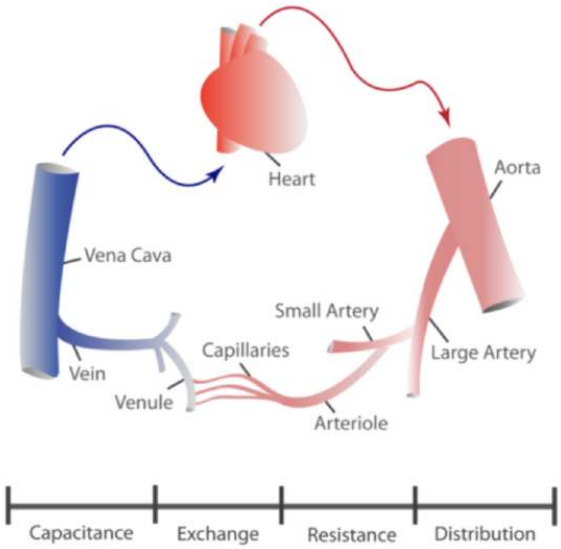


Figure **11.2.4**: This diagram represents the structure and functions of the different types of blood vessels in the cardiovascular system. Arteries carry blood from the heart and to capillaries. Veins carry blood from the capillaries back to the heart.

The blood vessels of the cardiovascular system are like a network of interconnected, one-way roads that range from superhighways to back alleys. Like a network of roads, the blood vessels have the job of allowing the transport of materials from one place to another. There are three major types of blood vessels: arteries, veins, and capillaries. They are illustrated in Figure **11.2.4**.

- Arteries are blood vessels that carry blood away from the heart (except for the arteries that actually supply blood to the heart muscle). Most arteries carry oxygen-rich blood, and one of their main functions is distributing oxygen to tissues throughout the body. The smallest arteries are called arterioles.
- Veins are blood vessels that carry blood toward the heart. Most veins carry deoxygenated blood. The smallest veins are called venules.
- Capillaries are the smallest blood vessels. They connect arterioles and venules. As they pass through tissues, they exchange substances including oxygen with cells.

TWO CIRCULATIONS

Cells throughout the body need a constant supply of oxygen. They get oxygen from capillaries in the systemic circulation. The systemic circulation is just one of two interconnected circulations that make up the human cardiovascular system. The other circulation is the pulmonary system. This is where the blood picks up oxygen to carry to cells. It takes blood about 20 seconds to make one complete transit through both circulations.

PULMONARY CIRCULATION

The **pulmonary circulation** involves only the heart and lungs and the major blood vessels that connect them. It is illustrated in Figure **11.2.5**. Blood moves through the pulmonary circulation from the heart to the lungs, and back to the heart again, becoming oxygenated in the process. Specifically, the right ventricle of the heart pumps deoxygenated blood into the right and left pulmonary arteries. These arteries carry the blood to the right and left lungs, respectively. Oxygenated blood then returns from the right and left lungs through the two right and two left pulmonary veins. All four pulmonary veins enter the left atrium of the heart.

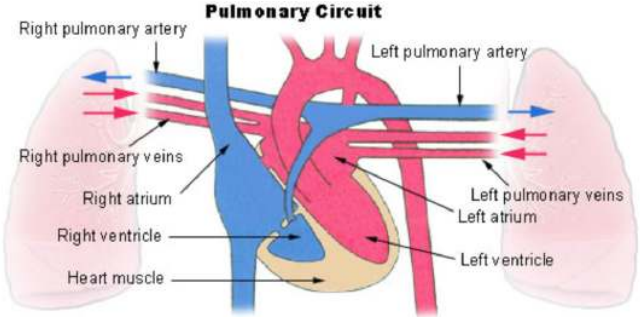


Figure **11.2.5**: This diagram shows the heart, lungs, and major vessels that make up the pulmonary circulation. The colored arrows indicate the direction of blood flow. Oxygenated blood (in red) flows from the lungs to the left side of the heart. Deoxygenated blood (in blue) flows from the right side of the heart to the lungs.

What happens to the blood while it is in the lungs? It passes through increasingly smaller arteries and finally through capillary networks surrounding the alveoli (Figure **11.2.6**). This is where gas exchange takes place. The deoxygenated blood in the capillaries picks up oxygen from the alveoli and gives up carbon dioxide to the alveoli. As a result, the blood returning to the heart in the pulmonary veins is almost completely saturated with oxygen.

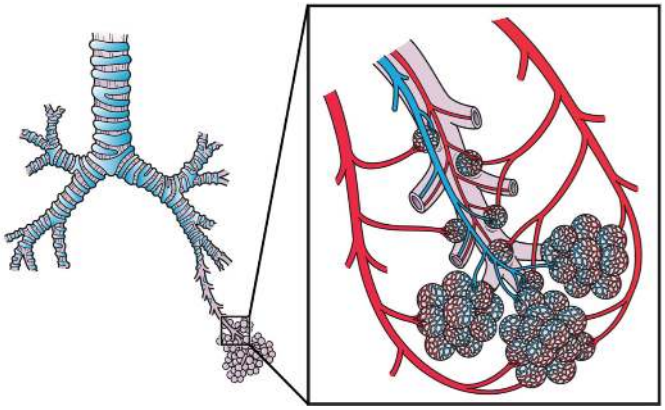


Figure **11.2.6**: This diagram illustrates clusters of alveoli in the lungs where gas exchange takes place with blood in capillaries as it passes through the pulmonary circulation.

SYSTEMIC CIRCULATION

The oxygenated blood that enters the left atrium of the heart in the pulmonary circulation then passes into the **systemic circulation.** This is the part of the cardiovascular system that transports blood to and from all of the tissues of the body to provide oxygen and nutrients and pick up wastes. It consists of the heart and blood vessels that supply the metabolic needs of all the cells in the body, including those of the heart and lungs.

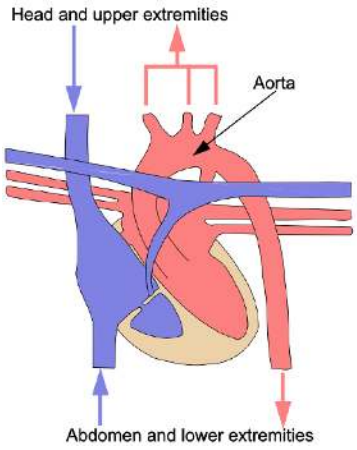


Figure **11.2.7**: The systemic circulation includes the aorta (red), which carries oxygenated blood away from the heart to the rest of the body; and the inferior and superior venae cavae (blue), which return deoxygenated blood to the heart from the body. The colored arrows in the diagram indicate the direction of blood flow, red for oxygenated and blue for deoxygenated.

As shown in Figure **11.2.7**, in the systemic circulation, the left atrium pumps oxygenated blood to the left ventricle, which pumps the blood directly into the aorta, the body's largest artery. Major arteries branching off the aorta carry the blood to the head and upper

extremities. The aorta continues down through the abdomen and carries blood to the abdomen and lower extremities. The blood then returns to the heart through the network of increasingly larger veins of the systemic circulation. All of the returning blood eventually collects in the superior vena cava (upper body) and inferior vena cava (lower body), which empty directly into the right atrium of the heart.

BLOOD

Blood is a fluid connective tissue that circulates throughout the body in blood vessels by the pumping action of the heart. Blood carries oxygen and nutrients to all the body's cells, and it carries carbon dioxide and other wastes away from the cells to be excreted. Blood also transports many other substances, defends the body against infection, repairs body tissues, and controls the body's pH, among other functions.

The fluid part of blood is called plasma. It is a yellowish, watery liquid that contains many dissolved substances and blood cells. Types of blood cells in plasma include red blood cells, white blood cells, and platelets, all of which are illustrated in Figure **11.2.8** and explained in the text.

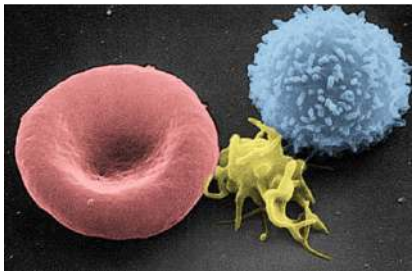


Figure **11.2.8**: The three types of cells in the blood are pictured here: red blood cell (left), platelet (center), and white blood cell (right).

- Red blood cells have the main function of carrying oxygen in the blood. Red blood cells consist mostly of hemoglobin, a protein containing iron that binds with oxygen.
- White blood cells are far fewer in number than red blood cells. They defend the body in various ways. For example, white blood cells called phagocytes swallow and destroy pathogens, dead cells, and other debris in the blood.
- Platelets are cell fragments involved in blood clotting. They stick to tears in blood vessels and to each other, forming a plug at the site of injury. They also release chemicals that are needed for clotting to occur.

REVIEW

1. What is the cardiovascular system? What are its main components?
2. Describe the heart and how it functions.
3. List the three major types of blood vessels and their basic functions.
4. Compare and contrast the pulmonary and systemic circulations.
5. What is blood? What are its chief constituents?
6. *True or False.* The circulatory system brings blood to and from the body, while the cardiovascular system brings blood to and from the lungs only.
7. *True or False.* Arteries carry mainly oxygenated blood.
8. Name three different types of substances that are transported by the cardiovascular system.
9. Describe where and how the pulmonary and systemic circulation systems meet.
10. Which of the following carries blood to the lungs? Choose all that apply.

    A. Left pulmonary artery

    B. Left pulmonary vein

    C. Right pulmonary artery

    D. Right pulmonary vein

11. Put the following structures in order of how blood flows from the heart out to the body and back again.

    capillaries; venules; aorta; veins; arteries

12. Explain why the heart and lungs need blood from the systemic circulation.
13. *Choose one.* Blood vessels carrying deoxygenated blood from the body back to the heart get increasingly (larger/smaller).
14. Blood becomes oxygenated in the lungs through gas exchange into:

    A. Arterioles

    B. Capillaries

    C. Venules

    D. Bronchioles

15. Which type of blood cell carries oxygen?

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11.3: HEART

LUB DUB

Lub dub, lub dub, lub dub... That's how the sound of a beating heart is typically described. In a normal, healthy heart, those are the only two sounds that should be audible when listening to the heart through a stethoscope. If a physician assistant hears something different from the normal lub dub sounds, it's a sign of a possible heart abnormality. What causes the heart to produce the characteristic lub dub sounds? Read on to find out.



Figure **11.3.1**: Listening to a heartbeat

The **heart** is a muscular organ behind the sternum (breastbone), slightly to the left of the center of the chest. A normal adult heart is about the size of a fist. The function of the heart is to pump blood through the blood vessels of the cardiovascular system. The continuous flow of blood through the system is necessary to provide all the cells of the body with oxygen and nutrients and to remove their metabolic wastes.

STRUCTURE OF THE HEART

The heart has a thick muscular wall that consists of several layers of tissue. Internally, the heart is divided into four chambers through which blood flows. Blood flows in just one direction through the chambers due to heart valves.

HEART WALL

As shown in Figure **11.3.2**, the wall of the heart is made up of three layers, called the endocardium, myocardium, and pericardium.

- The endocardium is the innermost layer of the heart wall. It is made up primarily of simple epithelial cells. It covers the heart chambers and valves. A thin layer of connective tissue joins the endocardium to the myocardium.
- The myocardium is the middle and thickest layer of the heart wall. It consists of cardiac muscle surrounded by a framework of collagen. There are two types of cardiac muscle cells in the myocardium: cardiomyocytes, which have the ability to contract easily; and pacemaker cells, which conduct electrical impulses that cause the cardiomyocytes to contract. About 99 percent of cardiac muscle cells are cardiomyocytes, and the remaining 1 percent are pacemaker cells. The myocardium is supplied with blood vessels and nerve fibers via the pericardium.
- The epicardium is the third layer which is a part of the pericardium, a protective sac that encloses and protects the heart. The pericardium consists of two membranes (visceral pericardium called epicardium and parietal pericardium), between which there is a fluid-filled cavity. The fluid helps to cushion the heart and also lubricates its outer surface.

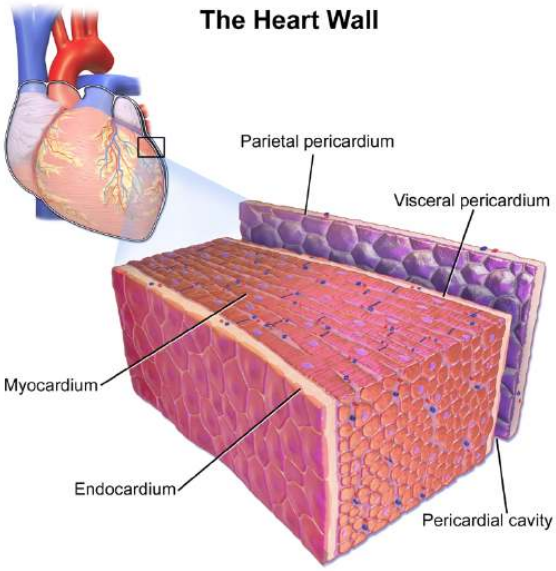


Figure **11.3.2**: The wall of the heart is made up mainly of the myocardium, which consists largely of cardiac muscle.

HEART CHAMBERS

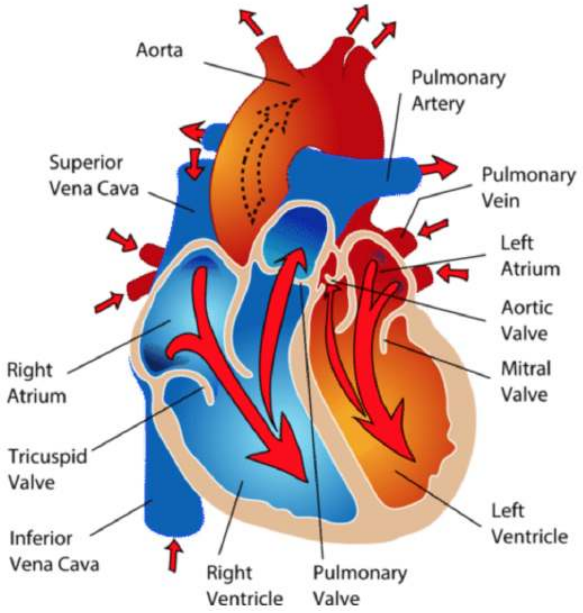


Figure **11.3.3**: This cross-sectional diagram of the heart shows its four chambers and four valves. The red arrows indicate the direction of blood flow through the heart chambers.

As shown in Figure **11.3.3**, the four chambers of the heart include two upper chambers called **atria (singular, atrium**) and two lower chambers called ventricles. The atria are also referred to as receiving chambers because blood coming into the heart first enters these two chambers. The right atrium receives blood from the upper and lower body through the superior vena cava and inferior vena cava, respectively; and the left atrium receives blood from the lungs through the pulmonary veins. The **ventricles** are also referred to as discharging chambers because the blood leaving the heart passes out through these two chambers. The right ventricle discharges blood to the lungs through the pulmonary artery, and the left ventricle discharges blood to the rest of the body through the aorta. The four chambers are separated from each other by dense connective tissue consisting mainly of collagen.

HEART VALVES

Figure **11.3.3** also shows the location of the four valves of the heart. The heart valves allow blood to flow from the atria to the ventricles and from the ventricles to the pulmonary artery and aorta. The valves are constructed in such a way that blood can flow through them in only one direction, thus preventing the backflow of blood. The four valves are the:

1. tricuspid valve, which allows blood to flow from the right atrium to the right ventricle.
2. the mitral valve, which allows blood to flow from the left atrium to the left ventricle.
3. pulmonary valve, which allows blood to flow from the right ventricle to the pulmonary artery.
4. the aortic valve, which allows blood to flow from the left ventricle to the aorta.

The tricuspid and mitral valves are also called atrioventricular (or AV) valves because they are found between the atrium and the ventricle. The pulmonary and aortic valves are also called semilunar valves because they are shaped like half-moons.

CORONARY CIRCULATION

The cardiomyocytes of the muscular walls of the heart are very active cells because they are responsible for the constant beating of the heart. These cells need a continuous supply of oxygen and nutrients. The carbon dioxide and waste products they produce also must be continuously removed. The blood vessels that carry blood to and from the heart muscle cells make up the coronary circulation. Note that the blood vessels of the coronary circulation supply heart tissues with blood and are different from the blood vessels that carry blood to and from the chambers of the heart as part of the general circulation. **Coronary arteries** supply oxygen-rich blood to the heart muscle cells. Coronary veins remove deoxygenated blood from the heart muscle cells.

- There are two coronary arteries: a right coronary artery that supplies the right side of the heart and a left coronary artery that supplies the left side of the heart. These arteries branch repeatedly into smaller and smaller arteries and finally into capillaries, which exchange gases, nutrients, and waste products with cardiomyocytes.
- At the back of the heart, small cardiac veins drain into larger veins and finally into the great cardiac vein, which empties into the right atrium. At the front of the heart, small cardiac veins drain directly into the right atrium.

BLOOD CIRCULATION THROUGH THE HEART

Figure **11.3.4** shows how blood circulates through the chambers of the heart. The right atrium collects blood from two large veins, the superior vena cava (from the upper body) and the inferior vena cava (from the lower body). The blood that collects in the right atrium is pumped through the tricuspid valve into the right ventricle. From the right ventricle, the blood is pumped through the pulmonary valve into the pulmonary artery. The pulmonary artery carries the blood to the lungs, where it enters the pulmonary circulation, gives up carbon dioxide, and picks up oxygen. The oxygenated blood travels back from the lungs through the pulmonary veins (of which there are four) and enters the left atrium of the heart. From the left atrium, the blood is pumped through the mitral valve into the left ventricle. From the left ventricle, the blood is pumped through the aortic valve into the aorta, which subsequently branches into smaller arteries that carry the blood throughout the rest of the body. After passing through capillaries and exchanging substances with cells, the blood returns to the right atrium via the superior vena cava and inferior vena cava, and the process begins anew.

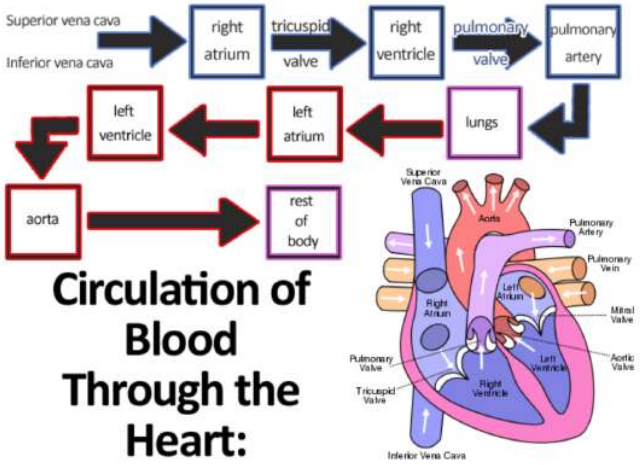


Figure **11.3.4**: The flow chart in this diagram summarizes the pathway blood takes as it flows into, through, and out of the heart. Trace the path of blood flow in the diagram of the heart as you follow it through the flow chart.

CARDIAC CYCLE

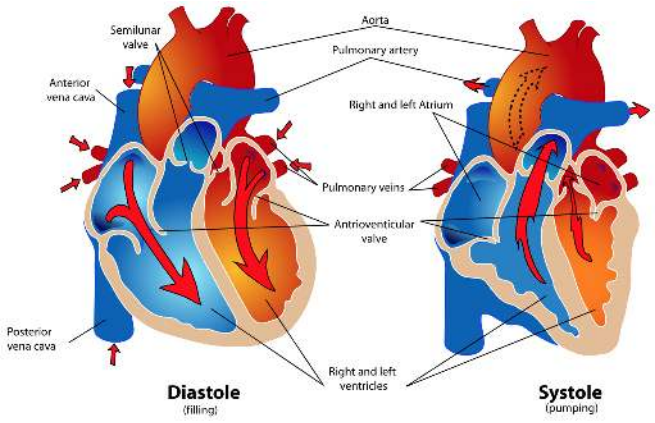


Figure **11.3.5**: Diastole is referred to as the filling stage because this is when the ventricles fill with blood. Systole is referred to as the pumping stage because this is when the ventricles pump blood out of the heart.

The cardiac cycle refers to a single complete heartbeat, which includes one iteration of the lub and dub sounds heard through a stethoscope. During the cardiac cycle, the atria and ventricles work in a coordinated fashion so that blood is pumped efficiently through and out of the heart. The cardiac cycle includes two parts, called diastole and systole, which are illustrated in Figure **11.3.5**.

- During **diastole,** the atria contract and pump blood into the ventricles, while the ventricles relax and fill with blood from the atria.
- During **systole,** the atria relax and collect blood from the lungs and body, while the ventricles contract and pump blood out of the heart.

ELECTRICAL STIMULATION OF THE HEART

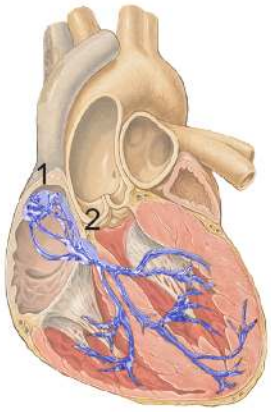


Figure **11.3.6**: In this drawing of the heart, the numbers refer to (1) the sinoatrial node and (2) the atrioventricular node. The blue lines in the drawing indicate the path of transmission of electrical signals through the heart.

The normal, rhythmical beating of the heart is called **sinus rhythm.** It is established by the heart's **pacemaker** cells, which are located in an area of the heart called the sinoatrial node (Figure **11.3.6**). The pacemaker cells create electrical signals by the movement of electrolytes (sodium, potassium, and calcium ions) into and out of the cells. For each cardiac cycle, an electrical signal rapidly travels first from the sinoatrial node to the right and left atria so they contract together. Then the signal travels to another node, called the atrioventricular node (also shown in Figure **11.3.6**), and from there to the right and left ventricles, which also contract together, just a split second after the atria contract.

The normal sinus rhythm of the heart is influenced by the autonomic nervous system through sympathetic and parasympathetic nerves. These nerves arise from two paired cardiovascular centers in the medulla of the brainstem. The parasympathetic nerves act to decrease the heart rate, and the sympathetic nerves act to increase the heart rate. Parasympathetic input normally predominates. Without it, the pacemaker cells of the heart would generate a resting heart rate of about 100 beats per minute, instead of a normal resting heart rate of about 72 beats per minute. The cardiovascular centers receive input from receptors throughout the body and act through the sympathetic nerves to increase the heart rate as needed. For example, increased physical activity is detected by receptors in muscles, joints, and tendons. These receptors send nerve impulses to the cardiovascular centers, causing sympathetic nerves to increase the heart rate. This allows more blood to flow to the muscles.

Besides the autonomic nervous system, other factors can also affect the heart rate. For example, thyroid hormones and adrenal hormones such as epinephrine can stimulate the heart to beat faster. The heart rate also increases when blood pressure drops or the body is dehydrated or overheated. On the other hand, cooling of the body and relaxation, among other factors, can contribute to a decrease in the heart rate.

FEATURE: HUMAN BIOLOGY IN THE NEWS

When a patient's heart is too diseased or damaged to sustain life, a heart transplant is likely to be the only long-term solution. The first successful heart transplant was undertaken in South Africa in 1967. For the past two decades in the United States, about 2,400 hearts were transplanted each year. The problem is that far too few hearts are available for transplant, and many patients die each year waiting for a life-saving heart to become available.

Hearts for transplant have to be used within four hours of the death of the donor. In addition, hearts can only come from brain-dead individuals whose hearts are removed while they are still healthy. Then the hearts are placed on ice inside picnic coolers to be transported to a waiting recipient. The four-hour window means that traffic jams, bad weather, or other unforeseen delays often result in a heart being in less than optimal condition by the time it arrives at its destination. Unfortunately, there is no way to know if the heart will start up again after it is transplanted until it is actually placed in the recipient's body. In up to seven percent of cases, a transplanted heart does not work and has to be removed.

A medical device company in Massachusetts named TransMedic was featured in many news stories when it developed the Organ Care System, commonly referred to as "heart in a box." The system takes a new approach to maintain

donated hearts until they are transplanted. The box is heated and contains a device that pumps oxygenated blood through the heart while it is being transported to the recipient. This extends the time up to 12 hours that the heart can remain healthy and usable. It also allows the heart to be monitored so it is kept in optimal condition while it is on the route. The end result, ideally, is that the recipient gets a healthier heart with less chance of failure of the new organ and a lower risk of death.

As of mid-2016, the heart-in-a-box system had already been used for several successful heart transplants in other countries. At that time, the system was also undergoing clinical trials in the United States to assess its effectiveness in promoting positive recipient outcomes. Developers of the heart-in-a-box predict that the system could increase the number of usable donor hearts by as much as 30 percent, thus greatly increasing the number of patients who are saved from death due to heart failure.

REVIEW

1. What is the heart, where is located, and what is its function?
2. Outline the structure of the heart.
3. Describe the coronary circulation.
4. Summarize how blood flows into, through, and out of the heart.
5. Define the cardiac cycle, and identify its two parts.
6. Explain what controls the beating of the heart.
7. a. What are the two types of cardiac muscle cells in the myocardium?

   b. What are the differences between these two types of cells?
8. Match each of the three layers of the walls of the heart (endocardium, myocardium, and pericardium) with the description that best matches it below.

   a. Protects the heart

   b. Covers the heart valves

   c. Responsible for the beating of the heart
9. Is the blood flowing through the mitral valve oxygenated or deoxygenated? Explain your reasoning.
10. *True or False.* The coronary arteries carry blood to the heart.
11. *True or False.* Systole is when the heart is contracting, diastole is when the heart is fully relaxed.
12. Explain why the blood from the cardiac veins empties into the right atrium of the heart. Focus on function rather than anatomy in your answer.

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11.4: BLOOD VESSELS

BULGING VEINS

Why do bodybuilders have such prominent veins? Bulging muscles push surface veins closer to the skin. Couple that with a virtual lack of subcutaneous fat, and you have bulging veins as well as bulging muscles. Veins are one of three major types of blood vessels in the cardiovascular system.



Figure **11.4.1**: 2012 Hong Kong Bodybuilding Championship participant

TYPES OF BLOOD VESSELS

Blood vessels are part of the cardiovascular system that transports blood throughout the human body. There are three major types of blood vessels: veins, arteries, and capillaries.

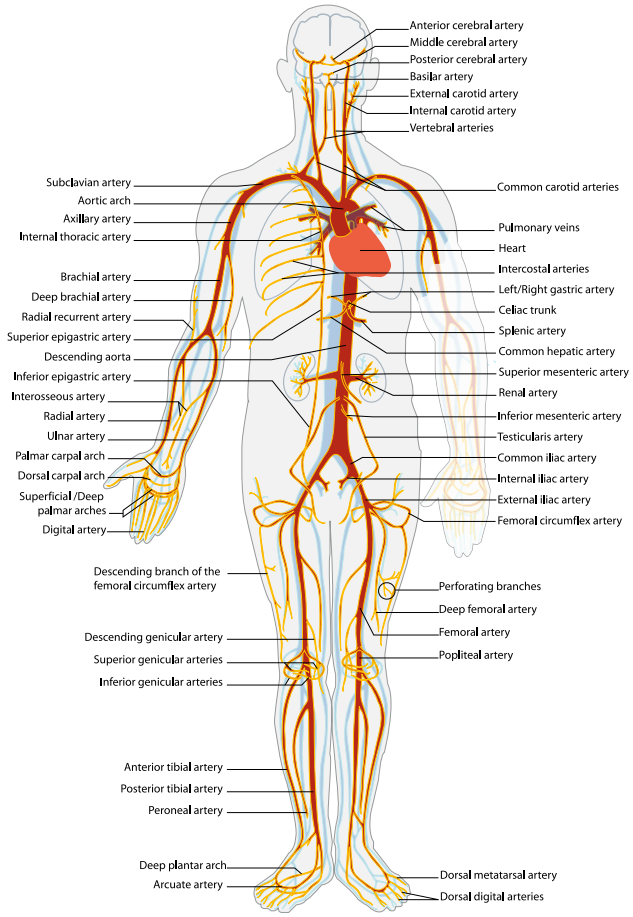


Figure **11.4.2**: This figure shows the heart and the major arteries of the cardiovascular system. The pulmonary veins are included in the diagram because, like arteries, they carry oxygenated blood.

Arteries are defined as blood vessels that carry blood away from the heart. Blood flows through arteries largely because it is under pressure from the pumping action of the heart. It should be noted that coronary arteries, which supply heart muscle cells with blood, travel toward the heart but not as part of the blood flow that travels through the chambers of the heart. Most arteries, including coronary arteries, carry oxygenated blood, but there are a few exceptions, most notably the pulmonary artery. This artery carries deoxygenated blood from the heart to the lungs, where it picks up oxygen and releases carbon dioxide. In virtually all other arteries, the hemoglobin in red blood cells is highly saturated with oxygen (95-100 percent). These arteries distribute oxygenated blood to tissues throughout the body.

The largest artery in the body is the aorta, which is connected to the heart and extends down into the abdomen (Figure **11.4.2**). The aorta has high-pressure, oxygenated blood pumped directly into it from the left ventricle of the heart. The aorta has many branches, and the branches subdivide repeatedly, with the subdivisions growing smaller and smaller in diameter. The smallest arteries are called arterioles.

VEINS

Veins are defined as blood vessels that carry blood toward the heart. Blood traveling through veins is not under pressure from the beating heart. It gets help moving along by the squeezing action of skeletal muscles, for example, when you walk or breathe. It is also prevented from flowing backward by valves in the larger veins, as illustrated in Figure **11.4.3**. Veins are called capacitance blood vessels because the majority (about 60 percent) of the body's total volume of blood is contained within veins.

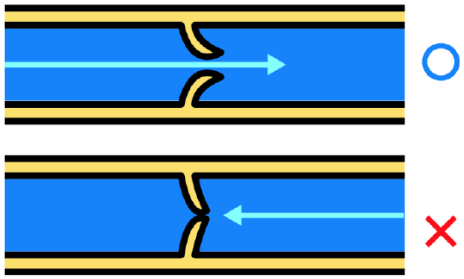


Figure **11.4.3**: The two flaps that make up a venous valve can open in just one direction, so blood can flow in only one direction through the vein.

Most veins carry deoxygenated blood, but there are a few exceptions, including the four pulmonary veins. These veins carry oxygenated blood from the lungs to the heart, which then pumps the blood to the rest of the body. In virtually all other veins, hemoglobin is relatively unsaturated with oxygen (about 75 percent).

The two largest veins in the body are the **superior vena cava**, which carries blood from the upper body directly to the right atrium of the heart, and the **inferior vena cava**, which carries blood from the lower body directly to the right atrium. The inferior vena cava is labeled in the figure below. The superior vena cava is not labeled in Figure **11.4.4** but is clearly visible entering the right atrium of the heart. Like arteries, veins form a complex, branching system of larger and smaller vessels. The smallest veins are called venules. They receive blood from capillaries and transport it to larger veins. Each venule receives blood from multiple capillaries.

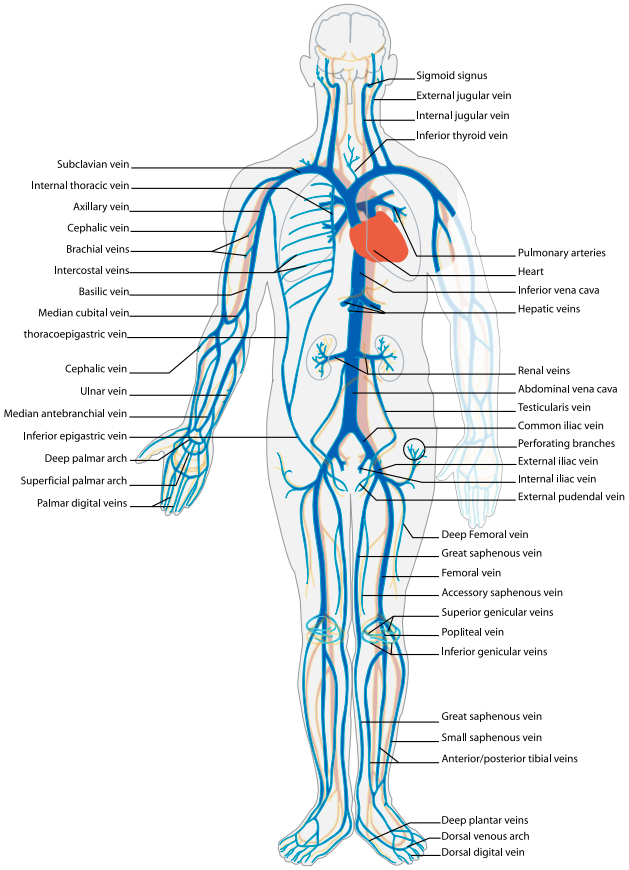


Figure **11.4.4**: This diagram shows the heart and major veins of the cardiovascular system. The pulmonary arteries are included in the diagram because, like veins, they carry deoxygenated blood.

CAPILLARIES

Capillaries are the smallest blood vessels in the cardiovascular system. They are so small that only one red blood cell at a time can squeeze through a capillary, and then only if the red blood cell deforms. Capillaries connect arterioles and venules, as shown in Figure **11.4.5**. Capillaries generally form a branching network of vessels, called a capillary bed, that provides a large surface area for the exchange of substances between the blood and surrounding tissues.

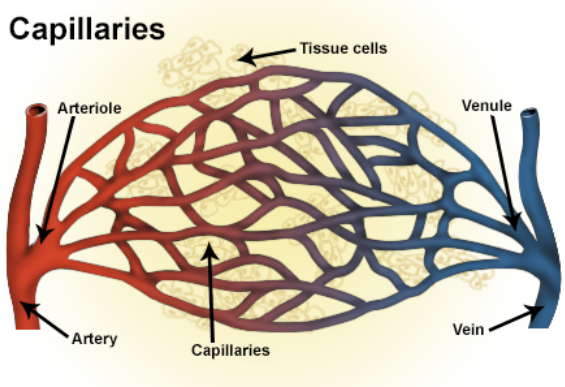


Figure **11.4.5**: Capillaries form beds of tiny blood vessels that exchange substances with the cells of tissues.

STRUCTURE OF BLOOD VESSELS

All blood vessels are basically hollow tubes with an internal space, called a lumen, through which blood flows. The lumen of an artery is shown in cross-section in the photomicrograph below. The width of blood vessels varies, but they all have a lumen. The walls of blood vessels differ depending on the type of vessel. In general, arteries and veins are more similar to one another than capillaries in the structure of their walls.

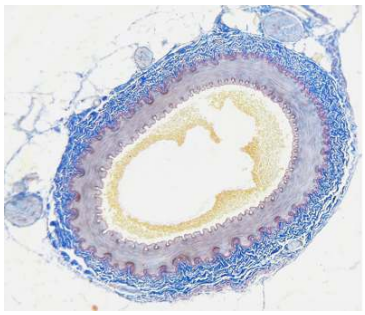


Figure **11.4.6**: The lumen is the white space in the center of this cross-sectional slice of an artery. You can see that the walls of the artery have multiple layers.

WALLS OF ARTERIES AND VEINS

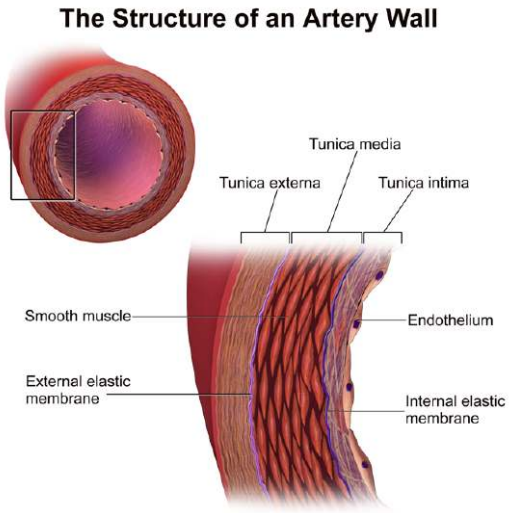


Figure **11.4.7**: The wall of an artery is made of three layers: tunica intima, tunica media, and tunica externa. A vein has the same three layers as the artery shown here, but the middle layer (tunica media) of a vein is thinner and lacks smooth muscle tissue.

The walls of both arteries and veins have three layers: the tunica intima, tunica media, and tunica adventitia. You can see the three layers for an artery in Figure **11.4.7**.

1. The tunica intima is the inner layer of arteries and veins. It is also the thinnest layer, consisting of a single layer of endothelial cells surrounded by a thin layer of connective tissues. It reduces friction between the blood and the inside of the blood vessel walls.
2. The tunica media is the middle layer of arteries and veins. In arteries, this is the thickest layer. It consists mainly of elastic fibers and connective tissues. In arteries, this is the thickest layer because it also contains smooth muscle tissues, which control the diameter of the vessels.
3. The tunica externa (also called tunica adventitia) is the outer layer of arteries and veins. It consists of connective tissue and also contains nerves. In veins, this is the thickest layer. In general, the tunica externa protects and strengthens vessels and attaches them to surrounding structures.

CAPILLARY WALLS

The walls of capillaries consist of little more than a single layer of epithelial cells. Being just one cell thick, the walls are well suited for the exchange of substances between the blood inside them and the cells of surrounding tissues. Substances including water, oxygen, glucose, and other nutrients as well as waste products such as carbon dioxide can pass quickly and easily through the extremely thin walls of capillaries.

BLOOD PRESSURE

The blood in arteries is normally under pressure because of the beating of the heart. The pressure is highest when the heart contracts and pumps out blood, and lowest when the heart relaxes and refills with blood. (You can feel this variation in pressure in your wrist or neck when you count your pulse.) **Blood pressure** is a measure of

the force that blood exerts on the walls of arteries. It is generally measured in millimeters of mercury (mm Hg) and expressed as a double number: a higher number for systolic pressure when the ventricles contract; and a lower number for diastolic pressure when the ventricles relax. Normal blood pressure is generally defined as less than 120 mm Hg (systolic)/80 mm Hg (diastolic) when measured in the arm at the level of the heart. It decreases as blood flows farther away from the heart and into smaller arteries.

As arteries grow smaller, there is increasing resistance to blood flow through them because of the friction of the blood against the arterial walls. This resistance restricts blood flow so less blood reaches smaller, downstream vessels, thus reducing blood pressure before the blood flows into the tiniest vessels, the capillaries. Without this reduction in blood pressure, capillaries would not be able to withstand the pressure of the blood without bursting. By the time blood flows through the veins, it is under very little pressure. The pressure of blood against the walls of veins is always about the same and normally no more than 10 mm Hg.

VASOCONSTRICTION AND VASODILATION

Smooth muscles in the walls of arteries can contract or relax to cause vasoconstriction (narrowing of the lumen of blood vessels) or vasodilation (widening of the lumen of blood vessels). This allows the arteries — especially the arterioles — to contract or relax as needed to help regulate blood pressure. In this regard, the arterioles act like an adjustable nozzle on a garden hose. When they narrow, the increased friction with the arterial walls causes less blood to flow downstream from the narrowing, resulting in a drop in blood pressure. These actions are controlled by the autonomic nervous system in response to pressure-sensitive sensory receptors in the walls of larger arteries.

Arteries can also dilate or constrict to help regulate body temperature by allowing more or less blood to flow from the warm body core to the body's surface. In addition, vasoconstriction and vasodilation play roles in the fight-or-flight response, under the control of the sympathetic nervous system. For example, vasodilation allows more blood to flow to skeletal muscles and vasoconstriction reduces blood flow to digestive organs.

FEATURE: MY HUMAN BODY

The lumpy appearance of this man's leg is caused by *varicose veins*. Do you have varicose veins? If you do, you may wonder whether they are a sign of a significant health problem. You may also wonder whether you should have them treated, and if so, what treatments are available. As is usually the case, when it comes to your health, "knowledge is power."



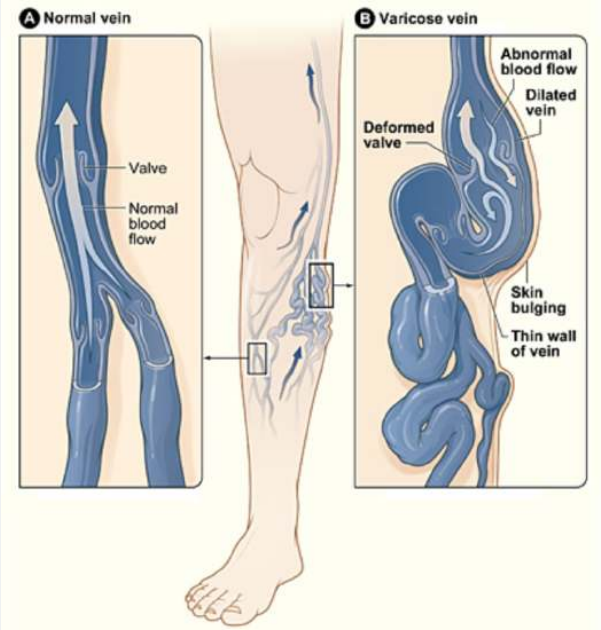


Figure **11.4.8**: Varicose veins form when a deformed valve allows blood to pool creating a bulge in the vein.

First, the "back story:" varicose veins are veins that have become enlarged and twisted because their valves have become ineffective (see Figure 11.4.8). As a consequence, blood pools in the veins and stretches them out. Varicose veins occur most frequently in the superficial veins of the legs, but they may also occur in other parts of the body. They are most common in older adults, females, and people who have a family history of the condition. Obesity and pregnancy also increase the risk of developing varicose veins. A job that requires standing for long periods of time, chronic constipation, and long-term alcohol consumption are additional risk factors.

Varicose veins usually are not serious. In many people, they are only a cosmetic issue. However, in severe cases, varicose veins may cause pain and other problems. For example, the affected leg(s) may feel heavy and achy, especially after long periods of standing. Ankles may become swollen by the end of the day. Minor injuries may bleed more than normal. The skin over varicosity may become red, dry, and itchy. In very severe cases, skin ulcers may develop.

If you are concerned about varicose veins, call them to the attention of your doctor, who can determine the best course of action for your case. There are many potential treatments for varicose veins. Some of the treatments have potential adverse side effects; and with many of the treatments, varicose veins

may return. Which treatment is best for a given patient depends in part on the severity of the condition.

- If varicose veins are not serious, then conservative treatment options may be recommended. These include avoiding standing or sitting for long periods, frequently elevating the legs, and wearing graduated compression stockings.
- For more serious cases, less conservative but non-surgical options may be advised. These include sclerotherapy, in which medicine is injected into the veins to make them shrink. Another non-surgical approach is endovenous thermal ablation. In this type of treatment, laser light, radio-frequency energy, or steam is used to heat the walls of the veins, causing them to shrink and collapse.
- For the most serious cases, surgery may be the best option. The most invasive surgery is vein stripping, in which all or part of the main trunk of a vein is tied off and removed from the leg while the patient is under general anesthesia. In a less invasive surgery, called ambulatory phlebectomy, short segments of a vein are removed through tiny incisions under local anesthesia.

REVIEW

1. What are the blood vessels? Name the three major types of blood vessels.
2. Describe arteries. Identify the largest artery in the body.
3. How are veins defined? What are the two largest veins in the body?
4. Compare and contrast how blood moves through arteries and veins.
5. What are capillaries, and what is their function?
6. Compare and contrast the structure of the walls of arteries, veins, and capillaries.
7. What is blood pressure, and how is it expressed? What blood pressure is considered normal?
8. Identify the functions of vasoconstriction and vasodilation of arteries.
9. Does the blood in most veins have any oxygen at all? Explain your answer.
10. *True or False.* Only one red blood cell can pass through the lumen of a capillary at a given time.
11. *True or False.* The pulmonary artery carries oxygenated blood.
12. Which tissue in blood vessels is responsible for vasodilation and vasoconstriction? Where is it located?
13. The blood pressure at the arterioles is generally _____ the blood pressure at the aorta.
    A. lower than
    B. higher than
    C. the same as
    D. not related to
14. Explain why it is important that the walls of capillaries are very thin.
15. Most of the blood in the body is in the:
    A. Capillaries
    B. Arteries
    C. Heart
    D. Veins

EXPLORE MORE

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11.5: BLOOD

VAMPIRES

From Bram Stoker's famous novel about Count Dracula to the campy TV series *Buffy the Vampire Slayer*, fantasies featuring vampires, like the one in Figure **11.5.1**, have been popular for decades. In fact, vampires are found in centuries-old myths from many cultures. In such myths, vampires are generally described as creatures that drink blood, preferably of the human variety, for sustenance. Dracula, for example, is based on Eastern European folklore about a human who attains immortality (and eternal damnation) by drinking the blood of others.



Figure **11.5.1**: Dracula

FUNCTIONS OF BLOOD

Blood performs many important functions in the body. Major functions of blood include:

- supplying tissues with oxygen, which is needed by all cells for aerobic cellular respiration.
- supplying cells with nutrients, including glucose, amino acids, and fatty acids.
- removing metabolic wastes from cells, including carbon dioxide, urea, and lactic acid.
- helping to defend the body from pathogens and other foreign substances.
- forming clots to seal broken blood vessels and stop bleeding.
- transporting hormones and other messenger molecules.
- regulating the pH of the body, which must be kept within a narrow range (7.35 to 7.45).
- helping to regulate body temperature (through vasoconstriction and vasodilation).

WHAT IS BLOOD?

Blood is a fluid connective tissue that circulates throughout the body through blood vessels of the cardiovascular system. What makes blood so special that it features in widespread myths? Although blood accounts for less than 10 percent of human body weight, it is quite literally the elixir of life. As blood travels through the vessels of the cardiovascular system, it delivers vital substances such as nutrients and oxygen to all of the cells and carries away their metabolic wastes. It is no exaggeration to say that without blood, cells could not survive. Indeed, without the oxygen carried in the blood, cells of the brain start to die within just a matter of minutes.

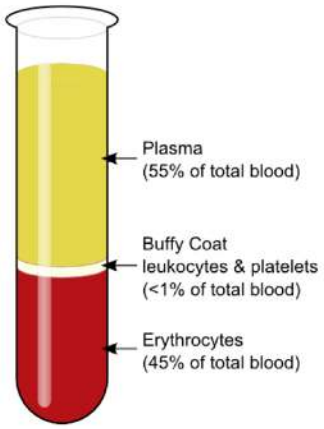


Figure **11.5.2**: If blood is centrifuged (spun at high speed), it separates into its major components based on density, as shown here: plasma, leukocytes (white blood cells) and platelets, and erythrocytes (red blood cells). Plasma makes up about 55% of the blood. Leukocytes and platelets make up less than 1%. Erythrocytes make up about 45%.

The average adult body contains between 4.7 and 5.7 liters (5-6 quarts) of blood. More than half of that amount is fluid. Most of the rest of that amount consists of cells. The relative amounts of the various components in the blood are illustrated in Figure **11.5.2**. The components are also described in the text.

BLOOD PLASMA

Plasma is the liquid component of human blood and makes up about 55 percent of blood by volume. It is about 92 percent water and contains many dissolved substances. Most of these substances are proteins, but plasma also contains trace amounts of glucose, mineral ions, hormones, carbon dioxide, and other substances.

FORMED ELEMENTS

The formed elements in the blood include red blood cells, white blood cells, and platelets. These different types of elements are pictured in Figure **11.5.3** and described in the sections that follow.

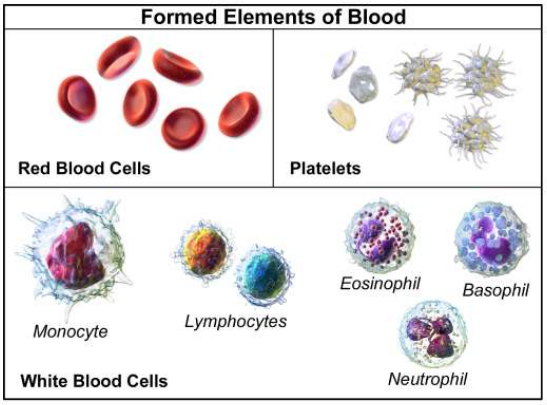


Figure **11.5.3**: Highly magnified blood cells in this image include donut-shaped red blood cells, rough-surfaced white blood cells, and small disc-shaped platelets.

RED BLOOD CELLS

The most numerous cells in the blood are **red blood cells,** also called erythrocytes. One microliter of blood contains between 4.2 and 6.1 million red blood cells, and red blood cells make up about a quarter of all the cells in the human body. The cytoplasm of a mature red blood cell is almost completely filled with hemoglobin, the iron-containing protein that binds with oxygen and gives the cell its red color. Mature red blood cells lack a cell nucleus and most organelles in order to provide maximum space for hemoglobin. They are little more than sacks of hemoglobin.

Red blood cells also carry proteins called antigens that determine blood type. Blood type is a genetic characteristic. The best known human blood type systems are the ABO and Rhesus systems. These are described in the next section.

WHITE BLOOD CELLS (WBC)

White blood cells are cells in the blood that defend the body against invading microorganisms and other threats. There are far fewer white blood cells (also called leukocytes) than red blood cells in the blood. There are normally only about 1,000 to 11,000 white blood cells per microliter of blood. Unlike red blood cells, white blood cells have a nucleus. White blood cells are part of the body's immune system. They destroy and remove old or abnormal cells and cellular debris, as well as attack pathogens and foreign substances. There are two categories of WBCs, granulocytes (contain visible granules in the cytoplasm) and agranulocytes (do not contain granules). The Granulocytes include neutrophils, eosinophils, and basophils. The agranulocytes include lymphocytes and monocytes. The five types differ in their specific immune functions. The relative percent and functions of WBCs are summarized in Table **11.5.1**:

Table **11.5.1**: Major Types of White Blood Cells

Type of Leukocyte	Percent of All Leukocytes	Main Function(s)
Neutrophil	62	Phagocytize (engulf and destroy) bacteria and fungi in the blood
Eosinophil	2	Attack and kill large parasites; carry out allergic responses
Basophil	<1	Release histamines in inflammatory responses
Lymphocyte	30	Attack and destroy virus-infected and tumor cells; create lasting immunity to specific pathogens
Monocyte	5	Phagocytize pathogens and debris in tissues

PLATELETS

Platelets, also called thrombocytes, are actually cell fragments. Like red blood cells, they lack a nucleus and are more numerous than white blood cells. There are about 150,000 to 400,000 platelets per microliter of blood.

The main function of platelets is blood clotting or **coagulation.** This is the process by which blood changes from a liquid to a gel, forming a plug in a damaged blood vessel. If blood clotting is successful, it results in hemostasis, which is the cessation of blood loss from the damaged vessel. A blood clot consists of both platelets and proteins, especially the protein fibrin. You can see a scanning electron microscope micrograph of a blood clot in Figure **11.5.4**.

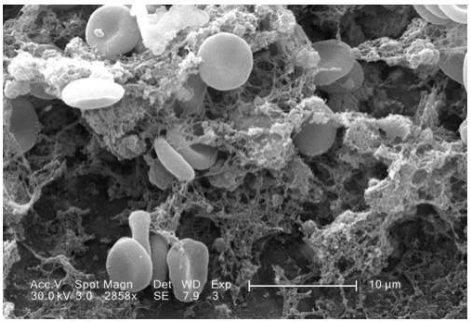


Figure **11.5.4**: Red blood cells become trapped in a coagulating clot so they cannot escape through a break in a blood vessel.

Coagulation begins almost instantly after an injury to the endothelium of a blood vessel occurs. Platelets become activated and change their shape from spherical to star-shaped, as shown in Figure **11.5.5**. This helps them aggregate with one another at the site of injury to start forming a plug in the vessel wall. Activated platelets also release substances into the blood that activate additional platelets and start a sequence of reactions leading to fibrin formation. Strands of fibrin crisscross the platelet plug and strengthen it, much as rebar strengthens concrete.

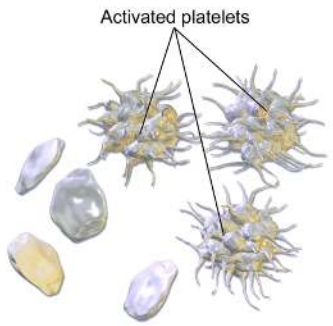


Figure 11.5.5: The shape of platelets after they are activated helps them to stick together and form a plug for a damaged blood vessel.

FORMATION AND DEGRADATION OF BLOOD CELLS

Blood is considered to be a connective tissue because blood cells form inside bones. All three types of blood cells are made in the red marrow of bones in a process called hematopoiesis. The formation of blood cells occurs by the proliferation of stem cells in the marrow. These stem cells are self-renewing: when they divide, some of the daughter cells remain stem cells, so the pool of stem cells is not used up. Other daughter cells follow various pathways to differentiate into a variety of types of blood cells. Once the cells have differentiated, they cannot divide to form copies of themselves.

Eventually, blood cells die and must be replaced through the formation of new blood cells from proliferating stem cells. After blood cells die, the dead cells are phagocytized (engulfed and destroyed) by white blood cells and removed from the circulation. This most often takes place in the spleen and liver.

BLOOD DISORDERS

Many human disorders primarily affect the blood. They include cancers, genetic disorders, poisoning by toxins, infections, and nutritional deficiencies.

- **Leukemia** is a group of cancers of the blood-forming tissues in the bone marrow. It is the most common type of cancer in children, although most cases occur in adults. Leukemia is generally characterized by large numbers of abnormal white blood cells. Symptoms may include excessive bleeding and bruising, fatigue, fever, and an increased risk of infections. Leukemia is thought to be caused by a combination of genetic and environmental factors.
- **Hemophilia** refers to any of several genetic disorders that cause dysfunction in the blood clotting process. People with hemophilia are prone to potentially uncontrollable bleeding even with otherwise inconsequential injuries. They also commonly suffer bleeding into the spaces between joints, which can cause crippling.
- Carbon monoxide poisoning occurs when inhaled carbon monoxide (for example, in fumes from a faulty home furnace) binds irreversibly to the hemoglobin in red blood cells. As a result, oxygen cannot bind to the red cells for transport throughout the body, and this can quickly lead to suffocation. Carbon monoxide is extremely dangerous because it is colorless and odorless so it cannot be detected in the air by human senses.
- HIV is a virus that infects certain types of white blood cells and interferes with the body's ability to defend itself from pathogens and other causes of illness. HIV infection may eventually lead to AIDS or acquired immunodeficiency syndrome. AIDS is characterized by rare infections and cancers that people with a healthy immune system almost never acquire.

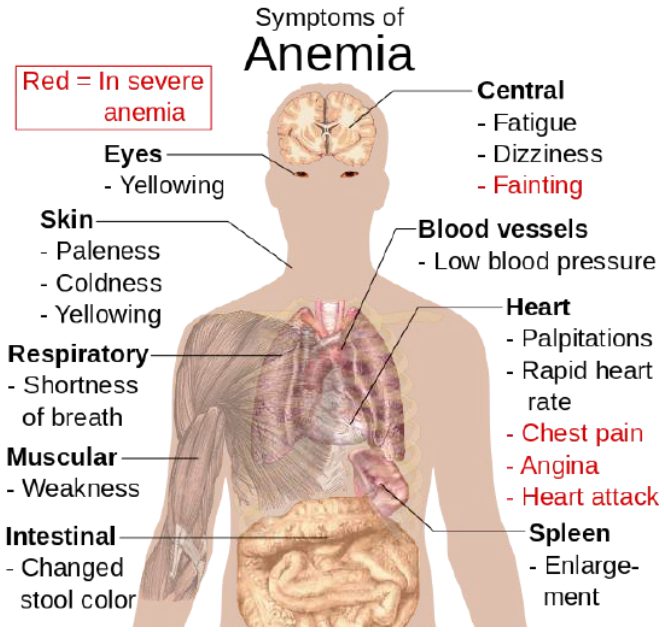


Figure **11.5.6**: Anemia has wide-ranging effects on the human body because oxygen is essential for the normal functioning of cells in every organ system. The most severe symptoms include fainting, chest pain, angina, and heart attack.

- **Anemia** is a disorder in which the blood has an inadequate volume of red blood cells. This reduces the amount of oxygen that the blood can carry and may cause weakness and fatigue. These and other signs and symptoms of anemia are shown in the figure below. Anemia has many possible causes, including excessive bleeding, inherited disorders such as sickle cell hemoglobin, or nutritional deficiencies (iron, folate, or B12). Severe anemia may require transfusions of donated blood.

FEATURE: MYTH VS. REALITY

Donating blood saves lives. In fact, with each blood donation, as many as three lives may be saved. The feeling that comes from knowing you have saved lives is well worth the short amount of time it takes to make a blood donation. Nonetheless, only a minority of potential donors actually donate blood. There are many myths about blood donation that contribute to the small percentage of donors. Knowing the facts may reaffirm your decision to donate if you are already a donor. If you aren't a donor already, getting the facts may help you decide to become one.

Myth: Your blood might become contaminated with an infection during the donation.

Reality: There is no risk of contamination because only single-use, disposable catheters, tubing, and other equipment are used to collect blood for a donation.

Myth: You are too old (or too young) to donate blood.

Reality: There is no upper age limit on donating blood as long as you are healthy. The lower age limit is 16 years.

Myth: You can't donate blood if you have high blood pressure.

Reality: As long as your blood pressure is below 180/100 at the time of donation, you can give blood. Even if you take blood pressure medication to keep your blood pressure below this level, you can donate.

Myth: You can't give blood if you have high cholesterol.

Reality: Having high cholesterol does not affect your ability to donate blood. Taking cholesterol-lowering medication also does not disqualify you.

Myth: You can't donate blood if you have had a flu shot.

Reality: Having a flu shot has no effect on your ability to donate blood. You can even donate on the same day that you receive a flu shot.

Myth: You can't donate blood if you take medication.

Reality: As long as you are healthy, in most cases taking medication does not preclude you from donating blood.

Myth: Your blood isn't needed if it's a common blood type.

Reality: All types of blood are in constant demand.

REVIEW

1. What is blood? Why is blood considered to be a connective tissue?
2. Identify four physiological roles of blood in the body.
3. Describe plasma and its components.
4. Identify red blood cells and their major function.
5. What are white blood cells? Which body system besides the cardiovascular system includes white blood cells?
6. Explain how platelets cause coagulation.
7. Summarize the formation and degradation of blood cells.
8. Identify three disorders of the blood.
9. For each of the descriptions below, choose the blood cell that best fits the description. Blood cells: red blood cells; white blood cells; platelets
   A. Has a nucleus
   B. Responsible for blood clotting
   C. Carbon monoxide binds to a protein in these cells
10. What is another name for erythrocytes? What is another name for leukocytes?
11. *True or False.* Plasma refers to the cytoplasm within blood cells.
12. *True or False.* Platelets are cell fragments.

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11.6: BLOOD TYPES

GIVING THE GIFT OF LIFE

Did you ever donate blood as the individual in Figure **11.6.1** is doing? If you did, then you probably know that your blood type is an important factor in blood transfusions. People vary in the type of blood they inherit, and this determines which type(s) of blood they can safely receive in a transfusion. Do you know your blood type?



Figure **11.6.1**: Donating Blood

WHAT ARE BLOOD TYPES?

Blood type (or blood group) is a genetic characteristic associated with the presence or absence of certain molecules, called antigens, on the surface of red blood cells. These molecules may help maintain the integrity of the cell membrane, act as receptors, or have other biological functions. A **blood group system** refers to all of the gene(s), alleles, and possible genotypes and phenotypes that exist for a particular set of blood type antigens. Human blood group systems include the well-known ABO and Rhesus (Rh) systems, as well as at least 33 others that are less well known.

ANTIGENS AND ANTIBODIES

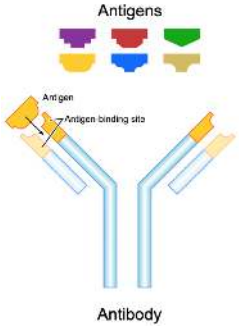


Figure **11.6.2**: Model of antigen and matching antibody

Antigens such as those on the red blood cells are molecules that the immune system identifies as either self (produced by your own body) or non-self (not produced by your own body). Blood group antigens may be proteins, carbohydrates, glycoproteins (proteins attached to chains of sugars), or glycolipids (lipids attached to chains of sugars), depending on the particular blood group system. If antigens are identified as nonself, the immune system responds by forming antibodies that are specific to the non-self antigens. **Antibodies** are large, Y-shaped proteins produced by the immune system that recognize and bind to non-self antigens. The analogy of a lock and key is often used to represent how an antibody and antigen fit together, as shown in Figure **11.6.2**. When antibodies bind to antigens, it marks them for destruction by other immune system cells. Nonself antigens may enter your body on pathogens such as bacteria or viruses, on foods, or on red blood cells in a blood transfusion from someone with a different blood type than your own. The last way is virtually impossible nowadays because of effective blood typing and screening protocols.

GENETICS OF BLOOD TYPE

An individual's blood type depends on which alleles for a blood group system were inherited from their parents. Generally, blood type is controlled by alleles for a single gene or for two or more very closely linked genes. Closely linked genes are almost always inherited together because there is little or no recombination between them. Like other genetic traits, a person's blood type is generally fixed for life, but there are rare instances in which blood type can change. This could happen, for example, if an individual receives a bone marrow transplant to treat a disease such as leukemia. If the bone marrow comes from a donor who has a different blood type, the patient's blood type may eventually convert to the donor's blood type because red blood cells are produced in the bone marrow.

ABO BLOOD GROUP SYSTEM

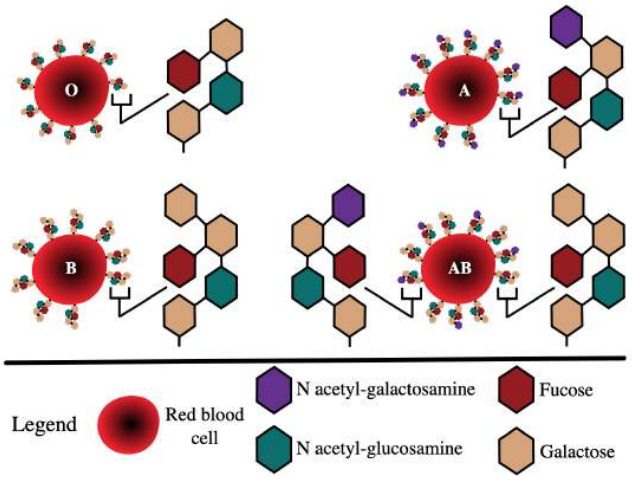


Figure **11.6.3**: ABO antigen molecules

The **ABO blood group system** is the best known human blood group system. Antigens in this system are glycoproteins. These antigen compounds are shown in Figure **11.6.3**. There are four common blood types for the ABO system:

1. Type A, in which only the A antigen is present
2. Type B, in which only the B antigen is present

3. Type AB, in which both the A and B antigens are present
4. Type O, in which neither the A nor the B antigen is present

GENETICS OF THE ABO SYSTEM

The ABO blood group system is controlled by a single gene on chromosome 9. There are three common alleles for the gene, often represented by the letters I^A (or A), I^B (or B), and i (or O). With three alleles, there are six possible genotypes for the ABO blood group. However, alleles I^A and I^B are both dominant to allele i and codominant to each other. This results in just four possible phenotypes (blood types) for the ABO system. These genotypes and phenotypes are shown in Table **11.6.1**.

Table **11.6.1**: **ABO Blood Group System**

Genotype	Phenotype (Blood Type, or Group)
I^Ai	A
I^AI^A	A
I^AI^B	AB
I^Bi	B
I^BI^B	B
ii	O

The diagram in Figure **11.6.4** shows an example of how ABO blood type is inherited. In this particular example, the father has blood type A (genotype AO) and the mother has blood type B (genotype BO). This mating type can produce children with each of the four possible ABO phenotypes, although in any given family not all phenotypes may be present in the children.

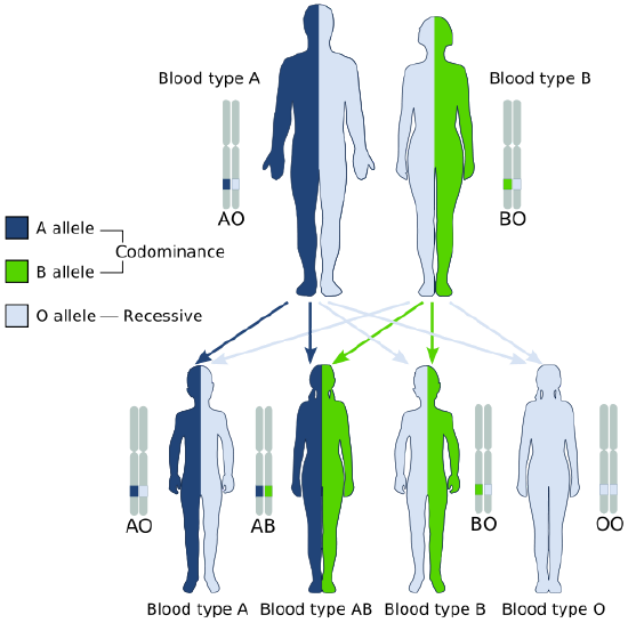


Figure **11.6.4**: Example of ABO blood group inheritance. A male who is type A (genotype of AO) and a female who is type B (genotype BO) can have children with blood types: A, AB, B, and O.

MEDICAL SIGNIFICANCE OF ABO BLOOD TYPE

The ABO system is the most important blood group system in blood transfusions. If red blood cells containing a particular ABO antigen are transfused into a person who lacks that antigen, the person's immune system will recognize the antigen on the red blood cells as non-self. Antibodies specific to that antigen will attack the red blood cells, causing them to agglutinate, or clump and break apart. If a unit of incompatible blood were to be accidentally transfused into a patient, a severe reaction (called acute hemolytic transfusion reaction) is likely to occur in which many red blood cells are destroyed. This may result in kidney failure, shock, and even death. Fortunately, such medical accidents virtually never occur today.

ABO antibodies are likely to already be present in a recipient's blood for antigens that the person lacks. These antibodies are produced in the first years of life by sensitization to similar antigens commonly occurring in the environment. Anti-A antibodies are thought to originate from an immune response to an antigen on the influenza virus, and anti-B antibodies are thought to originate from an immune response to an antigen found on bacteria such as *E. coli*. Once the antibodies have been produced, they circulate in the plasma. The relationship between ABO red blood cell antigens and plasma antibodies is shown in Table **11.6.2**.

Table **11.6.2**: The antibodies that circulate in the plasma are for different antigens than those on red blood cells, which are recognized as self-antigens.

Blood group	A	B	AB	O
Antibodies in plasma	Anti-B	Anti-A	None	Anti-A and Anti-B
Antigens on the red blood cell	A antigen	B antigen	A and B antigen	None

Which blood types are compatible and which are not? Type O blood contains both anti-A and anti-B antibodies, so people with type O blood can only receive type O blood. However, they can donate blood to people of any ABO blood type. That's why individuals with type O blood are called **universal donors.** Type AB blood contains neither anti-A nor anti-B antibodies, so people with type AB blood can receive blood from people of any ABO blood type. That's why individuals with type AB blood are called **universal recipients.** However, they can donate blood only to people who also have type AB blood. These and other relationships between blood types of donors and recipients are summarized in Figure **11.6.5**.

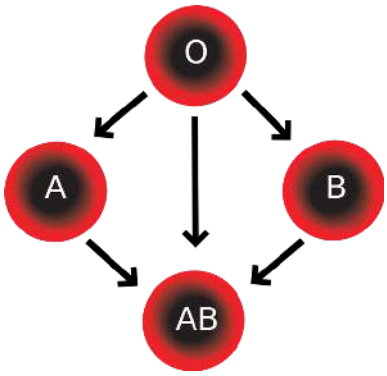


Figure **11.6.5**: You can always donate blood to someone who has the same blood type as yours, but you may or may not be able to donate to people who have other blood types, as indicated in this diagram.

ABO blood type antigens are found not only on red blood cells but also on platelets, in other body fluids such as tears and urine, and on cells of other types of tissues. Blood type compatibility is important to consider for successful organ transplantation. If a transplanted organ has nonself antigens for ABO, it may be attacked by antibodies and rejected by the body.

RHESUS BLOOD GROUP SYSTEM

Another well-known blood group system is the **Rhesus (Rh) blood group system**. The Rhesus system has dozens of different antigens but only five main antigens (named D, C, c, E, and e). The major Rhesus antigen is the D antigen. People with the D antigen are called Rh-positive (Rh+), and people who lack the D antigen are called Rh-negative (Rh-). Rhesus antigens are thought to play a role in transporting ions across cell membranes by acting as channel proteins.

The Rhesus blood group system is controlled by two linked genes on chromosome 1. One gene, called RHD, produces a single antigen, antigen D. The other gene, called RHCE, produces the other four relatively common Rhesus antigens (C, c, E, and e), depending on which alleles for this gene are inherited.

RHESUS BLOOD GROUP AND TRANSFUSIONS

After the ABO system, the Rhesus system is the second most important blood group system in blood transfusions. The D antigen is the one most likely to provoke an immune response in people who lack the antigen. People who have the D antigen (Rh+) can be safely transfused with either Rh+ or Rh- blood, whereas people who lack the D antigen (Rh-) can be safely transfused only with Rh- blood.

Unlike anti-A and anti-B antibodies to ABO antigens, anti-D antibodies for the Rhesus system are not usually produced by sensitization to environmental substances. However, people who lack the D antigen (Rh-) may produce anti-D antibodies if exposed to Rh+ blood. This may happen accidentally in a blood transfusion, although this is extremely unlikely today. It may also happen during pregnancy with an Rh+ fetus if some of the fetal blood cells pass into the mother's blood circulation.

HEMOLYTIC DISEASE OF THE NEWBORN

If a woman who is Rh- is carrying an Rh+ fetus, the fetus may be at risk. This is especially likely if the mother has formed anti-D antibodies during a prior pregnancy because of a mixing of maternal and fetal blood during childbirth. Unlike antibodies against ABO antigens, antibodies against the Rhesus D antigen can cross the placenta and enter the blood of the fetus. This may cause **hemolytic disease of the newborn (HDN)**, also called erythroblastosis fetalis, an illness in which fetal red blood cells are destroyed by maternal antibodies, causing anemia. This illness may range from mild to severe. If it is severe, it may cause brain damage and is sometimes fatal for the fetus or newborn. Fortunately, HDN can be prevented by preventing the formation of anti-D antibodies in the Rh- mother. This is achieved through an injection into the mother of a medication called Rho(D) immune globulin.

FEATURE: MYTH VS. REALITY

Myth: Your nutritional needs can be determined by your ABO blood type. Knowing your blood type allows you to choose the appropriate foods that will help you lose weight, increase your energy, and live a longer, healthier life.

Reality: This idea was proposed in 1996 in a *New York Times* bestseller *Eat Right for Your Type*, by Peter D'Adamo, a naturopath. Naturopathy is a method of treating disorders that involve the use of herbs, sunlight, fresh air, and other natural substances. Some medical doctors consider naturopathy a pseudoscience. A major scientific review of the blood type diet could find no evidence to support it. In one study, adults eating the diet designed for blood type A showed improved health, but this occurred in everyone regardless of their blood type. Because the blood type diet is based solely on blood type, it fails to account for other factors that might require dietary adjustments or restrictions. For example, people with diabetes but different blood types would follow different diets, and one or both of the diets might conflict with standard diabetes dietary recommendations and be dangerous.

Myth: ABO blood type is associated with certain personality traits. For example, people with blood type A are patient and responsible but may also be stubborn and tense, whereas people with blood type B are energetic and creative but may also be irresponsible and unforgiving. In selecting a spouse, both your own and your potential mate's blood type should be taken into account to ensure the compatibility of your personality.

Reality: The belief that blood type is correlated with personality is widely held in Japan and other East Asian countries (the Japanese booth pictured below offers fortunes based on blood type). The idea was originally introduced in the 1920s in a study commissioned by the Japanese government but later shown to have no scientific support. The idea was revived in the 1970s by a Japanese broadcaster who wrote popular books about it. There is no scientific basis for the idea, and it is generally dismissed as pseudoscience by the scientific community. Nonetheless, it remains popular in East Asian countries, like astrology in many other countries.

REVIEW

1. Define blood type and blood group system.
2. Explain the relationship between antigens and antibodies.
3. Identify the alleles, genotypes, and phenotypes in the ABO blood group system.
4. Discuss the medical significance of the ABO blood group system.
5. Give examples of how different ABO blood types vary in their susceptibility to diseases.
6. Describe the Rhesus blood group system.
7. Relate Rhesus blood groups to blood transfusions.
8. What causes hemolytic disease of the newborn?

9. A woman is blood type O and Rh- and her husband is blood type AB and Rh+. Answer the following questions about this couple and their offspring.

   a. What are the possible genotypes of their offspring in terms of ABO blood group?

   b. What are the possible phenotypes of their offspring in terms of ABO blood group?

   c. Can the woman donate blood to her husband? Explain your answer.

   d. Can the man donate blood to his wife? Explain your answer.

10. *True or False.* The D antigen is part of the ABO blood group system.
11. Explain why hemolytic disease of the newborn may be more likely to occur in a second pregnancy than in a first.

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11.7: CARDIOVASCULAR DISEASE

HEART ATTACK ON A PLATE

Eating this greasy cheeseburger smothered in bacon may not literally cause a heart attack. However, regularly eating high-fat, low-fiber foods such as this may increase the risk of a heart attack or other type of cardiovascular disease. In fact, unhealthy lifestyle choices such as this may account for as many as 90 percent of cases of cardiovascular disease.



Figure **11.7.1**: Bacon Cheeseburger

WHAT IS CARDIOVASCULAR DISEASE?

Cardiovascular disease is a class of diseases that involve the cardiovascular system. They include diseases of the coronary arteries that supply the heart muscle with oxygen and nutrients; diseases of arteries such as the carotid artery that provide blood flow to the brain; and diseases of the peripheral arteries that carry blood throughout the body. Worldwide, cardiovascular disease is the leading cause of death, causing about a third of all deaths each year.

Most cases of the cardiovascular disease occur in people over the age of 60, with disease onset typically being about a decade earlier in males than females. The LGBT (lesbian, gay, bisexual, and transgender) community belongs to almost every race, ethnicity, religion, age, and socioeconomic group. The LGBT youth are at a higher risk for cardiovascular diseases, obesity, anxiety, and depression as compared to the general population. LGBT youth receive poor quality of care due to stigma, lack of healthcare providers' awareness, and insensitivity to the unique needs of this community. Young LGBT individuals find it difficult to report their sexual identity to their clinicians. Some clinicians are not well trained in addressing the concerns of members of this community.

You can't control your age or sex, but you can control other factors that increase the risk of cardiovascular disease. Not smoking, maintaining a healthy weight, eating a healthy diet, taking medications as needed to control diabetes and cholesterol, and getting regular exercise are all ways to prevent cardiovascular disease or keep it from progressing. It should be noted that high blood lipid levels are definitely risk factors for cardiovascular disease. High levels of cholesterol in the diet do not appear to lead directly to high levels of cholesterol in the blood. Clearly, cardiovascular disease is multifactorial in terms of its causes.

PRECURSORS OF CARDIOVASCULAR DISEASE

There are two very common conditions that are precursors to virtually all cases of cardiovascular disease: hypertension (hypertension) and atherosclerosis (hardening of blood wall). Both conditions affect the arteries and their ability to maintain normal blood flow.

HYPERTENSION

Hypertension is a chronic medical condition in which the blood pressure in the arteries is persistently elevated, as defined in Table **11.7.1**. Hypertension usually does not cause symptoms, so more than half of the people with high blood pressure are unaware of their condition. Hypertension is typically diagnosed when blood pressure is routinely measured during a medical visit for some other health problem.

Table **11.7.1**: Classification of Blood Pressure (in Adults)

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Normal blood pressure	90-119	60-79
Prehypertension	120-139	80-89
Hypertension	140 or higher	90 or higher

High blood pressure is classified as either primary or secondary high blood pressure. At least 90% of cases are primary high blood pressure, which is caused by some combination of genetic and lifestyle factors. Numerous genes have been identified as having small effects on blood pressure. Lifestyle factors that increase the risk of high blood pressure include excess dietary salt and alcohol consumption in addition to the risk factors for cardiovascular disease stated above. Secondary high blood pressure, which makes up the remaining 10% of cases of hypertension, is attributable to chronic kidney disease or an endocrine disorder such as Cushing's disease.

Treating hypertension is important for reducing the risk of all types of cardiovascular disease, especially stroke. These and other complications of persistent high blood pressure are shown in Figure **11.7.2**. Lifestyle changes, such as reducing salt intake and adopting a healthier diet may be all that is needed to lower blood pressure to the normal range. In many cases, however, medications are also required.

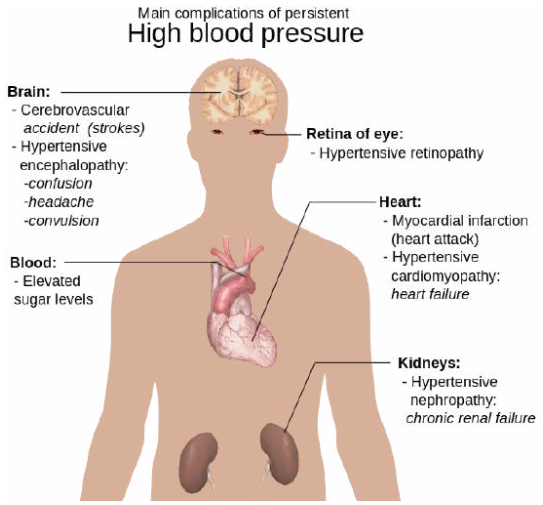


Figure **11.7.2**: If high blood pressure is not brought under control, it can eventually cause hypertensive retinopathy, myocardial infarction, heart failure, nephropathy, stokes, confusion, headache, convulsion, and elevated sugar levels.

ATHEROSCLEROSIS

Atherosclerosis is a condition in which artery walls thicken and stiffen as a result of the buildup of plaques inside the arteries. Plaques consist of white blood cells, cholesterol, and other fats. Typically, there is also a proliferation of smooth muscle cells that make the plaque fibrous as well as fatty. Over time, the plaques may harden with the addition of calcium crystals. This reduces the elasticity of the artery walls. As plaques increase in size, the artery walls dilate to compensate so blood flow is not affected. Eventually, however, the lumen of the arteries is likely to become so narrowed by plaque buildup that blood flow is reduced or even blocked entirely. Figure **11.7.3** illustrates the formation of a plaque in a coronary artery.

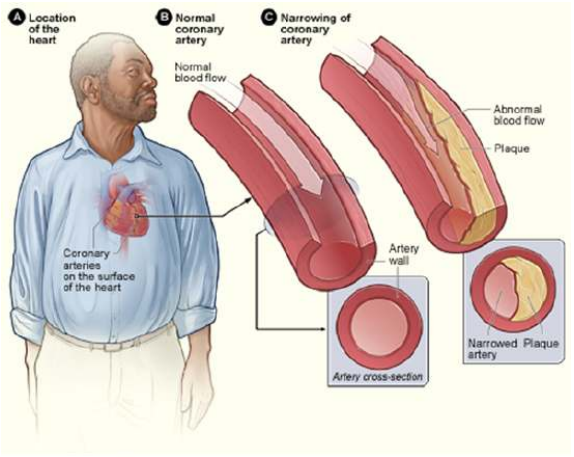


Figure **11.7.3**: Plaque accumulation in a coronary artery may reduce blood flow to cardiac muscle cells.

In most people, plaques start to form in arteries during childhood and progress throughout life. Individuals may develop just a few plaques or dozens of them. Plaques typically remain asymptomatic for decades. Signs and symptoms appear only after there is severe narrowing (stenosis) or complete blockage of arteries. As plaques increase in size and interfere with blood flow, they commonly lead to the formation of blood clots. These may plug arteries at the site of the plaque or travel elsewhere in the circulation. Sometimes plaques rupture or become detached from an arterial wall and become lodged in a smaller, downstream artery. Blockage of arteries by plaques or clots may cause a heart attack, stroke, or other potentially life-threatening cardiovascular events. If blood flow to the kidneys is affected, it may lead to chronic kidney disease.

The process in which plaques form is not yet fully understood, but it is thought that it begins when low-density lipoproteins (LDLs) accumulate inside endothelial cells in artery walls, causing inflammation. The inflammation attracts white blood cells that start to form a plaque. Continued inflammation and a cascade of other immune responses cause the plaque to keep growing. Risk factors for the development of atherosclerosis include hypertension, high cholesterol (especially LDL cholesterol), diabetes, and smoking. The chance of developing atherosclerosis also increases with age, male sex, and a family history of cardiovascular disease.

Treatment of atherosclerosis often includes both lifestyle changes and medications to lower cholesterol, control blood pressure, and reduce the risk of blood clot formation. In extreme cases or when other treatments are inadequate, surgery may be recommended. Surgery may involve the placement of stents in arteries to keep them open and improve blood flow or the use of grafts to divert blood flow around blocked arteries.

CORONARY ARTERY DISEASE

Coronary artery diseases are a group of diseases that result from atherosclerosis of coronary arteries. Treatment of the diseases mainly involves treating underlying atherosclerosis. Two of the most common coronary artery diseases are angina and myocardial infarction.

ANGINA

Angina is chest pain or pressure that occurs when heart muscle cells do not receive adequate blood flow and become starved of oxygen (a condition called ischemia). It is illustrated in Figure **11.7.4**. There may also be a pain in the back, neck, shoulders, or jaw; and in some cases, the pain may be accompanied by shortness of breath, sweating, or nausea. The main goals of the treatment of angina are relieving the symptoms and slowing the progression of underlying atherosclerosis.

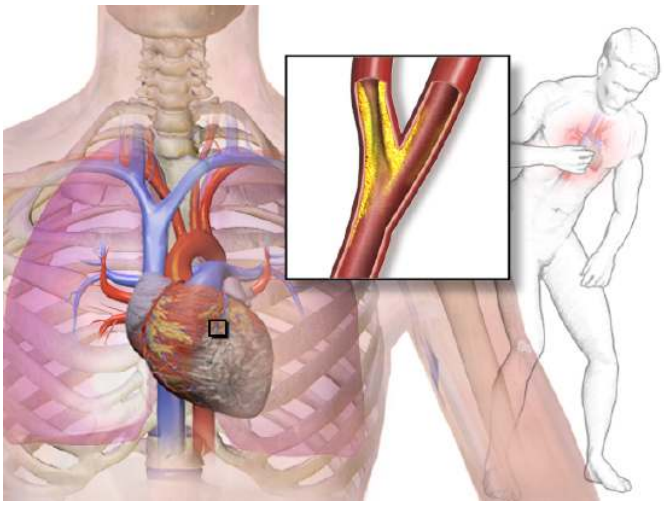


Figure **11.7.4**: Angina is a pain in the chest due to reduced blood flow in coronary arteries so the heart muscle does not receive adequate oxygen.

Angina may be classified as either stable angina or unstable angina:

- Stable angina is angina in which pain is precipitated by exertion (say, from brisk walking or running) and improves quickly with rest or the administration of nitroglycerin, which dilates coronary arteries and improves blood flow. Stable angina may develop into unstable angina.
- Unstable angina is angina in which pain occurs during rest, lasts more than 15 minutes, and is of new onset. This type of angina is more dangerous and may be a sign of an imminent heart attack. It requires urgent medical attention.

MYOCARDIAL INFARCTION

A **myocardial infarction (MI)**, commonly known as a heart attack, occurs when blood flow stops to a part of the heart causing damage to the heart muscle and the death of myocardial cells. An MI usually occurs because of complete blockage of a coronary artery, often due to a blood clot or the rupture of a plaque (Figure **11.7.5**). An MI typically causes chest pain and pressure, among other possible symptoms, but at least one-quarter of MIs do not cause any symptoms.

In the worst case, an MI may cause sudden death. Even if the patient survives, an MI often causes permanent damage to the heart. This puts the heart at risk of heart arrhythmias, heart failure, and cardiac arrest.

- Heart arrhythmias are abnormal heart rhythms, which are potentially life-threatening. Heart arrhythmias often can be interrupted with a cardiac defibrillator, which delivers an electrical shock to the heart, in effect “rebooting” it.
- Heart failure occurs when the pumping action of the heart is impaired so tissues do not get adequate oxygen. This is a chronic condition that tends to get worse over time, although it can be managed with medications.
- Cardiac arrest occurs when the heart no longer pumps blood or pumps blood so poorly that vital organs can no longer function. This is a medical emergency requiring immediate intervention.

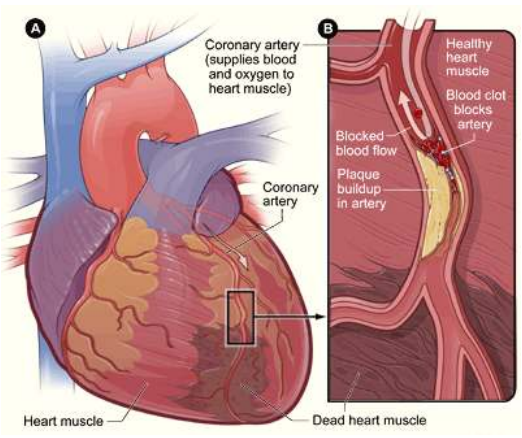


Figure **11.7.5**: A myocardial infarction occurs when cardiac muscle cells die due to blockage of a coronary artery.

OTHER CARDIOVASCULAR DISEASES

Hypertension and atherosclerosis often cause other cardiovascular diseases. These commonly include stroke and peripheral artery disease.

STROKE

A **stroke,** also known as a cerebrovascular accident or brain attack, occurs when blocked or broken arteries in the brain result in the death of brain cells. There are two main types of stroke: ischemic stroke and hemorrhagic stroke. Ischemic storke is illustrated in Figure **11.7.6**.

1. An ischemic stroke occurs when an embolus (blood clot) breaks off from a plaque or forms in the heart because of arrhythmia and travels to the brain where it becomes lodged in an artery. This blocks blood flow to the part of the brain that is served by arteries downstream from the blockage. Lack of oxygen causes the death of brain cells. Treatment with a clot-busting drug within a few hours of the stroke may prevent permanent damage. Almost 90 percent of strokes are ischemic strokes.
2. A hemorrhagic stroke occurs when an artery in the brain ruptures and causes bleeding in the brain. This deprives downstream tissues of adequate blood flow and also puts pressure on brain tissue. Both factors can lead to the death of brain cells. Surgery to temporarily open the cranium may be required to relieve the pressure. Only about 10 percent of strokes are hemorrhagic strokes, but they are more likely to be fatal than ischemic strokes.

In both types of stroke, the part of the brain that is damaged loses is the ability to function normally. Signs and symptoms of stroke may include an inability to move, feel, or see on one side of the body; problems understanding speech or difficulty speaking; memory problems; confusion; and dizziness. Hemorrhagic strokes may also cause a severe headache. The symptoms of a stroke usually occur within seconds or minutes of the brain injury. Depending on the severity of the stroke and how quickly treatment is provided, the symptoms may be temporary or permanent. If the symptoms of a stroke go away on their own in less than an hour or two, the stroke is

called a transient ischemic attack. Stroke is the leading cause of disability in the United States, but rehabilitation with physical, occupational, speech, or other types of therapy may significantly improve functioning.

The main risk factor for stroke is high blood pressure. Therefore, keeping blood pressure within the normal range, whether with lifestyle changes or medications, is the best way to reduce the risk of stroke. Another possible cause of stroke is the use of illicit drugs such as amphetamines or cocaine. Having had a stroke in the past greatly increases one's risk of future strokes. Men are also more likely than women to have strokes.

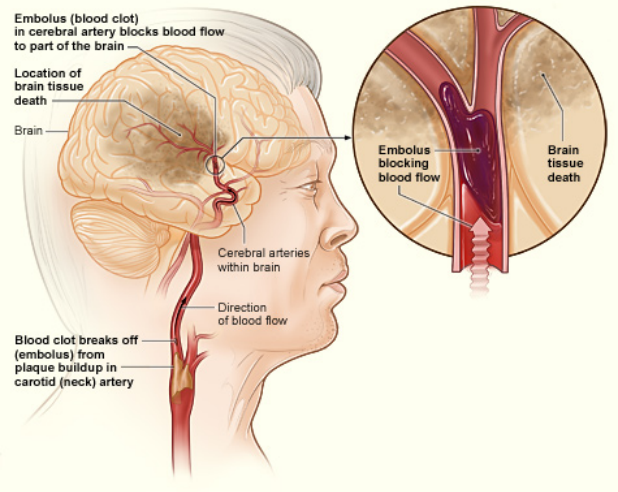


Figure **11.7.6**: In an ischemic stroke, brain cells die due to a blocked artery in the brain. The blockage happens when a blood clot breaks from a buildup in the carotid artery and blocks blood flow to part of the brain. As a result, the brain tissue dies. The traveling clot is called embolus.

PERIPHERAL ARTERY DISEASE

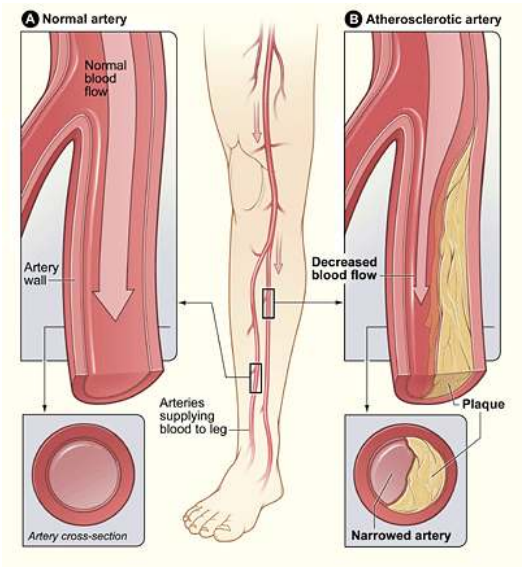


Figure **11.7.7**: Peripheral artery disease (PAD) develops when plaque accumulates in the wall of the leg artery. PAD typically causes pain and other symptoms because of decreased blood flow in the leg or other areas of the body served by peripheral arteries.

Peripheral artery disease (PAD) is the narrowing of the arteries other than those that supply the heart or brain due to atherosclerosis. Figure **11.7.7** shows how the PAD occurs. PAD most commonly affects the legs, but other arteries may also be involved. The classic symptom is leg pain when walking, which usually resolves with rest. This symptom is known as intermittent claudication. Other symptoms may include skin ulcers, bluish skin, cold skin, or poor nail and hair growth in the affected leg(s). However, up to half of all cases of PAD do not have any symptoms.

The main risk factor for PAD is smoking. Other risk factors include diabetes, high blood pressure, and high blood cholesterol. The underlying mechanism is usually atherosclerosis. PAD is typically diagnosed when blood pressure readings taken at the ankle are lower than blood pressure readings taken at the upper arm. It is important to diagnose PAD and treat underlying atherosclerosis because people with this disorder have a four to five times higher risk of myocardial infarction or stroke. Surgery to expand the affected arteries or to graft vessels in order to bypass blockages may be recommended in some cases.

FEATURE: MY HUMAN BODY

You read in this concept about the many dangers of hypertension. Do you know whether you have hypertension? The only way to know for sure is to have your blood pressure measured. Measuring blood pressure is quick and painless, but several measurements are needed to accurately diagnose hypertension. Some people have what is called "white coat disease." Their blood pressure rises just because they are being examined by a physician (in a white coat). Blood pressure also fluctuates from time to time due to factors such as hydration, stress, and time of day. Repeatedly measuring and recording your own blood pressure at home can provide your doctor with valuable diagnostic data. Digital blood pressure monitors for home use, like the one pictured in Figure **11.7.8**, are relatively inexpensive, easy to use, and available at most pharmacies.



Figure **11.7.8**: This personal blood pressure monitor is worn on the wrist.

REVIEW

1. What is cardiovascular disease? How much mortality do cardiovascular diseases cause?
2. List risk factors for cardiovascular disease.
3. What is hypertension?

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4. Define atherosclerosis.
5. What is coronary artery disease?
6. Identify two specific coronary artery diseases.
7. Explain how a stroke occurs and how it affects the patient.
8. Describe the cause of peripheral artery disease.
9. What are two cardiovascular diseases that can be caused by atherosclerosis? Explain specifically how atherosclerosis contributes to each of them.
10. *True or False.* A heart attack is the same thing as cardiac arrest.
11. *True or False.* Plaques in arteries can cause blood clots.
12. What are the similarities between angina and ischemic stroke?
13. How can kidney disease be caused by problems in the cardiovascular system?
14. In peripheral artery disease, the blood pressure at the ankle is typically _____ the blood pressure at the upper arm.

    A. erratic compared to B. the same as

    C. higher than D. lower than
15. Name three components of the plaque that can build up in arteries.

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11.8: CASE STUDY CONCLUSION- FLIGHT AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: FLIGHT RISK

At the beginning of this chapter, you learned about Antônio and Ahaya, who met while sitting next to each other on a plane. During the flight, Ahaya got up to take frequent walks and was doing leg exercises to try to avoid the medical condition depicted in Figure 11.8.1—**deep vein thrombosis** (DVT). DVT occurs when a blood clot forms in a deep vein, usually in the leg. It can be very dangerous—even deadly.

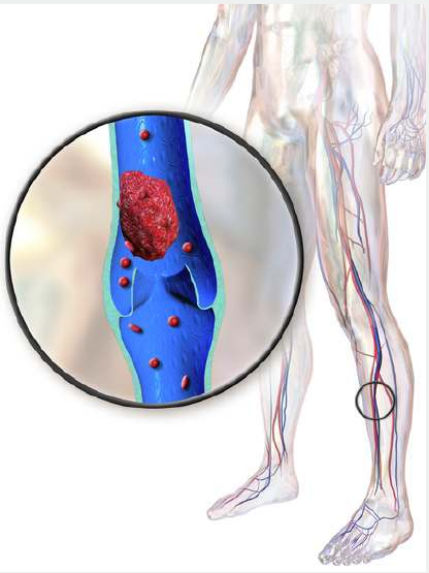


Figure **11.8.1**: Illustration of a blood clot in a deep vein in the leg, which is called deep vein thrombosis (DVT).

As you learned in this chapter, a blood clot is an aggregation of platelets and proteins. Blood clots are helpful to prevent blood loss when a blood vessel is damaged. But in some situations, they can be extremely dangerous. For example, blood clots can cause heart attacks or strokes by blocking the flow of blood to the heart or brain, respectively.

When DVT occurs, one of the major risks is pulmonary embolism (PE). PE is when the blood clot breaks off, travels through the blood vessels, and lodges in a pulmonary artery, like the blood clot shown in Figure **11.8.2**. Recall what the pulmonary arteries do: they carry deoxygenated blood from the heart to the lungs, where the blood picks up oxygen and releases carbon dioxide due to gas exchange between the capillaries and the alveoli of the lungs. Imagine what would happen if this flow of blood to the lungs was partially or completely blocked by a blood clot. Depending on the size of the blood clot and where it is lodged, a PE can cause a variety of serious consequences ranging from lung damage to instant death, because of the disruption of the pulmonary circulation.

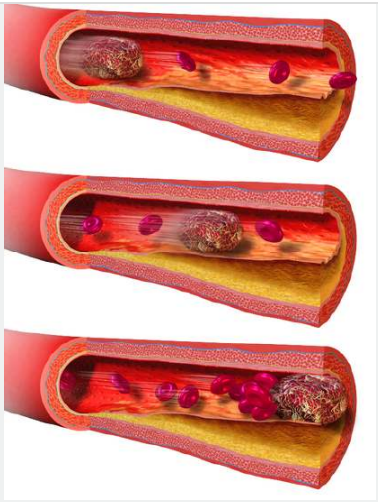


Figure **11.8.2**: Illustration of how a moving blood clot can get stuck in a blood vessel. When this occurs in a pulmonary artery, it is called a pulmonary embolism (PE).

Ahaya has a higher risk of DVT and its consequences because he has heart failure. As you have learned, heart failure is a chronic condition in which the pumping action of the heart is impaired. One reason that heart failure is thought to increase the risk of DVT is that the blood is not being pushed strongly enough through the cardiovascular system, allowing blood clots to form more easily.

Ahaya needs to be particularly concerned about DVT while on a long plane flight. Why do you think this is? Think about how blood flows through arteries and veins. Blood is pushed through arteries mainly due to the pumping action of the heart. Veins, on the other hand, rely on the movement of the surrounding skeletal muscles to help push blood through them. Sitting still for long periods of time in cramped quarters, such as on a plane, can cause blood to pool in the deep veins of the legs. This can lead to the formation of a blood clot.

CHAPTER SUMMARY

In this chapter, you learned about the structure, functions, and disorders of the cardiovascular system. Specifically, you learned that:

- The cardiovascular system is the organ system that transports materials to and from all the cells of the body. The main components of the cardiovascular system are the heart, blood vessels, and blood.
- The cardiovascular system has two interconnected circulations. The pulmonary circulation carries blood between the heart and lungs, where blood is oxygenated. The systemic circulation carries blood between the heart and the rest of the body, where it delivers oxygen.
- The heart is a muscular organ in the chest that consists mainly of cardiac muscle and pumps blood through blood vessels by repeated, rhythmic contractions.

- The wall of the heart consists of three layers. The middle layer, the myocardium, is the thickest layer and consists mainly of cardiac muscle.
- The interior of the heart consists of four chambers, with an upper atrium and lower ventricle on each side of the heart. Blood enters the heart through the atria, which pump it to the ventricles. Then the ventricles pump blood out of the heart. Four valves in the heart keep blood flowing in the correct direction and prevent backflow.
- Deoxygenated blood flows into the right atrium through veins from the upper and lower body (superior and inferior vena cava, respectively), and oxygenated blood flows into the left atrium through four pulmonary veins from the lungs. Each atrium pumps the blood to the ventricle below it. From the right ventricle, deoxygenated blood is pumped to the lungs through the two pulmonary arteries. From the left ventricle, oxygenated blood is pumped to the rest of the body through the aorta.
- The coronary circulation consists of blood vessels that carry blood to and from the heart muscle cells. There are two coronary arteries that supply the two sides of the heart with oxygenated blood. Cardiac veins drain deoxygenated blood back into the heart.
- The cardiac cycle refers to a single complete heartbeat. It includes diastole when the atria contract; and systole when the ventricles contract.
- The normal, rhythmic beating of the heart is called sinus rhythm. It is established by the heart's pacemaker cells in the sinoatrial node. Electrical signals from the pacemaker cells travel to the atria and cause them to contract. Then the signals travel to the atrioventricular node and from there to the ventricles, causing them to contract. Electrical stimulation from the autonomic nervous system and hormones from the endocrine system can also influence heartbeat.

- Blood vessels carry blood throughout the body. Major types of blood vessels are arteries, veins, and capillaries.
  - Arteries are blood vessels that usually carry blood away from the heart (except for coronary arteries that supply the heart muscle with blood). Most arteries carry oxygenated blood. The largest artery is the aorta, which is connected to the heart and extends into the abdomen. Blood moves through arteries due to pressure from the beating of the heart.
  - Veins are blood vessels that usually carry blood toward the heart. Most veins carry deoxygenated blood. The largest veins are the superior and inferior venae cavae. Blood moves through veins by the squeezing action of surrounding skeletal muscles. Valves in veins prevent the backflow of blood.
  - Capillaries are the smallest blood vessels. They connect arterioles and venules. They form capillary beds where substances are exchanged between the blood and surrounding tissues.
  - The walls of arteries and veins have three layers. The middle layer is thickest in arteries, in which it contains smooth muscle tissue that controls the diameter of the vessels. The outer layer is thickest in veins and consists mainly of connective tissue. The walls of capillaries consist of little more than a single layer of epithelial cells.
  - Blood pressure is a measure of the force that blood exerts on the walls of arteries. It is expressed as a double number, with the higher number representing systolic pressure when the ventricles contract and the lower number representing diastolic pressure when the ventricles relax. Normal blood pressure is generally defined as a pressure of 120/80 mm Hg or less.
  - Vasoconstriction (narrowing) and vasodilation (widening) of arteries can occur to help regulate blood pressure or body temperature or to change blood flow as part of the fight-or-flight response.
- Blood is a fluid connective tissue that circulates throughout the body in blood vessels. Blood supplies tissues with oxygen and nutrients and removes their metabolic wastes. Blood helps defend the body from pathogens and other threats, transports hormones and other substances, and helps to keep the body's pH and temperature in homeostasis. Blood consists of a liquid part, called plasma, and cells, including red blood cells, white blood cells, and platelets.
  - Plasma makes up more than half of blood by volume. It consists of water and many dissolved substances. Blood also contains blood cells and platelets.
  - Red blood cells are the most numerous cells in the blood and consist mostly of hemoglobin, which carries oxygen. Red blood cells also carry antigens that determine blood types. White blood cells are less numerous than red blood cells and are part of the body's immune system. They protect the body from abnormal cells, microorganisms, and other harmful substances. There are several different types of white blood cells that differ in their specific immune functions.
  - Platelets are cell fragments that play important roles in blood clotting or coagulation. They stick together at breaks in blood vessels to form a clot and stimulate the production of fibrin, which strengthens the clot.
  - All blood cells form by the proliferation of stem cells in red bone marrow in a process called hematopoiesis. When blood cells die, they are phagocytized by white blood cells and removed from circulation.
  - Disorders of the blood include leukemia, which is a cancer of the bone-forming cells; hemophilia, which is any of several genetic blood-clotting disorders; carbon monoxide poisoning, which prevents red blood cells from binding with oxygen and causes suffocation; HIV infection, which destroys certain white blood cells and can cause AIDS; and anemia, in which there are not enough red blood cells to carry adequate oxygen to body tissues.
- Blood type (or blood group) is a genetic characteristic associated with the presence or absence of antigens on the surface of red blood cells. A blood group system refers to all of the gene(s),

alleles, and possible genotypes and phenotypes that exist for a particular set of blood type antigens.

- Cardiovascular disease is a class of diseases that involve the cardiovascular system. Worldwide, it is the leading cause of death. Most cases occur in people over age 60, and onset is typically about a decade earlier in males than females. Other risk factors include smoking, obesity, diabetes, high blood cholesterol, and lack of exercise.
- Antigens are molecules that the immune system identifies as either self or nonself. If antigens are identified as nonself, the immune system responds by forming antibodies that are specific to the nonself antigens, leading to the destruction of cells bearing the antigens.
- The ABO blood group system is a system of red blood cell antigens controlled by a single gene with three common alleles on chromosome 9. There are four possible ABO blood types: A, B, AB, and O. The ABO system is the most important blood group system in blood transfusions. People with type O blood are universal donors, and people with type AB blood are universal recipients.
- The Rhesus blood group system is a system of red blood cell antigens controlled by two genes with many alleles on chromosome 1. There are five common Rhesus antigens, of which antigen D is most significant. Individuals who have antigen D are called Rh+, and individuals who lack antigen D are called Rh-. Rh- mothers of Rh+ fetuses may produce antibodies against the D antigen in the fetal blood, causing hemolytic disease of the newborn (HDN).

- Two common conditions that lead to most cases of cardiovascular disease are hypertension and atherosclerosis. Hypertension is blood pressure that is persistently at or above 140/90 mm Hg. Atherosclerosis is a buildup of fatty, fibrous plaques in arteries that may reduce or block blood flow. Treating these conditions is important for preventing cardiovascular disease.
  - Coronary artery disease is a group of diseases that result from atherosclerosis of coronary arteries. Two of the most common are angina and myocardial infarction (heart attack). In angina, cardiac cells receive inadequate oxygen, which causes chest pain. In a heart attack, cardiac cells die because blood flow to part of the heart is blocked. A heart attack may cause death or lead to heart arrhythmias, heart failure, or cardiac arrest.
  - A stroke occurs when blocked or broken arteries in the brain result in the death of brain cells. This may occur when an artery is blocked by a clot or plaque or when an artery ruptures and bleeds in the brain. In both cases, part of the brain is damaged and functions such as speech and controlled movements may be impaired, either temporarily or permanently.
  - Peripheral artery disease occurs when atherosclerosis narrows peripheral arteries, usually in the legs, often causing pain when walking. It is important to diagnose this disease so underlying atherosclerosis can be treated before it causes a heart attack or stroke.

In this chapter, you learned that the cardiovascular system carries nutrients to the cells of the body. Read the next chapter about the Digestive System to learn about how your body transforms your meals into the nutrients that cells need to function.

CHAPTER SUMMARY REVIEW QUESTIONS

1. Alex goes to the doctor and learns that his blood pressure is 135/90 mm Hg. Answer the following questions about his blood pressure.
   A. Is this normal blood pressure? Why or why not?
   B. Which number refers to the systolic pressure and which number refers to the diastolic pressure?
   C. Describe what the atria and ventricles of Alex's heart are doing when the pressure is at 135 mm Hg.
   D. Alex's doctor would like him to lower his blood pressure. Why do you think he would like Alex to do this and what are some ways in which he may be able to lower his blood pressure?
2. What are the three functions of the cardiovascular system?
3. What is the watery part of the blood called?
4. Which are the chambers of the heart that receive blood? Which are the chambers of the heart that pump blood out of the heart?
5. Which chambers of the heart contain deoxygenated blood?
   A. Right and left atria
   B. Right and left ventricles
   C. Right atrium and right ventricle
   D. Left atrium and left ventricle
6. What are two different places in the cardiovascular system where valves are located?
7. Valves prevent blood from flowing backward in the cardiovascular system. Why do you think this is important?
8. Explain how pacemaker cells in the heart work together with the nervous system to regulate the beating of the heart.
9. *True or False.* Red marrow is the source of white blood cells.
10. *True or False.* Plaques that build up in arteries are made completely of fats.
11. The aorta is:
    A. An artery
    B. A chamber of the heart
    C. A vein
    D. A valve
12. Compare the coronary arteries, pulmonary arteries, and arteries elsewhere in the body in terms of their target tissues (i.e. where they bring blood to) and whether they are carrying oxygenated or deoxygenated blood.
13. The superior vena cava empties into which structure of the heart? The inferior vena cava empties into which structure of the heart?
    A. right atrium; left atrium
    B. right atrium; right atrium

C. right atrium; right ventricle
D. right ventricle; left ventricle

14. Venules receive blood from what?
15. Define blood type and blood group system. Explain the relationship between antigens and antibodies.
16. Identify the alleles, genotypes, and phenotypes in the ABO blood group system.
17. Discuss the medical significance of the ABO blood group system.
18. Give examples of how different ABO blood types vary in their susceptibility to diseases.
19. Describe the Rhesus blood group system.
20. Relate Rhesus blood groups to blood transfusions.
21. What causes hemolytic disease of the newborn?
22. A woman is blood type O and Rh- and her husband is blood type AB and Rh+. Answer the following questions about this couple and their offspring.
    A. What are the possible genotypes of their offspring in terms of ABO blood group?
    B. What are the possible phenotypes of their offspring in terms of ABO blood group?
    C. Can the woman donate blood to her husband? Explain your answer.
    D. Can the man donate blood to his wife? Explain your answer.
23. *True or False.* The D antigen is part of the ABO blood group system.
24. Explain why hemolytic disease of the newborn may be more likely to occur in a second pregnancy than in a first.
25. Anemia causes weakness and fatigue due to a reduction in the amount of oxygen that gets to the cells of the body. Explain how oxygen is transported to the cells of the body and which blood cells are affected in anemia.
26. What are the two conditions that are precursors to virtually all cases of cardiovascular disease?
27. What is another name for a heart attack?
    A. Heart arrhythmia
    B. Myocardial infarction
    C. Angina
    D. Heart failure
28. *True or False.* Strokes can be due to a blood clot or to a broken artery.
29. *True or False.* After an injury to a blood vessel, platelets respond by losing their nuclei.
30. What are the main differences between coronary circulation, pulmonary circulation, and systemic circulation?
31. Define the term *sinus rhythm.*
32. Which is generally a more serious and immediately life-threatening condition: heart failure or cardiac arrest? Explain your answer.
33. Match each of the following descriptions to the disease or disorder from the list below that *best* matches it. Use each disease or disorder only once. Diseases and disorders: hypertension; atherosclerosis; coronary artery disease; peripheral artery disease
    A. Blood flow to the muscle cells of the heart is impaired.
    B. Blood pressure is too high.
    C. Arteries in the legs specifically become more narrow.
    D. Plaque builds up in arteries (in general).

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CHAPTER OVERVIEW

12: Special Senses

12.1: Introduction to the Special Senses

12.2: Taste and Smell

12.3: Hearing and Vestibular Sensation

12.4: Vision

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12.1: Introduction to the Special Senses



Figure 12.1.1 This shark uses its senses of sight and smell to hunt, but it also relies on its ability to sense the electric fields of prey, a sense not present in most land animals. (credit: modification of work by Hermanus Backpackers Hostel, South Africa)

In more advanced animals, the senses are constantly at work, making the animal aware of stimuli—such as light, or sound, or the presence of a chemical substance in the external environment—and monitoring information about the organism's internal environment. All bilaterally symmetric animals have a sensory system, and the development of any species' sensory system has been driven by natural selection; thus, sensory systems differ among species according to the demands of their environments. The shark, unlike most fish predators, is electrosensitive—that is, sensitive to electrical fields produced by other animals in its environment. While it is helpful to this underwater predator, electrosensitivity is a sense not found in most land animals. in this chapter, information about smell, taste, hearing, and vision is presented.

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12.2: Taste and Smell

Taste, also called **gustation**, and smell, also called **olfaction**, are the most interconnected senses in that both involve molecules of the stimulus entering the body and bonding to receptors. Smell lets an animal sense the presence of food other chemicals in the environment that can impact their survival. Similarly, the sense of taste allows animals to discriminate between types of foods. While the value of a sense of smell is obvious, what is the value of a sense of taste? Different tasting foods have different attributes, both helpful and harmful. For example, sweet-tasting substances tend to be highly caloric, which could be necessary for survival in lean times. Bitterness is associated with toxicity, and sourness is associated with spoiled food. Salty foods are valuable in maintaining homeostasis by helping the body retain water and by providing ions necessary for cells to function.

Tastes and Odors

Both taste and odor stimuli are molecules taken in from the environment. The primary tastes detected by humans are sweet, sour, bitter, salty and umami. The first four tastes need little explanation. The identification of **umami** as a fundamental taste occurred fairly recently—it was identified in 1908 by Japanese scientist Kikunae Ikeda while he worked with seaweed broth, but it was not widely accepted as a taste that could be physiologically distinguished until many years later. The taste of umami, also known as savoriness, is attributable to the taste of the amino acid L-glutamate. In fact, monosodium glutamate, or MSG, is often used in cooking to enhance the savory taste of certain foods. What is the adaptive value of being able to distinguish umami? Savory substances tend to be high in protein.

All odors that we perceive are molecules in the air we breathe. If a substance does not release molecules into the air from its surface, it has no smell. And if a human or other animal does not have a receptor that recognizes a specific molecule, then that molecule has no smell. Humans have about 350 olfactory receptor subtypes that work in various combinations to allow us to sense about 10,000 different odors. Compare that to mice, for example, which have about 1,300 olfactory receptor types, and therefore probably sense more odors. Both odors and tastes involve molecules that stimulate specific chemoreceptors. Although humans commonly distinguish taste as one sense and smell as another, they work together to create the perception of flavor. A person's perception of flavor is reduced if he or she has congested nasal passages.

Reception and Transduction

Odorants (odor molecules) enter the nose and dissolve in the olfactory epithelium, the mucosa at the back of the nasal cavity (as illustrated in Figure 12.2.1). The **olfactory epithelium** is a collection of specialized olfactory receptors in the back of the nasal cavity that spans an area about 5 cm^2 in humans. Recall that sensory cells are neurons. An **olfactory receptor**, which is a dendrite of a specialized neuron, responds when it binds certain molecules inhaled from the environment by sending impulses directly to the olfactory bulb of the brain. Humans have about 12 million olfactory receptors, distributed among hundreds of different receptor types that respond to different odors. Twelve million seems like a large number of receptors, but compare that to other animals: rabbits have about 100 million, most dogs have about 1 billion, and bloodhounds—dogs selectively bred for their sense of smell—have about 4 billion. The overall size of the olfactory epithelium also differs between species, with that of bloodhounds, for example, being many times larger than that of humans.

Olfactory neurons are **bipolar neurons** (neurons with two processes from the cell body). Each neuron has a single dendrite buried in the olfactory epithelium, and extending from this dendrite are 5 to 20 receptor-laden, hair-like cilia that trap odorant molecules. The sensory receptors on the cilia are proteins, and it is the variations in their amino acid chains that make the receptors sensitive to different odorants. Each olfactory sensory neuron has only one type of receptor on its cilia, and the receptors are specialized to detect specific odorants, so the bipolar neurons themselves are specialized. When an odorant binds with a receptor that recognizes it, the sensory neuron associated with the receptor is stimulated. Olfactory stimulation is the only sensory information that directly reaches the cerebral cortex, whereas other sensations are relayed through the thalamus.

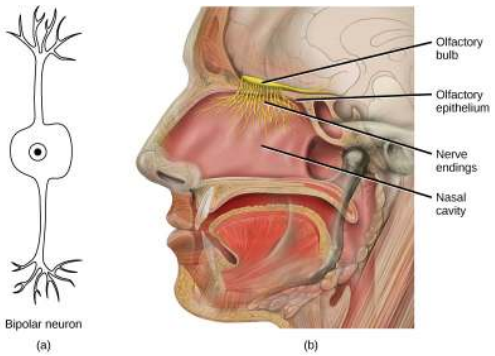


Figure 12.2.1. In the human olfactory system, (a) bipolar olfactory neurons extend from (b) the olfactory epithelium, where olfactory receptors are located, to the olfactory bulb. (credit: modification of work by Patrick J. Lynch, medical illustrator; C. Carl Jaffe, MD, cardiologist)

EVOLUTION CONNECTION

PheromonesA **pheromone** is a chemical released by an animal that affects the behavior or physiology of animals of the same species. Pheromonal signals can have profound effects on animals that inhale them, but pheromones apparently are not consciously perceived in the same way as other odors. There are several different types of pheromones, which are released in urine or as glandular secretions. Certain pheromones are attractants to potential mates, others are repellants to potential competitors of the same sex, and still others play roles in mother-infant attachment. Some pheromones can also influence the timing of puberty, modify reproductive cycles, and even prevent embryonic implantation. While the roles of pheromones in many nonhuman species are important, pheromones have become less important in human behavior over evolutionary time compared to their importance to organisms with more limited behavioral repertoires.

The vomeronasal organ (VNO, or Jacobson's organ) is a tubular, fluid-filled, olfactory organ present in many vertebrate animals that sits adjacent to the nasal cavity. It is very sensitive to pheromones and is connected to the nasal cavity by a duct. When molecules dissolve in the mucosa of the nasal cavity, they then enter the VNO where the pheromone molecules among them bind with specialized pheromone receptors. Upon exposure to pheromones from their own species or others, many animals, including cats, may display the flehmen response (shown in Figure 12.2.2), a curling of the upper lip that helps pheromone molecules enter the VNO.

Pheromonal signals are sent, not to the main olfactory bulb, but to a different neural structure that projects directly to the amygdala (recall that the amygdala is a brain center important in emotional reactions, such as fear). The pheromonal signal then continues to areas of the hypothalamus that are key to reproductive physiology and behavior. While some scientists assert that the VNO is apparently functionally vestigial in humans, even though there is a similar structure located near human nasal cavities, others are researching it as a possible functional system that may, for example, contribute to synchronization of menstrual cycles in women living in close proximity.



Figure 12.2.2. The flehmen response in this tiger results in the curling of the upper lip and helps airborne pheromone molecules enter the vomeronasal organ. (credit: modification of work by "chadh"/Flickr)

Taste

Detecting a taste (gustation) is fairly similar to detecting an odor (olfaction), given that both taste and smell rely on chemical receptors being stimulated by certain molecules. The primary organ of taste is the taste bud. A **taste bud** is a cluster of gustatory receptors (taste cells) that are located within the bumps on the tongue called **papillae** (singular: papilla) (illustrated in Figure 12.2.3). There are several structurally distinct papillae. Filiform papillae, which are located across the tongue, are tactile,

providing friction that helps the tongue move substances, and contain no taste cells. In contrast, fungiform papillae, which are located mainly on the anterior two-thirds of the tongue, each contain one to eight taste buds and also have receptors for pressure and temperature. The large circumvallate papillae contain up to 100 taste buds and form a V near the posterior margin of the tongue.

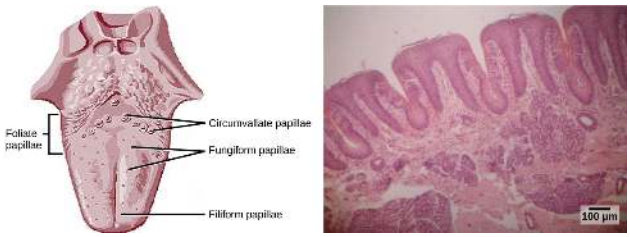


Figure 12.2.3. (a) Foliate, circumvallate, and fungiform papillae are located on different regions of the tongue. (b) Foliate papillae are prominent protrusions on this light micrograph. (credit a: modification of work by NCI; scale-bar data from Matt Russell)

In addition to those two types of chemically and mechanically sensitive papillae are foliate papillae—leaf-like papillae located in parallel folds along the edges and toward the back of the tongue, as seen in the Figure 12.2.3 micrograph. Foliate papillae contain about 1,300 taste buds within their folds. Finally, there are circumvallate papillae, which are wall-like papillae in the shape of an inverted "V" at the back of the tongue. Each of these papillae is surrounded by a groove and contains about 250 taste buds.

Each taste bud's taste cells are replaced every 10 to 14 days. These are elongated cells with hair-like processes called microvilli at the tips that extend into the taste bud pore (illustrate in Figure 12.2.4). Food molecules (**tastants**) are dissolved in saliva, and they bind with and stimulate the receptors on the microvilli. The receptors for tastants are located across the outer portion and front of the tongue, outside of the middle area where the filiform papillae are most prominent.

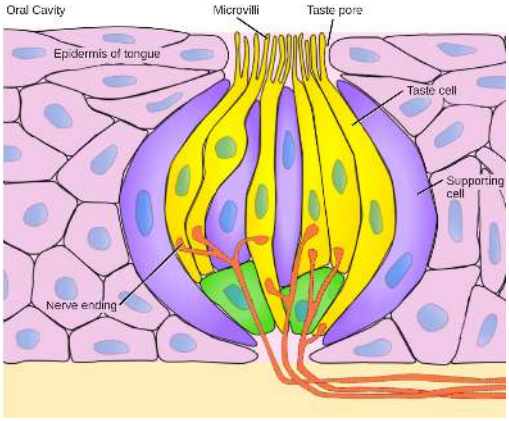


Figure 12.2.4. Pores in the tongue allow tastants to enter taste pores in the tongue. (credit: modification of work by Vincenzo Rizzo)

In humans, there are five primary tastes, and each taste has only one corresponding type of receptor. Thus, like olfaction, each receptor is specific to its stimulus (tastant). Transduction of the five tastes happens through different mechanisms that reflect the molecular composition of the tastant. A salty tastant (containing NaCl) provides the sodium ions (Na^+) that enter the taste neurons and excite them directly. Sour tastants are acids and belong to the thermoreceptor protein family. Binding of an acid or other sour-tasting molecule triggers a change in the ion channel and these increase hydrogen ion (H^+) concentrations in the taste neurons, thus depolarizing them. Sweet, bitter, and umami tastants require a G-protein coupled receptor. These tastants bind to their respective receptors, thereby exciting the specialized neurons associated with them.

Both tasting abilities and sense of smell change with age. In humans, the senses decline dramatically by age 50 and continue to decline. A child may find a food to be too spicy, whereas an elderly person may find the same food to be bland and unappetizing.

Section Summary

There are five primary tastes in humans: sweet, sour, bitter, salty, and umami. Each taste has its own receptor type that responds only to that taste. Tastants enter the body and are dissolved in saliva. Taste cells are located within taste buds, which are found on three of the four types of papillae in the mouth.

Regarding olfaction, there are many thousands of odorants, but humans detect only about 10,000. Like taste receptors, olfactory receptors are each responsive to only one odorant. Odorants dissolve in nasal mucosa, where they excite their corresponding olfactory sensory cells. When these cells detect an odorant, they send their signals to other structures which ultimately are conveyed to the CNS.

Review Questions

Which of the following has the fewest taste receptors?

a. fungiform papillae
b. circumvallate papillae
c. foliate papillae
d. filiform papillae

How many different taste molecules do taste cells each detect?

a. one
b. five
c. ten
d. It depends on the spot on the tongue

Salty foods activate the taste cells by _____.

a. exciting the taste cell directly
b. causing hydrogen ions to enter the cell
c. causing sodium channels to close
d. binding directly to the receptors

Free Response

From the perspective of the recipient of the signal, in what ways do pheromones differ from other odorants?

What might be the effect on an animal of not being able to perceive taste?

Glossary

bipolar neuron
neuron with two processes from the cell body, typically in opposite directions

glomerulus
in the olfactory bulb, one of the two neural clusters that receives signals from one type of olfactory receptor

gustation
sense of taste

odorant
airborne molecule that stimulates an olfactory receptor

olfaction
sense of smell

olfactory bulb
neural structure in the vertebrate brain that receives signals from olfactory receptors

olfactory epithelium
specialized tissue in the nasal cavity where olfactory receptors are located

olfactory receptor
dendrite of a specialized neuron

papilla
one of the small bump-like projections from the tongue

pheromone
substance released by an animal that can affect the physiology or behavior of other animals

tastant
food molecule that stimulates gustatory receptors

taste bud
clusters of taste cells

umami
one of the five basic tastes, which is described as “savory” and which may be largely the taste of L-glutamate

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12.3: Hearing and Vestibular Sensation

Audition, or hearing, is important to humans and to other animals for many different interactions. It enables an organism to detect and receive information about danger, such as an approaching predator, and to participate in communal exchanges like those concerning territories or mating. On the other hand, although it is physically linked to the auditory system, the vestibular system is not involved in hearing. Instead, an animal's vestibular system detects its own movement, both linear and angular acceleration and deceleration, and balance.

Sound

Auditory stimuli are sound waves, which are mechanical, pressure waves that move through a medium, such as air or water. There are no sound waves in a vacuum since there are no air molecules to move in waves. The speed of sound waves differs, based on altitude, temperature, and medium, but at sea level and a temperature of 20º C (68º F), sound waves travel in the air at about 343 meters per second.

As is true for all waves, there are four main characteristics of a sound wave: frequency, wavelength, period, and amplitude. Frequency is the number of waves per unit of time, and in sound is heard as pitch. High-frequency (≥15.000Hz) sounds are higher-pitched (short wavelength) than low-frequency (long wavelengths; ≤100Hz) sounds. Frequency is measured in cycles per second, and for sound, the most commonly used unit is hertz (Hz), or cycles per second. Most humans can perceive sounds with frequencies between 30 and 20,000 Hz. Women are typically better at hearing high frequencies, but everyone's ability to hear high frequencies decreases with age. Dogs detect up to about 40,000 Hz; cats, 60,000 Hz; bats, 100,000 Hz; and dolphins 150,000 Hz, and American shad (*Alosa sapidissima*), a fish, can hear 180,000 Hz. Those frequencies above the human range are called **ultrasound**.

Amplitude, or the dimension of a wave from peak to trough, in sound is heard as volume and is illustrated in Figure 12.3.1. The sound waves of louder sounds have greater amplitude than those of softer sounds. For sound, volume is measured in decibels (dB). The softest sound that a human can hear is the zero point. Humans speak normally at 60 decibels.

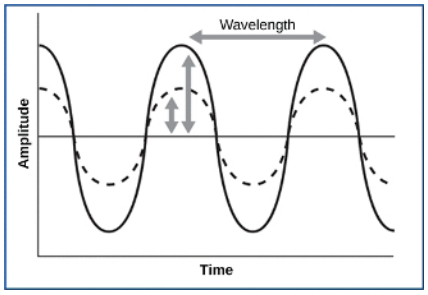


Figure 12.3.1. For sound waves, wavelength corresponds to pitch. Amplitude of the wave corresponds to volume. The sound wave shown with a dashed line is softer in volume than the sound wave shown with a solid line. (credit: NIH)

Reception of Sound

In mammals, sound waves are collected by the external, cartilaginous part of the ear called the **pinna**, then travel through the auditory canal and cause vibration of the thin diaphragm called the **tympanum** or ear drum, the innermost part of the **outer ear** (illustrated in Figure 12.3.2). Interior to the tympanum is the **middle ear**. The middle ear holds three small bones called the **ossicles**, which transfer energy from the moving tympanum to the inner ear. The three ossicles are the **malleus** (also known as the hammer), the **incus** (the anvil), and **stapes** (the stirrup). The aptly named stapes looks very much like a stirrup. The three ossicles are unique to mammals, and each plays a role in hearing. The malleus attaches at three points to the interior surface of the tympanic membrane. The incus attaches the malleus to the stapes. In humans, the stapes is not long enough to reach the tympanum. If we did not have the malleus and the incus, then the vibrations of the tympanum would never reach the inner ear. These bones also function to collect force and amplify sounds. The ear ossicles are homologous to bones in a fish mouth: the bones that support gills in fish are thought to be adapted for use in the vertebrate ear over evolutionary time. Many animals (frogs, reptiles, and birds, for example) use the stapes of the middle ear to transmit vibrations to the middle ear.

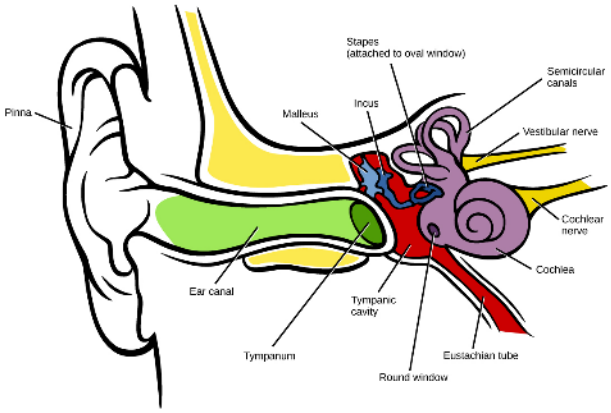


Figure 12.3.2. Sound travels through the outer ear to the middle ear, which is bounded on its exterior by the tympanic membrane. The middle ear contains three bones called ossicles that transfer the sound wave to the oval window, the exterior boundary of the inner ear. The organ of Corti, which is the organ of sound transduction, lies inside the cochlea. (credit: modification of work by Lars Chittka, Axel Brockmann)

Transduction of Sound

Vibrating objects, such as vocal cords, create sound waves or pressure waves in the air. When these pressure waves reach the ear, the ear transduces this mechanical stimulus (pressure wave) into a nerve impulse (electrical signal) that the brain perceives as sound. The pressure waves strike the tympanum, causing it to vibrate. The mechanical energy from the moving tympanum transmits the vibrations to the three bones of the middle ear. The stapes transmits the vibrations to a thin diaphragm called the **oval window**, which is the outermost structure of the **inner ear**. The structures of the inner ear are found in the **labyrinth**, a bony, hollow structure that is the most interior portion of the ear. Here, the energy from the sound wave is transferred from the stapes through the flexible oval window and to the fluid of the cochlea. The vibrations of the oval window create pressure waves in the fluid (perilymph) inside the cochlea. The **cochlea** is a whorled structure, like the shell of a snail, and it contains receptors for transduction of the mechanical wave into an electrical signal (as illustrated in Figure 12.3.3). Inside the cochlea, the **basilar membrane** is a mechanical analyzer that runs the length of the cochlea, curling toward the cochlea's center.

The mechanical properties of the basilar membrane change along its length, such that it is thicker, tauter, and narrower at the outside of the whorl (where the cochlea is largest), and thinner, floppier, and broader toward the apex, or center, of the whorl (where the cochlea is smallest). Different regions of the basilar membrane vibrate according to the frequency of the sound wave conducted through the fluid in the cochlea. For these reasons, the fluid-filled cochlea detects different wave frequencies (pitches) at different regions of the membrane. When the sound waves in the cochlear fluid contact the basilar membrane, it flexes back and forth in a wave-like fashion. Above the basilar membrane is the **tectorial membrane**.

ART CONNECTION

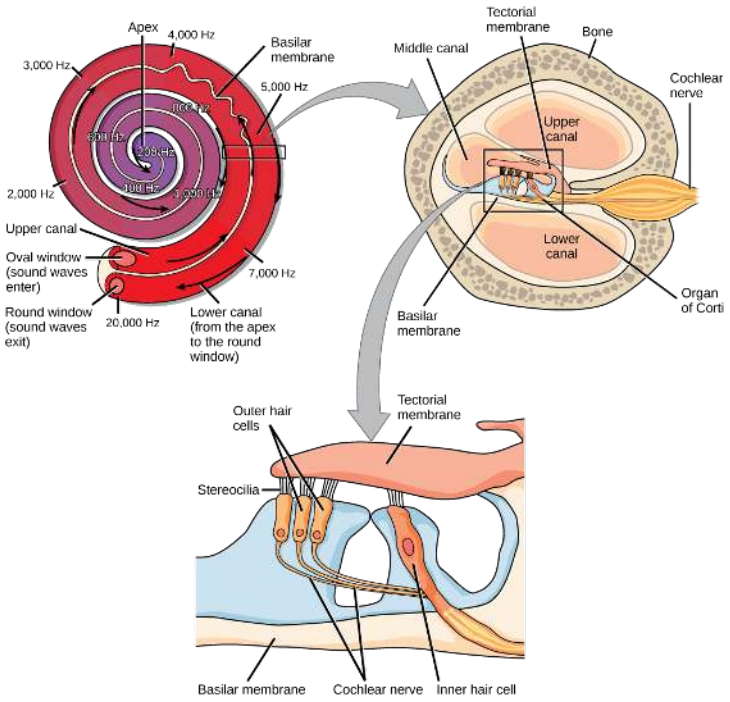


Figure 12.3.3. In the human ear, sound waves cause the stapes to press against the oval window. Vibrations travel up the fluid-filled interior of the cochlea. The basilar membrane that lines the cochlea gets continuously thinner toward the apex of the cochlea. Different thicknesses of membrane vibrate in response to different frequencies of sound. Sound waves then exit through the round window. In the cross section of the cochlea (top right figure), note that in addition to the upper canal and lower canal, the cochlea also has a middle canal. The organ of Corti (bottom image) is the site of sound transduction. Movement of stereocilia on hair cells results in an action potential that travels along the auditory nerve.

The site of transduction is in the **organ of Corti** (spiral organ). It is composed of hair cells held in place above the basilar membrane like flowers projecting up from soil, with their exposed short, hair-like **stereocilia** contacting or embedded in the tectorial membrane above them. The inner hair cells are the primary auditory receptors and exist in a single row, numbering approximately 3,500. The stereocilia from inner hair cells extend into small dimples on the tectorial membrane's lower surface. The outer hair cells are arranged in three or four rows. They number approximately 12,000, and they function to fine tune incoming sound waves. The longer stereocilia that project from the outer hair cells actually attach to the tectorial membrane. All of the stereocilia are mechanoreceptors, and when bent by vibrations they respond by opening a gated ion channel. As a result, the hair cell membrane is depolarized, and a signal is transmitted to the chochlear nerve. Intensity (volume) of sound is determined by how many hair cells at a particular location are stimulated.

The hair cells are arranged on the basilar membrane in an orderly way. The basilar membrane vibrates in different regions, according to the frequency of the sound waves impinging on it. Likewise, the hair cells that lay above it are most sensitive to a specific frequency of sound waves. Hair cells can respond to a small range of similar frequencies, but they require stimulation of greater intensity to fire at frequencies outside of their optimal range. The difference in response frequency between adjacent inner hair cells is about 0.2 percent. Compare that to adjacent piano strings, which are about six percent different. Place theory, which is the model for how biologists think pitch detection works in the human ear, states that high frequency sounds selectively vibrate the basilar membrane of the inner ear near the entrance port (the oval window). Lower frequencies travel farther along the membrane before causing appreciable excitation of the membrane. The basic pitch-determining mechanism is based on the location along the membrane where the hair cells are stimulated. The place theory is the first step toward an understanding of pitch perception. Considering the extreme pitch sensitivity of the human ear, it is thought that there must be some auditory "sharpening" mechanism to enhance the pitch resolution.

When sound waves produce fluid waves inside the cochlea, the basilar membrane flexes, bending the stereocilia that attach to the tectorial membrane. Their bending results in action potentials in the hair cells, and auditory information travels along the neural endings of the bipolar neurons of the hair cells (collectively, the auditory nerve) to the brain. When the hairs bend, they release an excitatory neurotransmitter at a synapse with a sensory neuron, which then conducts action potentials to the central nervous system.

The cochlear branch of the vestibulocochlear cranial nerve sends information on hearing. The auditory system is very refined, and there is some modulation or “sharpening” built in. The brain can send signals back to the cochlea, resulting in a change of length in the outer hair cells, sharpening or dampening the hair cells’ response to certain frequencies.

LINK TO LEARNING

Watch an animation of sound entering the outer ear, moving through the ear structure, stimulating cochlear nerve impulses, and eventually sending signals to the temporal lobe.

Higher Processing

The inner hair cells are most important for conveying auditory information to the brain. About 90 percent of the afferent neurons carry information from inner hair cells, with each hair cell synapsing with 10 or so neurons. Outer hair cells connect to only 10 percent of the afferent neurons, and each afferent neuron innervates many hair cells. The afferent, bipolar neurons that convey auditory information travel from the cochlea to the medulla, through the pons and midbrain in the brainstem, finally reaching the primary auditory cortex in the temporal lobe.

Vestibular Information

The stimuli associated with the vestibular system are linear acceleration (gravity) and angular acceleration and deceleration. Gravity, acceleration, and deceleration are detected by evaluating the inertia on receptive cells in the vestibular system. Gravity is detected through head position. Angular acceleration and deceleration are expressed through turning or tilting of the head.

The vestibular system has some similarities with the auditory system. It utilizes hair cells just like the auditory system, but it excites them in different ways. There are five vestibular receptor organs in the inner ear: the utricle, the saccule, and three semicircular canals. Together, they make up what’s known as the vestibular labyrinth that is shown in Figure 12.3.4. The utricle and saccule respond to acceleration in a straight line, such as gravity. The roughly 30,000 hair cells in the utricle and 16,000 hair cells in the saccule lie below a gelatinous layer, with their stereocilia projecting into the gelatin. Embedded in this gelatin are calcium carbonate crystals—like tiny rocks. When the head is tilted, the crystals continue to be pulled straight down by gravity, but the new angle of the head causes the gelatin to shift, thereby bending the stereocilia. The bending of the stereocilia stimulates the neurons, and they signal to the brain that the head is tilted, allowing the maintenance of balance. It is the vestibular branch of the vestibulocochlear cranial nerve that deals with balance.

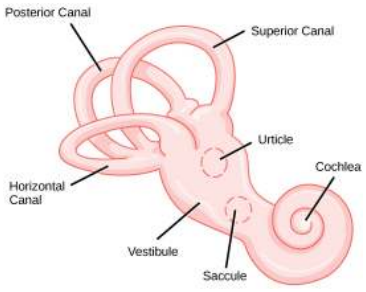


Figure 12.3.4. The structure of the vestibular labyrinth is shown. (credit: modification of work by NIH)

The fluid-filled **semicircular canals** are tubular loops set at oblique angles. They are arranged in three spatial planes. The base of each canal has a swelling that contains a cluster of hair cells. The hairs project into a gelatinous cap called the cupula and monitor angular acceleration and deceleration from rotation. They would be stimulated by driving your car around a corner, turning your head, or falling forward. One canal lies horizontally, while the other two lie at about 45 degree angles to the horizontal axis, as illustrated in Figure 12.3.4. When the brain processes input from all three canals together, it can detect angular acceleration or deceleration in three dimensions. When the head turns, the fluid in the canals shifts, thereby bending stereocilia and sending signals to the brain. Upon cessation accelerating or decelerating—or just moving—the movement of the fluid within the canals slows or stops. For example, imagine holding a glass of water. When moving forward, water may splash backwards onto the hand, and when

motion has stopped, water may splash forward onto the fingers. While in motion, the water settles in the glass and does not splash. Note that the canals are not sensitive to velocity itself, but to changes in velocity, so moving forward at 60mph with your eyes closed would not give the sensation of movement, but suddenly accelerating or braking would stimulate the receptors.

Higher Processing

Hair cells from the utricle, saccule, and semicircular canals also communicate through bipolar neurons to the cochlear nucleus in the medulla. Cochlear neurons send descending projections to the spinal cord and ascending projections to the pons, thalamus, and cerebellum. Connections to the cerebellum are important for coordinated movements. There are also projections to the temporal cortex, which account for feelings of dizziness; projections to autonomic nervous system areas in the brainstem, which account for motion sickness; and projections to the primary somatosensory cortex, which monitors subjective measurements of the external world and self-movement. People with lesions in the vestibular area of the somatosensory cortex see vertical objects in the world as being tilted. Finally, the vestibular signals project to certain optic muscles to coordinate eye and head movements.

LINK TO LEARNING



Click through this interactive tutorial to review the parts of the ear and how they function to process sound.

Section Summary

Audition is important for territory defense, predation, predator defense, and communal exchanges. The vestibular system, which is not auditory, detects linear acceleration and angular acceleration and deceleration. Both the auditory system and vestibular system use hair cells as their receptors.

Auditory stimuli are sound waves. The sound wave energy reaches the outer ear (pinna, canal, tympanum), and vibrations of the tympanum send the energy to the middle ear. The middle ear bones shift and the stapes transfers mechanical energy to the oval window of the fluid-filled inner ear cochlea. Once in the cochlea, the energy causes the basilar membrane to flex, thereby bending the stereocilia on receptor hair cells. This activates the receptors, which send their auditory neural signals to the brain.

The vestibular system has five parts that work together to provide the sense of direction, thus helping to maintain balance. The utricle and saccule measure head orientation: their calcium carbonate crystals shift when the head is tilted, thereby activating hair cells. The semicircular canals work similarly, such that when the head is turned, the fluid in the canals bends stereocilia on hair cells. The vestibular hair cells also send signals to the thalamus and to somatosensory cortex, but also to the cerebellum, the structure above the brainstem that plays a large role in timing and coordination of movement.

Art Connections

Figure Cochlear implants can restore hearing in people who have a nonfunctional cochlea. The implant consists of a microphone that picks up sound. A speech processor selects sounds in the range of human speech, and a transmitter converts these sounds to electrical impulses, which are then sent to the auditory nerve. Which of the following types of hearing loss would not be restored by a cochlear implant?

a. Hearing loss resulting from absence or loss of hair cells in the organ of Corti.
b. Hearing loss resulting from an abnormal auditory nerve.
c. Hearing loss resulting from fracture of the cochlea.
d. Hearing loss resulting from damage to bones of the middle ear.

Review Questions

In sound, pitch is measured in _____, and volume is measured in _____.

a. nanometers (nm); decibels (dB)

b. decibels (dB); nanometers (nm)
c. decibels (dB); hertz (Hz)
d. hertz (Hz); decibels (dB)

Auditory hair cells are indirectly anchored to the _____.

a. basilar membrane
b. oval window
c. tectorial membrane
d. ossicles

Which of the following are found both in the auditory system and the vestibular system?

a. basilar membrane
b. hair cells
c. semicircular canals
d. ossicles

Free Response

How would a rise in altitude likely affect the speed of a sound transmitted through air? Why?

How might being in a place with less gravity than Earth has (such as Earth's moon) affect vestibular sensation, and why?

Glossary

audition
sense of hearing

basilar membrane
stiff structure in the cochlea that indirectly anchors auditory receptors

cochlea
whorled structure that contains receptors for transduction of the mechanical wave into an electrical signal

incus
(also, anvil) second of the three bones of the middle ear

inner ear
innermost part of the ear; consists of the cochlea and the vestibular system

labyrinth
bony, hollow structure that is the most internal part of the ear; contains the sites of transduction of auditory and vestibular information

malleus
(also, hammer) first of the three bones of the middle ear

middle ear
part of the hearing apparatus that functions to transfer energy from the tympanum to the oval window of the inner ear

organ of Corti
in the basilar membrane, the site of the transduction of sound, a mechanical wave, to a neural signal

ossicle
one of the three bones of the middle ear

outer ear
part of the ear that consists of the pinna, ear canal, and tympanum and which conducts sound waves into the middle ear

oval window
thin diaphragm between the middle and inner ears that receives sound waves from contact with the stapes bone of the middle ear

pinna
cartilaginous outer ear

semicircular canal
one of three half-circular, fluid-filled tubes in the vestibular labyrinth that monitors angular acceleration and deceleration

stapes
(also, stirrup) third of the three bones of the middle ear

stereocilia
in the auditory system, hair-like projections from hair cells that help detect sound waves

tectorial membrane
cochlear structure that lies above the hair cells and participates in the transduction of sound at the hair cells

tympanum
(also, tympanic membrane or ear drum) thin diaphragm between the outer and middle ears

ultrasound
sound frequencies above the human detectable ceiling of approximately 20,000 Hz

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12.4: Vision

Vision is the ability to detect light patterns from the outside environment and interpret them into images. Humans are bombarded with sensory information, and the sheer volume of visual information can be problematic. Fortunately, our visual system is able to attend to the most-important stimuli. The importance of vision to humans is further substantiated by the fact that about one-third of the human cerebral cortex is dedicated to analyzing and perceiving visual information.

Light

As with auditory stimuli, light travels in waves. The compression waves that compose sound must travel in a medium—a gas, a liquid, or a solid. In contrast, light is composed of electromagnetic waves and needs no medium; light can travel in a vacuum (Figure 12.4.1). The behavior of light can be discussed in terms of the behavior of waves and also in terms of the behavior of the fundamental unit of light—a packet of electromagnetic radiation called a photon. A glance at the electromagnetic spectrum shows that visible light for humans is just a small slice of the entire spectrum, which includes radiation that we cannot see as light because it is below the frequency of visible red light and above the frequency of visible violet light.

Certain variables are important when discussing perception of light. Wavelength (which varies inversely with frequency) manifests itself as hue. Light at the red end of the visible spectrum has longer wavelengths (and is lower frequency), while light at the violet end has shorter wavelengths (and is higher frequency). The wavelength of light is expressed in nanometers (nm); one nanometer is one billionth of a meter. Humans perceive light that ranges between approximately 380 nm and 740 nm. Some other animals, though, can detect wavelengths outside of the human range. For example, bees see near-ultraviolet light in order to locate nectar guides on flowers, and some non-avian reptiles sense infrared light (heat that prey gives off).

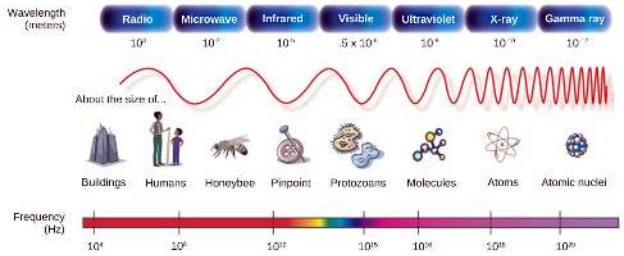


Figure 12.4.1. In the electromagnetic spectrum, visible light lies between 380 nm and 740 nm. (credit: modification of work by NASA)

Wave amplitude is perceived as luminous intensity, or brightness. The standard unit of intensity of light is the **candela**, which is approximately the luminous intensity of a one common candle.

Light waves travel 299,792 km per second in a vacuum, (and somewhat slower in various media such as air and water), and those waves arrive at the eye as long (red), medium (green), and short (blue) waves. What is termed “white light” is light that is perceived as white by the human eye. This effect is produced by light that stimulates equally the color receptors in the human eye. The apparent color of an object is the color (or colors) that the object reflects. Thus a red object reflects the red wavelengths in mixed (white) light and absorbs all other wavelengths of light.

Anatomy of the Eye

The photoreceptive cells of the eye, where transduction of light to nervous impulses occurs, are located in the **retina**(shown in Figure 12.4.2a) on the inner surface of the back of the eye. But light does not impinge on the retina unaltered. It passes through other layers that process it so that it can be interpreted by the retina (Figure 12.4.2b). The **cornea**, the front transparent layer of the eye, and the crystalline **lens**, a transparent convex structure behind the cornea, both refract (bend) light to focus the image on the retina. The **iris**, which is conspicuous as the colored part of the eye, is a circular muscular ring lying between the lens and cornea that regulates the amount of light entering the eye. In conditions of high ambient light, the iris contracts, reducing the size of the pupil at its center. In conditions of low light, the iris relaxes and the pupil enlarges.

ART CONNECTION

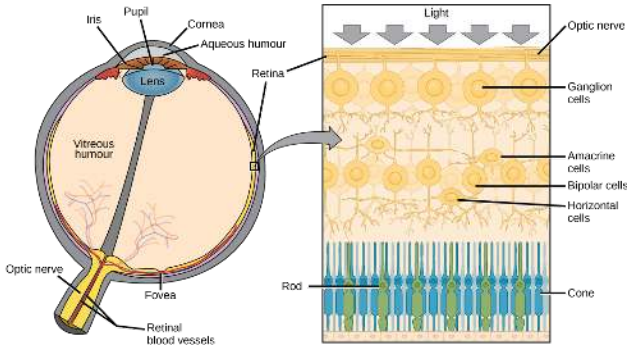


Figure 12.4.2. (a) The human eye is shown in cross section. (b) A blowup shows the layers of the retina.

The main function of the lens is to focus light on the retina and fovea centralis. The lens is dynamic, focusing and re-focusing light as the eye rests on near and far objects in the visual field. The lens is operated by muscles that stretch it flat or allow it to thicken, changing the focal length of light coming through it to focus it sharply on the retina. With age comes the loss of the flexibility of the lens, and a form of farsightedness called **presbyopia** results. Presbyopia occurs because the image focuses behind the retina. Presbyopia is a deficit similar to a different type of farsightedness called **hyperopia** caused by an eyeball that is too short. For both defects, images in the distance are clear but images nearby are blurry. **Myopia** (nearsightedness) occurs when an eyeball is elongated and the image focus falls in front of the retina. In this case, images in the distance are blurry but images nearby are clear.

There are two types of photoreceptors in the retina: **rods** and **cones**, named for their general appearance as illustrated in Figure 12.4.3. Rods are strongly photosensitive and are located in the outer edges of the retina. They detect dim light and are used primarily for peripheral and nighttime vision. Cones are weakly photosensitive and are located near the center of the retina. They respond to bright light, and their primary role is in daytime, color vision.

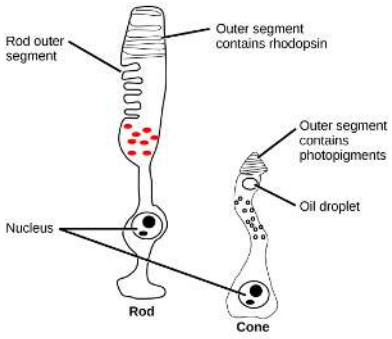


Figure 12.4.3. Rods and cones are photoreceptors in the retina. Rods respond in low light and can detect only shades of gray. Cones respond in intense light and are responsible for color vision. (credit: modification of work by Piotr Sliwa)

The **fovea** is the region in the center back of the eye that is responsible for acute vision. The fovea has a high density of just cones. When you bring your gaze to an object to examine it intently in bright light, the eyes orient so that the object's image falls on the fovea. This is the area of the retina that gives us high clarity of vision. However, when looking at a star in the night sky or other object in dim light, the object can be better viewed by the peripheral vision because it is the rods in higher concentrations in the other regions of the retina, rather than the cones at the center, that operate better in low light. In low-light conditions, the rods allow us to see in shades of gray because cones require bright light to be stimulated and don't respond in low light conditions.

LINK TO LEARNING

Review the anatomical structure of the eye, clicking on each part to practice identification.

Processing Visual Input

Trichromatic Coding

There are three types of cones (with different photopsins), and they differ in the wavelength to which they are most responsive, as shown in Figure 12.4.4. Some cones are maximally responsive to short light waves of 420 nm, so they are called S cones (“S” for “short”); others respond maximally to waves of 530 nm (M cones, for “medium”); a third group responds maximally to light of longer wavelengths, at 560 nm (L, or “long” cones). With only one type of cone, color vision would not be possible, and a two-cone (dichromatic) system has limitations. Primates use a three-cone (trichromatic) system, resulting in full color vision.

The color we perceive is a result of the ratio of activity of our three types of cones. The colors of the visual spectrum, running from long-wavelength light to short, are red (700 nm), orange (600 nm), yellow (565 nm), green (497 nm), blue (470 nm), indigo (450 nm), and violet (425 nm). Humans have very sensitive perception of color and can distinguish about 500 levels of brightness, 200 different hues, and 20 steps of saturation, or about 2 million distinct colors.

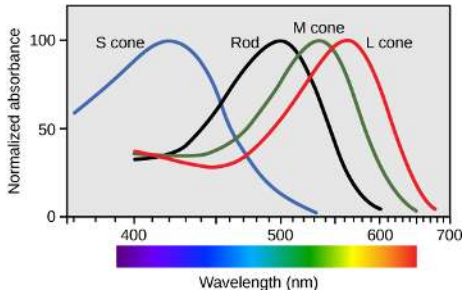


Figure 12.4.4. Human rod cells and the different types of cone cells each have an optimal wavelength. However, there is considerable overlap in the wavelengths of light detected.

Retinal Processing

Visual signals leave the cones and rods, travel to the bipolar cells, and then to ganglion cells. A large degree of processing of visual information occurs in the retina itself, before visual information is sent to the brain.

Higher Processing

The myelinated axons of ganglion cells make up the optic nerves. Within the nerves, different axons carry different qualities of the visual signal. Some axons constitute the magnocellular (big cell) pathway, which carries information about form, movement, depth, and differences in brightness. Other axons constitute the parvocellular (small cell) pathway, which carries information on color and fine detail. Some visual information projects directly back into the brain, while other information crosses to the opposite side of the brain. This crossing of optical pathways produces the distinctive optic chiasma (Greek, for “crossing”) found at the base of the brain and allows us to coordinate information from both eyes.

Once in the brain, visual information is processed in several places, and its routes reflect the complexity and importance of visual information to humans and other animals.

Section Summary

Vision is the only photo responsive sense. Visible light travels in waves and is a very small slice of the electromagnetic radiation spectrum. Light waves differ based on their frequency (wavelength = hue) and amplitude (intensity = brightness).

In the vertebrate retina, there are two types of light receptors (photoreceptors): cones and rods. Cones, which are the source of color vision, exist in three forms—L, M, and S—and they are differentially sensitive to different wavelengths. Cones are located in the retina, along with the dim-light, achromatic receptors (rods). Cones are found in the fovea, the central region of the retina, whereas rods are found everywhere else throughout the retina.

Visual signals travel from the eye over the axons of retinal ganglion cells, which make up the optic nerves. Ganglion cells come in several versions. Some ganglion cell axons carry information on form, movement, depth, and brightness, while other axons carry information on color and fine detail.

Art Connections

Figure Which of the following statements about the human eye is false?

a. Rods detect color, while cones detect only shades of gray.
b. When light enters the retina, it passes the ganglion cells and bipolar cells before reaching photoreceptors at the rear of the eye.
c. The iris adjusts the amount of light coming into the eye.
d. The cornea is a protective layer on the front of the eye.

Review Questions

Why do people over 55 often need reading glasses?

a. Their cornea no longer focuses correctly.
b. Their lens no longer focuses correctly.
c. Their eyeball has elongated with age, causing images to focus in front of their retina.
d. Their retina has thinned with age, making vision more difficult.

Why is it easier to see images at night using peripheral, rather than the central, vision?

a. Cones are denser in the periphery of the retina.
b. Bipolar cells are denser in the periphery of the retina.
c. Rods are denser in the periphery of the retina.
d. The optic nerve exits at the periphery of the retina.

Glossary

candela
(cd) unit of measurement of luminous intensity (brightness)

circadian
describes a time cycle about one day in length

cone
weakly photosensitive, chromatic, cone-shaped neuron in the fovea of the retina that detects bright light and is used in daytime color vision

cornea
transparent layer over the front of the eye that helps focus light waves

fovea
region in the center of the retina with a high density of photoreceptors and which is responsible for acute vision

hyperopia
(also, farsightedness) visual defect in which the image focus falls behind the retina, thereby making images in the distance clear, but close-up images blurry

iris
pigmented, circular muscle at the front of the eye that regulates the amount of light entering the eye

lens
transparent, convex structure behind the cornea that helps focus light waves on the retina

myopia

(also, nearsightedness) visual defect in which the image focus falls in front of the retina, thereby making images in the distance blurry, but close-up images clear

presbyopia

visual defect in which the image focus falls behind the retina, thereby making images in the distance clear, but close-up images blurry; caused by age-based changes in the lens

pupil

small opening though which light enters

retina

layer of photoreceptive and supporting cells on the inner surface of the back of the eye

rhodopsin

main photopigment in vertebrates

rod

strongly photosensitive, achromatic, cylindrical neuron in the outer edges of the retina that detects dim light and is used in peripheral and nighttime vision

superior colliculus

paired structure in the top of the midbrain, which manages eye movements and auditory integration

suprachiasmatic nucleus

cluster of cells in the hypothalamus that plays a role in the circadian cycle

tonic activity

in a neuron, slight continuous activity while at rest

vision

sense of sight

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CHAPTER OVERVIEW

13: IMMUNE SYSTEM

This chapter outlines the layered responses of the human immune system, including both innate and adaptive immune responses. It also describes the structures and functions of the lymphatic system, with a focus on its roles in host defense. In addition, the chapter examines three different types of immune system disorders.

13.1: Case Study- Your Defense System

13.2: Introduction to the Immune System

13.3: Lymphatic System

13.4: Innate Immune System

13.5: Adaptive Immune System

13.6: Disorders of the Immune System

13.7: Human Microbiome

13.8: Case Study Conclusion- Lymphoma and Chapter Summary

Thumbnail: From left to right: erythrocyte, platelet, and lymphocyte. (Public Domain; The National Cancer Institute at Frederick).

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13.1: CASE STUDY- YOUR DEFENSE SYSTEM

CASE STUDY: DEFENDING YOUR DEFENSES

Twenty-six-year-old Wei isn't feeling well. Wei uses he/him/his pronouns. He is more tired than usual, dragging through his workdays despite going to bed earlier and napping on the weekends. He doesn't have much of an appetite and has started losing weight. When he presses on the side of his neck, like the doctor is doing in Figure **13.1.1**, he notices an unusual lump.



Figure **13.1.1**: Palpating lymph nodes

Wei goes to his doctor, who performs a physical exam and determines that the lump is a swollen lymph node. Lymph nodes are part of the immune system, and they will often become enlarged when the body is fighting off an infection. Dr. Bouazizi thinks that the swollen lymph node and fatigue could be signs of a viral or bacterial infection, or indicate a type of cancer called lymphoma. However, an infection is a more likely cause, particularly in a young person like Wei. Dr. Bouazizi prescribes an antibiotic in case Wei has a bacterial infection and advises him to return in a few weeks if his lymph node does not shrink or if he is not feeling better.

Wei returns a few weeks later. He is not feeling better and his lymph node is still enlarged. Dr. Bouazizi is concerned and orders a biopsy of the enlarged lymph node. A lymph node biopsy for suspected lymphoma often involves the surgical removal of all or part of a lymph node, to determine whether the tissue contains cancerous cells.

The initial results of the biopsy indicate that Wei does have lymphoma. Although lymphoma is more common in older people, young adults and even children can get this disease. There are many types of lymphoma, with the two main types being Hodgkin and non-Hodgkin lymphoma. Non-Hodgkin lymphoma (NHL), in turn, has many subtypes depending on factors such as which cell types are affected. For instance, some subtypes of NHL affect immune system cells called B cells, while others affect different immune system cells called T cells.

Dr. Bouazizi explains to Wei that it is important to determine which type of lymphoma he has, in order to choose the best course of treatment. Wei's biopsied tissue will be further examined and tested to see which cell types are affected and which specific cell-surface proteins, called antigens, are present. This should help in identifying his specific type of lymphoma.

As you read this chapter, you will learn about the functions of the immune system, and the specific roles that its cells and organs—such as B and T cells and lymph nodes— play in defending the body. At the end of this chapter, you will learn what type of lymphoma Wei has and what some of his treatment options are, including treatments that make use of the biochemistry of the immune system to fight cancer with the immune system itself.

CHAPTER OVERVIEW: IMMUNE SYSTEM

In this chapter, you will learn about the immune system—the system that defends the body against infections and other causes of disease such as cancerous cells. Specifically, you will learn about:

- How the immune system identifies normal cells of the body as "self" and pathogens and damaged cells as "non-self."
- The two major subsystems of the general immune system: the innate immune system, which provides a quick but non-specific response; and the adaptive immune system, which is slower but provides a specific response that often results in long-lasting immunity.
- The specialized immune system that protects the brain and spinal cord called the neuroimmune system.
- The organs, cells, and responses of the innate immune system, which include physical barriers such as skin and mucus, chemical and biological barriers, inflammation, activation of the complement system of molecules, and non-specific cellular responses such as phagocytosis.
- The lymphatic system—which includes white blood cells called lymphocytes; lymphatic vessels that transport a fluid called lymph; and organs such as the spleen, tonsils, and lymph nodes —and its important role in the adaptive immune system.
- Specific cells of the immune system and their functions, including B cells, T cells, plasma cells, and natural killer cells.
- How the adaptive immune system can generate specific and often long-lasting immunity against pathogens through the production of antibodies.
- How vaccines work to generate immunity.
- How cells in the immune system detect and kill cancerous cells.
- Some strategies that pathogens employ to evade the immune system.
- Disorders of the immune system, including allergies, autoimmune diseases (such as diabetes and multiple sclerosis), and immunodeficiency resulting from conditions such as HIV infection.

As you read the chapter, think about the following questions:

1. What are the functions of lymph nodes?
2. What are B and T cells and how do they relate to lymph nodes?
3. What are cell-surface antigens? How do they relate to the immune system and to cancer?

ATTRIBUTIONS

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13.2: INTRODUCTION TO THE IMMUNE SYSTEM

WORM ATTACK!

Does this organism look like a space alien? A scary creature from a nightmare? In fact, it's a 1-cm long worm in the genus *Schistosoma*. It may invade and take up residence in the human body, causing a very serious illness known as schistosomiasis. The worm gains access to the human body while it is in a microscopic life stage. It enters through a hair follicle when the skin comes into contact with contaminated water. The worm then grows and matures inside the human organism, causing disease.



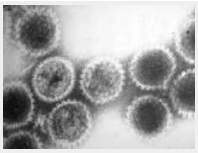
Figure **13.2.1**: Schistosome Parasite

HOST VS. PATHOGEN

The *Schistosoma* worm has a parasitic relationship with humans. In this type of relationship, one organism, called the parasite, lives on or in another organism, called the host. The parasite always benefits from the relationship and the host is always harmed. The human host of the *Schistosoma* worm is clearly harmed by the parasite when it invades the host's tissues. The urinary tract or intestines may be infected, and signs and symptoms may include abdominal pain, diarrhea, bloody stool, or blood in the urine. Those who have been infected a long time may experience liver damage, kidney failure, infertility, or bladder cancer. In children, *Schistosoma* infection may cause poor growth and difficulty learning. Table **13.2.1** lists some of the microscopic pathogens, their images, description, and the diseases that they cause.

Like the Schistosoma worm, many other organisms can make us sick if they manage to enter our body. Any such agent that can cause disease is called a **pathogen**. Most pathogens are microorganisms, although some, such as the Schistosoma worm, are much larger. In addition to worms, common types of pathogens of human hosts include bacteria, viruses, fungi, and single-celled organisms called protists. You can see examples of each of these types of pathogens in Table **13.2.1**. Fortunately for us, our immune system is able to keep most potential pathogens out of the body or to quickly destroy them if they do manage to get in. When you read this chapter, you'll learn how your immune system usually keeps you safe from harm — including from scary creatures like the Schistosoma worm!

Table **13.2.1**: Types of Pathogens

Type of Pathogen	Example and their Image	Description	Human Disease caused by pathogens of that type
Bacteria	 such as *Escherichia coli*	Single-celled organisms without a nucleus	Strep throat, staph infections, tuberculosis, food poisoning, tetanus, pneumonia, syphilis
Viruses	 such as Herpes simplex	Particles that reproduce by taking over living cells.	Common cold, flu, genital herpes, cold sores, measles, AIDS, genital warts, chickenpox, smallpox
Fungi	 such as *Trichophyton rubrum*	Organisms with a nucleus that grow as single cells or tread-like filaments	Ringworm, athlete's foot, tineas, candidiasis, histoplasmosis
Protozoa	 Such as *Giarida lamblia*	A single-celled organism with a nucleus	Malaria, Traveler's diarrhea, giardiasis, trypanosomiasis (sleeping sickness)

WHAT IS THE IMMUNE SYSTEM?

The **immune system** is a host defense system. It comprises many biological structures —ranging from individual white blood cells to entire organs — as well as many complex biological processes. The function of the immune system is to protect the host from pathogens and other causes of disease such as tumor cells. To function properly, the immune system must be able to detect a wide variety of pathogens. It also must be able to distinguish the cells of pathogens from the host's own cells and also to distinguish cancerous or damaged host cells from healthy cells. In humans and most other vertebrates, the immune system consists of layered defenses that have increased specificity for particular pathogens or tumor cells. The layered defenses of the human immune system are usually classified into two subsystems called the innate immune system and the adaptive immune system.

INNATE IMMUNE SYSTEM

Any discussion of the innate immune response usually begins with the physical barriers that prevent pathogens from entering the body, destroy them after they enter, or flush them out before they can establish themselves in the hospitable environment of the body's soft tissues. Barrier defenses are part of the body's most basic defense mechanisms. The barrier defenses are not a response to infections, but they are continuously working to protect against a broad range of pathogens.

The **phagocytes** are the body's fast acting first line of immunological defense against organisms that have breached barrier defenses and have entered the vulnerable tissues of the body. For example, certain leukocytes (white blood cells) engulf and destroy pathogens they encounter in the process called phagocytosis. The body's response again a pathogen's breach is also called **Inflammation**. Phagocytosis and Inflammation will be discussed in detail in concept *Innate Immune System*.

ADAPTIVE IMMUNE SYSTEM

The adaptive immune system is activated if pathogens successfully enter the body and manage to evade the general defenses of the innate immune system. An adaptive response is specific to the particular type of pathogen that has invaded the body or to cancerous cells. It takes longer to launch a specific attack, but once it is underway, its specificity makes it very effective. An adaptive response also usually leads to immunity. This is a state of resistance to a specific pathogen due to the ability of the adaptive immune system to "remember" the pathogen and immediately mount a strong attack tailored to that particular pathogen if it invades again in the future.

SELF VS. NON-SELF

Both innate and adaptive immune responses depend on the ability of the immune system to distinguish between self and non-self molecules. Self molecules are those components of an organism's body that can be distinguished from foreign substances by the immune system. Virtually all body cells have surface proteins that are part of a complex called the **major histocompatibility complex (MHC)**. These proteins are one way the immune system recognizes body cells as self. Non-self proteins, in contrast, are recognized as foreign because they are different from self-proteins.

ANTIGENS AND ANTIBODIES

Many non-self molecules comprise a class of compounds called antigens. Antigens, which are usually proteins, bind to specific receptors on immune system cells and elicit an adaptive immune response. Some adaptive immune system cells (B cells) respond to foreign antigens by producing antibodies. An antibody is a molecule that precisely matches and binds to a specific antigen. This may target the antigen (and the pathogen displaying it) for destruction by other immune cells.

Antigens on the surface of pathogens are how the adaptive immune system recognizes specific pathogens. Antigen specificity allows for the generation of responses tailored to the specific pathogen. It is also how the adaptive immune system ”remembers” the same pathogen in the future.

IMMUNE SURVEILLANCE

Another important role of the immune system is to identify and eliminate tumor cells. This is called **immune surveillance.** The transformed cells of tumors express antigens that are not found on normal body cells. The main response of the immune system to tumor cells is to destroy them. This is carried out primarily by aptly named killer T cells of the adaptive immune system.

LYMPHATIC SYSTEM

The lymphatic system is a human organ system that is a vital part of the adaptive immune system. It is also part of the cardiovascular system and plays a major role in the digestive system (see the concept Lymphatic System).

FEATURE: HUMAN BIOLOGY IN THE NEWS

“They'll have to rewrite the textbooks!”

That sort of response to scientific discovery is sure to attract media attention, and it did. It's what Kevin Lee, a neuroscientist at the University of Virginia, said in 2016 when his colleagues told him they had discovered human anatomical structures that had never before been detected. The structures were tiny lymphatic vessels in the meningeal layers surrounding the brain.

How these lymphatic vessels could have gone unnoticed when all human body systems have been studied so completely is amazing in its own right. The suggested implications of the discovery are equally amazing:

- The presence of these lymphatic vessels means that the brain is directly connected to the peripheral immune system, presumably allowing a close association between the human brain and human pathogens. This suggests an entirely new avenue by which humans and their pathogens may have influenced each other's evolution. The researchers speculate that our pathogens may have even influenced the evolution of our social behaviors.
- The researchers think there will also be many medical applications of their discovery. For example, the newly discovered lymphatic vessels may play a major role in neurological diseases that have an immune component, such as multiple sclerosis. The discovery might also affect how conditions such as autism spectrum disorders and schizophrenia are treated.

REVIEW

1. What is a pathogen?
2. State the purpose of the immune system.
3. Compare and contrast the innate and adaptive immune systems.
4. Explain how the immune system distinguishes self molecules from non-self molecules.
5. What are antigens?
6. Define tumor surveillance.
7. Briefly describe the lymphatic system and its role in immune function.
8. Identify the neuroimmune system.
9. Which of the following is NOT a function of the immune system?

   A. Protecting the body against fungi

B. Protecting the body against bacteria
C. Protecting the body against cancerous cells
D. None of the above

10. What does it mean that the immune system is not just composed of organs?
11. What are the general relationships between the terms *lymphocytes*, *leukocytes*, and *white blood cells*?
12. *True or False.* Phagocytosis occurs in the innate immune system.
13. *True or False.* Major histocompatibility complex proteins are antibodies.
14. *True or False.* Only the adaptive immune response requires the ability to distinguish between self and non-self.
15. Why is the immune system considered to be "layered?"

EXPLORE MORE

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ATTRIBUTIONS

1. Schistosome Parasite by Bruce Wetzel and Harry Schaefer, public domain via NCI NIH
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13.3: LYMPHATIC SYSTEM

TONSILLITIS

The white patches on either side of the throat in this picture are signs of tonsillitis. The tonsils are small structures in the throat that are very common sites of infection. The white spots on the tonsils pictured here are evidence of infection. The patches consist of large amounts of dead bacteria, cellular debris, and white blood cells; in a word, pus. Children with recurrent tonsillitis may have their tonsils removed surgically to eliminate this type of infection. The tonsils are organs of the lymphatic system.



Figure **13.3.1**:Tonsilitis

WHAT IS THE LYMPHATIC SYSTEM?

The **lymphatic system** is a collection of organs involved in the production, maturation, and harboring of white blood cells called lymphocytes. It also includes a network of vessels that transport or filter the fluid known as **lymph** in which lymphocytes circulate. Figure **13.3.2**shows major lymphatic vessels and other structures that make up the lymphatic system. Besides the tonsils, organs of the lymphatic system include the thymus, the spleen, and hundreds of lymph nodes that are distributed along the lymphatic vessels.

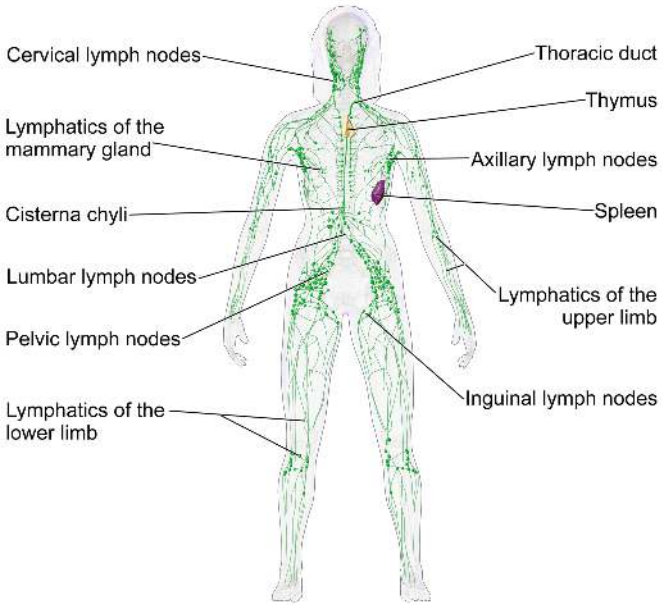


Figure **13.3.2**: The lymphatic system includes the thymus, spleen, lymph vessels, and nodes.

The lymphatic vessels form a transportation network similar in many respects to the blood vessels of the cardiovascular system. However, unlike the cardiovascular system, the lymphatic system is not a closed system. Instead, lymphatic vessels carry lymph in a single direction, always toward the upper chest, where the lymph empties from lymphatic vessels into blood vessels.

CARDIOVASCULAR FUNCTION OF THE LYMPHATIC SYSTEM

The return of lymph to the bloodstream is one of the major functions of the lymphatic system. When blood travels through capillaries of the cardiovascular system, it is under pressure, which forces some of the components of blood (such as water, oxygen, and nutrients) through the walls of the capillaries and into the tissue spaces between cells, forming tissue fluid, also called interstitial fluid (Figure **13.3.3**). Interstitial fluid bathes and nourishes cells and also absorbs their waste products. Much of the water from the interstitial fluid is reabsorbed into the capillary blood by osmosis. Most of the remaining fluid is absorbed by tiny lymphatic vessels called lymph capillaries. Once interstitial fluid enters the lymphatic vessels, it is called lymph. Lymph is very similar in composition to blood plasma. Besides water, lymph may contain proteins, waste products, cellular debris, and pathogens. It also contains numerous white blood cells, especially the subset of white blood cells known as lymphocytes. In fact, lymphocytes are the main cellular components of lymph.

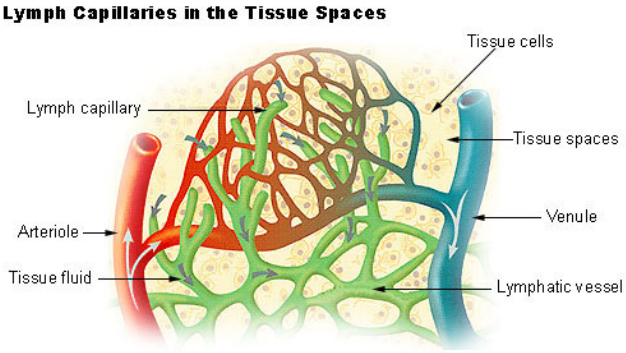


Figure **13.3.3**: Fluid and other substances in the blood are forced by blood pressure through the walls of capillaries and into the surrounding tissue spaces. Some of the tissue fluid is absorbed by tiny lymphatic vessels, forming lymph. The arrows show the direction of blood and lymph through the blood and lymphatic vessels.

The lymph that enters lymph capillaries in tissues is transported through the lymphatic vessel network to two large lymphatic ducts in the upper chest. From there, the lymph flows into two major veins (called subclavian veins) of the cardiovascular system. Unlike blood, lymph is not pumped through its network of vessels. Instead, lymph moves through lymphatic vessels via a combination of contractions of the vessels themselves and forces applied to the vessels externally by skeletal muscles. Lymphatic vessels also contain numerous valves that keep lymph flowing in just one direction, thereby preventing backflow.

DIGESTIVE FUNCTION OF THE LYMPHATIC SYSTEM

Lymphatic vessels called lacteals (Figure **13.3.4**) are present in the lining of the gastrointestinal tract, mainly in the small intestine. Each tiny villus in the lining of the small intestine has an internal bed of capillaries and lacteals. The capillaries absorb most nutrients from the digestion of food into the blood. The lacteals absorb mainly fatty acids from lipid digestion into the lymph, forming a fatty-acid-enriched fluid called chyle. Vessels of the lymphatic network then transport chyle from the small intestine to the main lymphatic ducts in the chest from which it drains into the blood circulation. The nutrients in chyle then circulate in the blood to the liver, where they are processed along with the other nutrients that reach the liver directly via the bloodstream.

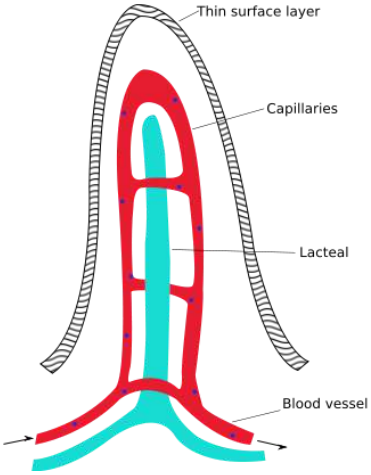


Figure **13.3.4**: Vessels called lacteals in the villi lining the small intestine are the main way that fatty acids from digestion are absorbed from the gastrointestinal tract. These nutrients eventually reach the blood circulation after traveling through the network of lymphatic vessels.

IMMUNE FUNCTION OF THE LYMPHATIC SYSTEM

The primary function of the lymphatic system is host defense as part of the immune system. This function of the lymphatic system is centered on the production, maturation, and circulation of lymphocytes. **Lymphocytes** are leukocytes that are involved in the adaptive immune system. They are responsible for the recognition of, and tailored defense against, specific pathogens or tumor cells. Lymphocytes may also create a lasting memory of pathogens so they can be attacked quickly and strongly if they ever invade the body again. In this way, lymphocytes bring about long-lasting immunity to specific pathogens.

There are two major types of lymphocytes, called B cells and T cells, which are illustrated in Figure **13.3.5**. Both B cells and T cells are involved in the adaptive immune response, but they play different roles. You can learn more about their immune functions by reading the concept Adaptive Immune System.

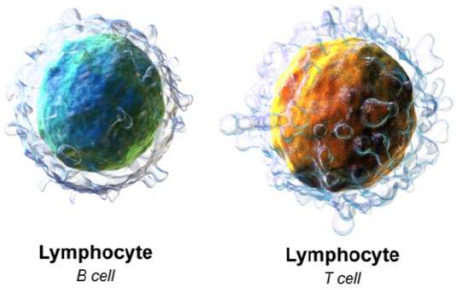


Figure **13.3.5**: Notice the large nucleus in the center of these relatively round cells.

PRODUCTION AND MATURATION OF LYMPHOCYTES

Like all other types of blood cells, including red blood cells as well as leukocytes, both B cells and T cells are produced from stem cells in the red marrow inside bones. After lymphocytes first form, they must go through a complicated maturation process before they are ready to search for pathogens. In this maturation process, they "learn" to distinguish self from non-self. Only those lymphocytes that successfully complete this maturation process go on to actually fight infections by pathogens.

B cells mature in the bone marrow, which is why they are called B cells. After they mature and leave the bone marrow, they travel first to the circulatory system and then enter the lymphatic system to search for pathogens. T cells, on the other hand, mature in the thymus, which is why they are called T cells. The **thymus** is illustrated in Figure **13.3.6**. It is a small lymphatic organ in the chest that consists of an outer cortex and inner medulla, all surrounded by a fibrous capsule. After maturing in the thymus, T cells enter the rest of the lymphatic system to join B cells in the hunt for pathogens. The bone marrow and thymus are called primary lymphoid organs because of their role in the production and/or maturation of lymphocytes.

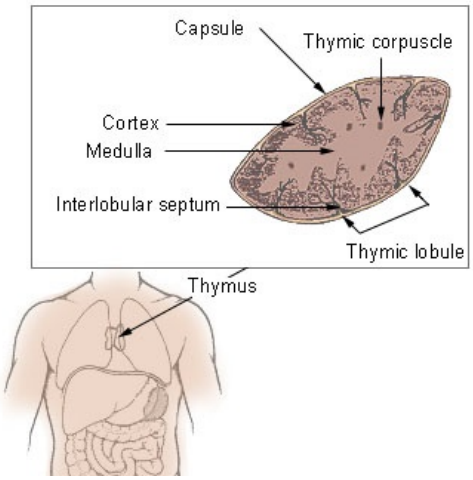


Figure **13.3.6**: The thymus (found in the chest) is an important organ of the lymphatic system because it is the location of T cell maturation.

LYMPHOCYTES IN SECONDARY LYMPHOID ORGANS

The tonsils, spleen, and lymph nodes are referred to as secondary lymphoid organs. These organs do not produce or mature lymphocytes. Instead, they filter lymph and store lymphocytes. It is in these secondary lymphoid organs that pathogens (or their antigens) activate lymphocytes and initiate adaptive immune responses. Activation leads to the cloning of pathogen-specific lymphocytes, which then circulate between the lymphatic system and the blood, searching for and destroying their specific pathogens by producing antibodies against them.

TONSILS

There are actually four pairs of human **tonsils.** Three of the four are shown in Figure **13.3.7**. The fourth pair, called tubal tonsils, is located at the back of the nasopharynx. The palatine tonsils are the tonsils that are visible on either side of the throat. All four pairs of tonsils encircle a part of the anatomy where the respiratory and gastrointestinal tracts intersect and where pathogens have ready access to the body. This ring of tonsils is called **Waldeyer's ring**.

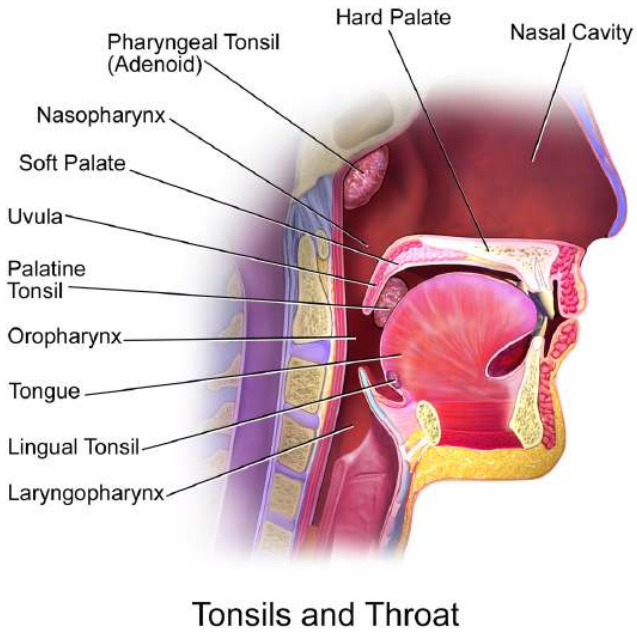


Figure **13.3.7**: Three of four pairs of human tonsils are shown in this figure. Lingual tonsils are below the tongue. Palatine tonsils are at the back of the mouth. Pharyngeal (adenoid) tonsils are in the back of the nasal cavity.

SPLEEN

The spleen (Figure **13.3.8**) is the largest of the secondary lymphoid organs and is centrally located in the body. Besides harboring lymphocytes and filtering lymph, the spleen also filters blood. Most dead or aged red blood cells are removed from the blood in the red pulp of the spleen. Lymph is filtered in the white pulp of the spleen. In the fetus, the spleen has the additional function of producing red blood cells. This function is taken over by bone marrow after birth.

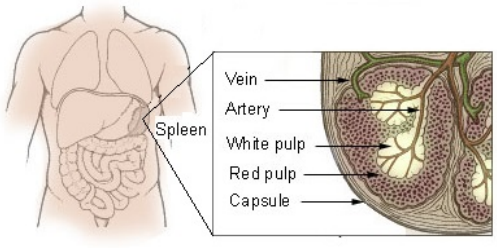


Figure **13.3.8**: The spleen (found behind the stomach) is a secondary lymphoid organ where pathogens are likely to encounter lymphocytes and trigger an adaptive immune response.

LYMPH NODES

Each **lymph node** is a small but organized collection of lymphoid tissue (see green circular structures in Figure **13.3.1**) that contains many lymphocytes. Lymph nodes are located at intervals along the lymphatic vessels, and lymph passes through them on their way back to the blood. There are at least 500 lymph nodes in the human body. Many of them are clustered at the base of the limbs and in the neck. Figure **13.3.9** shows the major lymph node concentrations. The figure includes the spleen and the region named Waldeyer's ring, consisting of the tonsils.

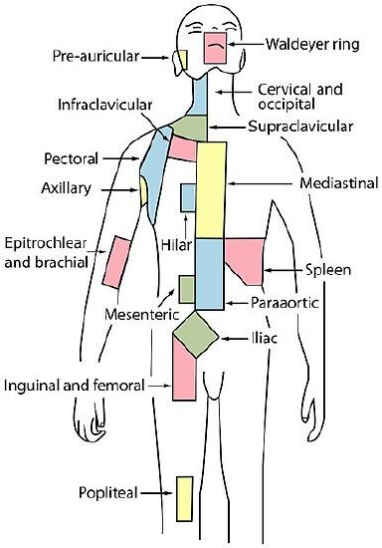


Figure **13.3.9**: In this diagram, lymph node regions are just shown for the left side of the body. The same regions are also found on the right side of the body.

FEATURE: MYTH VS. REALITY

Lymph nodes near the surface of the body are obvious signs of immune system activity when they become enlarged and sometimes tender to the touch. Because it is easy to see and feel swollen lymph nodes, an individual can monitor his or her own health. It is important to be able to know the myths and realities of swollen lymph nodes.

Myth: You should see a doctor immediately whenever you have swollen lymph nodes.

Reality: Lymph nodes are constantly filtering lymph so it is expected that they will change in size with varying amounts of debris or pathogens that may be present. A minor, unnoticed infection may cause swollen lymph nodes that may last for a few weeks. Generally, lymph nodes that return to their normal size within three weeks are not a cause for concern.

Myth: Swollen lymph nodes mean you have a bacterial infection.

Reality: Although infection is the most common cause of swollen lymph nodes, not all infections are caused by bacteria. For example, mononucleosis commonly causes swollen lymph nodes, and it is caused by viruses. There are also other causes of swollen lymph nodes besides infections, such as cancer and certain medications.

Myth: A swollen lymph node means you have cancer.

Reality: Cancer is far less likely to be the cause of a swollen lymph node than is an infection.

Myth: Cancer in a lymph node always originates somewhere else. There is no cancer of the lymph nodes.

Reality: Cancers do commonly spread from their site of origin to nearby lymph nodes and then to other organs, but cancer may also originate in the lymph nodes. This type of cancer is called lymphoma.

REVIEW

1. What is the lymphatic system?
2. Describe the composition of lymph.
3. Outline the cardiovascular function of the lymphatic system.
4. Describe the role of the lymphatic system in the absorption of nutrients from the digestive system.
5. Summarize the function of the lymphatic system in host defense.
6. Name primary lymphatic organs and their functions.
7. What are the secondary lymphatic organs? State their functions in the adaptive immune system.
8. How is interstitial fluid related to lymph?
9. B and T cells are types of:
   A. Leukocytes
   B. Lymphocytes
   C. White blood cells
   D. All of the above
10. For each of the following statements, indicate whether it applies to B cells, T cells, or both.
    A. These cells are born in the red bone marrow.
    B. These cells are part of the adaptive immune system.
    C. These cells mature in the bone marrow.
11. Explain the difference between lymphocyte maturation and lymphocyte activation.
12. *True or False*. The spleen produces lymphocytes.
13. *True or False*. Tonsils are glands that produce lymph.

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13.4: INNATE IMMUNE SYSTEM

PAPER CUT

It's just a paper cut, but the break in your skin could provide an easy way for pathogens to enter your body. If bacteria were to enter through the cut and infect the wound, your innate immune system would quickly respond with a dizzying array of general defenses.



Figure **13.4.1**: Papercut

The **innate immune system** is a subset of the human immune system that produces rapid but non-specific responses to pathogens. Innate responses are generic rather than tailored to a particular pathogen. Every pathogen that is encountered is responded to in the same general ways by the innate system. Although the innate immune system provides immediate and rapid defenses against pathogens, it does not confer long-lasting immunity to them. In most organisms, the innate immune system is the dominant system of host defense. Other than most vertebrates including humans, the innate immune system is the only system of host defense.

In humans, the innate immune system includes surface barriers, inflammation, the complement system, and a variety of cellular responses. Surface barriers of various types generally keep most pathogens out of the body. If these barriers fail, then other innate defenses are triggered. The triggering event is usually the identification of pathogens by pattern-recognition receptors on cells of the innate immune system. These receptors recognize molecules that are broadly shared by pathogens but distinguishable from host molecules. Alternatively, the other innate defenses may be triggered when damaged, injured, or stressed cells send out alarm signals, many of which are recognized by the same receptors as those that recognize pathogens.

BARRIERS TO PATHOGENS

The body's first line of defense consists of three different types of barriers that keep most pathogens out of body tissues. The types of barriers are mechanical, chemical, and biological barriers.

MECHANICAL BARRIERS

Mechanical barriers are the first line of defense against pathogens, and they physically block pathogens from entering the body. The skin is the most important mechanical barrier. In fact, it is the single most important defense the body has. The outer layer of skin, the epidermis, is tough and very difficult for pathogens to penetrate. It consists of dead cells that are constantly being shed from the body surface. This helps remove bacteria and other infectious agents that have adhered to the skin. The epidermis also lacks blood vessels and is usually lacking moisture, so it does not provide a suitable environment for most pathogens. Hair, which is an accessory organ of the skin, also helps to keep out pathogens. Hairs inside the nose may trap larger pathogens and other particles in the air before they can enter the airways of the respiratory system.

Mucous membranes provide a mechanical barrier to pathogens and other particles at body openings. These membranes also line the respiratory, gastrointestinal, urinary, and reproductive tracts. Mucous membranes secrete mucus, which is a slimy and somewhat sticky substance that traps pathogens. Many mucous membranes also have hair-like cilia that sweep mucus and trapped pathogens toward body openings where they can be removed from the body. When you sneeze or cough, mucus, and pathogens are mechanically ejected from the nose and throat, as you can see in the photo below. Other mechanical defenses include tears, which wash pathogens from the eyes, and urine, which flushes pathogens out of the urinary tract.



Figure **13.4.2**: A sneeze can expel many pathogens from the respiratory tract. That's why you should always cover your mouth and nose and when you sneeze.

CHEMICAL BARRIERS

Chemical barriers also protect against infection by pathogens. They destroy pathogens on the outer body surface, at body openings, and on inner body linings. Sweat, mucus, tears, saliva, and breastmilk all contain antimicrobial substances, such as the enzyme lysozyme, that kill pathogens, especially bacteria. Sebaceous glands in the dermis of the skin secrete acids that form a very fine, slightly acidic film on the surface of the skin that acts as a barrier to bacteria, viruses, and other potential contaminants that might penetrate the skin. Urine and vaginal secretions are also too acidic for many pathogens to endure. Semen contains zinc, which most pathogens cannot tolerate, as well as defensins, which are antimicrobial proteins that act mainly by disrupting bacterial cell membranes. In the stomach, stomach acid and digestive enzymes called proteases, which break down proteins, kill most pathogens that enter the gastrointestinal tract in food or water.

BIOLOGICAL BARRIERS

Biological barriers are living organisms that help protect the body from pathogens. Trillions of harmless bacteria normally live on the human skin and in the urinary, reproductive, and gastrointestinal tracts. These bacteria use up food and surface space that help prevent pathogenic bacteria from colonizing the body. Some of these harmless bacteria also secrete substances that change the conditions

of their environment, making it less hospitable to potentially harmful bacteria. For example, they may release toxins or change the pH. All of these effects of harmless bacteria reduce the chances that pathogenic microorganisms will be able to reach sufficient numbers to cause illness.

INFLAMMATION

If pathogens manage to breach the barriers protecting the body, then one of the first active responses of the innate immune system kicks in. This response is **inflammation.** The main function of inflammation is to establish a physical barrier against the spread of infection. It also eliminates the initial cause of cell injury, clears out dead cells and tissues damaged from the original insult and the inflammatory process, and initiates tissue repair. Inflammation is often a response to infection by pathogens, but there are other possible causes, including burns, frostbite, and exposure to toxins.

The signs and symptoms of inflammation include redness, swelling, warmth, pain, and frequently some loss of function. These symptoms are caused by increased blood flow into infected tissue and a number of other processes, illustrated in Figure **13.4.3** and described below in the text.

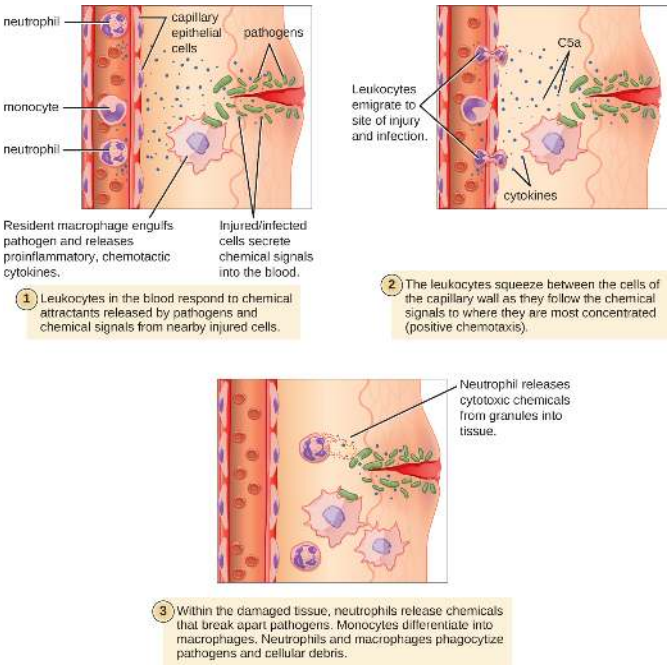


Figure **13.4.3**: This drawing shows what happens during the inflammatory response.

Inflammation is triggered by chemicals such as **cytokines** and **histamines,** which are released by injured or infected cells or by immune system cells such as macrophages (described in Figure **13.4.5**) that are already present in tissues. These chemicals cause capillaries to dilate and become leaky, increasing blood flow to the infected area and allowing blood to enter the tissues. Pathogen-destroying leukocytes, complement proteins, and tissue-repairing proteins migrate into tissue spaces from the bloodstream to attack pathogens and repair their damage. Cytokines also promote chemotaxis, which is migration to the site of infection by leukocytes that destroy pathogens. Some cytokines have anti-viral, antifungal, and antibacterial effects, such as shutting down protein synthesis in host cells, which viruses need in order to survive and replicate.

COMPLEMENT SYSTEM

The **complement system** is a complex biochemical mechanism named for its ability to "complement" the killing of pathogens directly by creating holes in the body of the pathogen and by assisting antibodies. Antibodies are produced as part of an adaptive immune response. The complement system consists of more than two dozen proteins that are normally found in the blood and synthesized in the liver. The proteins usually circulate as non-functional precursor molecules until activated.

CELLULAR RESPONSES

Cellular responses of the innate immune system involve a variety of different types of leukocytes. Many of these leukocytes circulate in the blood and act like independent, single-celled organisms, searching out and destroying pathogens in the human host. These and other immune cells of the innate system identify pathogens or debris and then help to eliminate them in some way. One way is phagocytosis.

PHAGOCYTOSIS

Phagocytosis is an important feature of innate immunity that is performed by cells classified as phagocytes. In the process of phagocytosis, phagocytes engulf and digest pathogens or other harmful particles. Phagocytes generally patrol the body searching for pathogens, but they can also be called to specific locations by the release of cytokines when inflammation occurs. Some phagocytes reside permanently in certain tissues.

As shown in Figure **13.4.4**, when a pathogen such as a bacterium is encountered by a phagocyte, the phagocyte extends a portion of its plasma membrane, wrapping the membrane around the pathogen until it is enveloped. Once inside the phagocyte, the pathogen becomes enclosed within an intracellular vesicle called a phagosome. The phagosome then fuses with another vesicle called a lysosome, forming a phagolysosome. Digestive enzymes and acids from the lysosome kill and digest the pathogen in the phagolysosome. The final step of phagocytosis is the excretion of soluble debris from the destroyed pathogen through exocytosis.

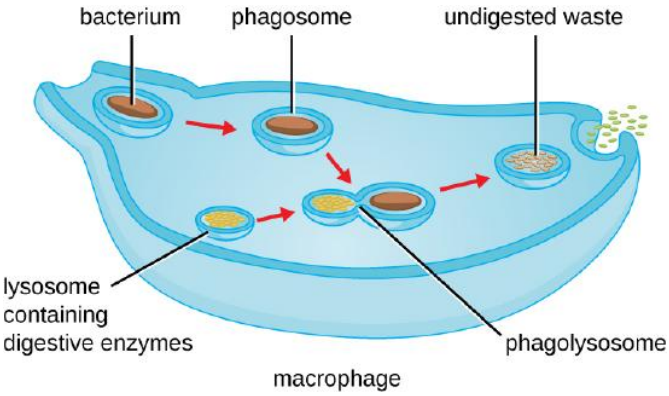


Figure **13.4.4**: Phagocytosis is a multi-step process in which a pathogen is engulfed and digested by immune cells called phagocytes.

LEUKOCYTES

Types of leukocytes that kill pathogens by phagocytosis include neutrophils, macrophages, and dendritic cells. Macrophages and dendritic cells are the derivatives of monocytes. Figure **13.4.5** shows five major types of leukocytes, lymphocytes, basophils, eosinophils, neutrophils, and monocytes. Because lymphocytes are mainly involved in the adaptive immune system, they are not discussed in this concept.

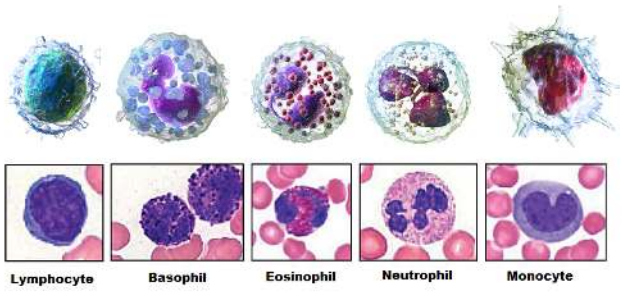


Figure **13.4.5**: Five types of leukocytes: from left to right, lymphocyte, basophil, eosinophil, neutrophil, and monocytes.

NEUTROPHILS

Neutrophils are leukocytes that travel throughout the body in the blood and are usually the first immune cells to arrive at the site of an infection. As shown in Figure **13.4.5**, these cells contain granules and carry a multilobed nucleus. They are the most numerous types of phagocytes and normally make up at least half of the total circulating leukocytes. The bone marrow of a normal healthy adult produces more than 100 billion neutrophils per day. During acute inflammation, more than 10 times that many neutrophils may be produced each day. Many neutrophils are needed to fight infections because after a neutrophil phagocytizes just a few pathogens, it generally dies.

MACROPHAGES

Macrophages are large phagocytic leukocytes that develop from monocytes. Macrophages spend much of their time within the interstitial fluid in tissues of the body. As shown in Figure **13.4.5**, monocytes do not contain granules and carry a big kidney-shaped nucleus. They are the most efficient phagocytes and can phagocytize a substantial number of pathogens or other cells. Macrophages are also versatile cells that produce a wide array of chemicals — including enzymes, complement proteins, and cytokines — in addition to their phagocytic action. As phagocytes, macrophages act as scavengers that rid tissues of worn-out cells and other debris as well as pathogens. In addition, macrophages act as antigen-presenting cells that activate the adaptive immune system. (To learn more about antigen-presenting cells, see the concept Adaptive Immune System.)

EOSINOPHILS

Eosinophils are non-phagocytic leukocytes that are related to neutrophils. They specialize in defending against parasites. As shown in Figure **13.4.5**, these cells contain granules and carry a bilobed earmuff-shaped nucleus. These leukocytes are very effective in killing large parasites such as worms by secreting a range of highly toxic substances when activated. Eosinophils may become overactive and cause allergies or asthma.

BASOPHILS

Basophils are non-phagocytic leukocytes that are also related to neutrophils. They are the least numerous of all white blood cells. As shown in Figure **13.4.5**, these cells contain granules and carry a bilobed nucleus. Basophils secrete two types of chemicals that aid in body defenses: histamines and heparin. Histamines are responsible for dilating blood vessels and increasing their permeability in inflammation. Heparin inhibits blood clotting and also promotes the movement of leukocytes into an area of infection.

DENDRITIC CELLS

Like macrophages, dendritic cells develop from monocytes (see Figure **13.4.6**. They reside in tissues that have contact with the external environment, so they are located mainly in the skin, nose, lungs, stomach, and intestines. Their plasma membrane has extensions. Besides engulfing and digesting pathogens, dendritic cells also act as antigen-presenting cells that trigger adaptive immune responses.

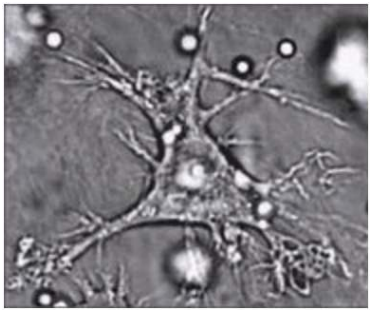


Figure **13.4.6**: dendritic cell

MAST CELLS

Mast cells are non-phagocytic leukocytes that help to initiate inflammation by secreting histamines. In some people, histamines trigger allergic reactions as well as inflammation. Mast cells may also secrete chemicals that help defend against parasites.

NATURAL KILLER CELLS

Natural killer cells are in the subset of leukocytes called lymphocytes, which are produced by the lymphatic system. Natural killer cells destroy cancerous or virus-infected host cells, although they do not directly attack invading pathogens. Natural killer cells recognize these host cells by a condition they exhibit called “missing self.” Cells with missing self have abnormally low levels of cell-surface proteins of the major histocompatibility complex (MHC), which normally identify body cells as self.

REVIEW

1. What is the innate immune system?
2. Identify the body’s first line of defense.
3. Define and give examples of mechanical and chemical barriers of the innate immune system.
4. What are biological barriers, and how do they protect the body?
5. State the purposes of inflammation.
6. What triggers inflammation, and what signs and symptoms does it cause?
7. Define the complement system. How does it help destroy pathogens?
8. List six different types of leukocytes and state their roles in innate immune responses.
9. Describe two ways that pathogens may evade the innate immune system.
10. Explain how mucus can contribute to the immune system as both a mechanical barrier and a chemical barrier.
11. Which type of immune system cell can both phagocytize pathogens and produce chemicals that promote inflammation?

    A. Macrophages

    B. Natural killer cells

    C. Basophils

    D. Mast cells
12. What are the ways in which phagocytes can encounter pathogens in the body?
13. Describe different two ways in which enzymes play a role in the innate immune response.
14. *True or False.* Complement proteins can be produced by macrophages.
15. *True or False.* The main function of inflammation is to secrete repair proteins at the site of damage.

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13.5: ADAPTIVE IMMUNE SYSTEM

THE KISS OF DEATH

The photomicrograph in Figure **13.5.1** shows a group of killer T cells (green and red) surrounding a cancer cell (blue, center). When a killer T cell makes contact with the cancer cell, it attaches to and spreads over the dangerous target. The killer T cell then uses special chemicals stored in vesicles (red) to deliver the killing blow. This event has thus been nicknamed "the kiss of death." After the target cell is killed, the killer T cells move on to find the next victim. Killer T cells like these are important players in the adaptive immune system.

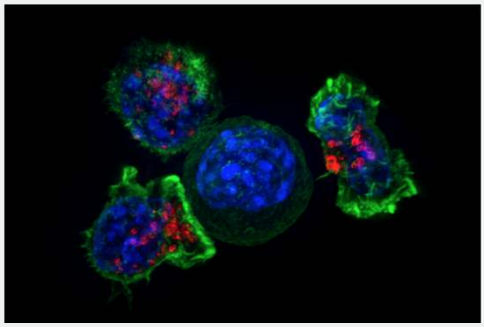


Figure **13.5.1**: Three Killer T cells surrounding Cancer Cells

The **adaptive immune system** (also called **specific immunity**) is a subsystem of the overall immune system. It is composed of highly specialized cells and processes that eliminate specific pathogens and tumor cells. An adaptive immune response is set in motion by antigens that the immune system recognizes as foreign. Unlike an innate immune response, an adaptive immune response is highly specific to a particular pathogen (or its antigen). An important function of the adaptive immune system that is not shared by the innate immune system is the creation of immunological memory or immunity. This occurs after the initial response to a specific pathogen. It allows a faster, stronger response on subsequent encounters with the same pathogen, usually before the pathogen can cause symptoms of illness.

Lymphocytes are the main cells of the adaptive immune system. They are leukocytes that arise and mature in organs of the lymphatic system, including the bone marrow and thymus. The human body normally has about 2 trillion lymphocytes, which constitute about a third of all leukocytes. Most of the lymphocytes are normally sequestered within tissue fluid or organs of the lymphatic system, including the tonsils, spleen, and lymph nodes. Only about 2 percent of the lymphocytes are normally circulating in the blood. There are two main types of lymphocytes involved in adaptive immune responses, called T cells and B cells. T cells destroy infected cells or release chemicals that regulate immune responses. B cells secrete antibodies that bind with antigens of pathogens so they can be removed by other immune cells or processes.

T CELLS

There are multiple types of **T cells** or T lymphocytes. Major types are killer (or cytotoxic) T cells and helper T cells. Both types develop from immature T cells that become activated by exposure to an antigen.

T CELL ACTIVATION

T cells must be activated. After the pathogen is phagocytized and digested by macrophages, a part of the pathogen is displayed on the surface of the macrophage. The proteins that display the antigen (part of the pathogen) are called Major Histocompatibility Complex (MHC). There are two types of MHC, MHCI and MHCII. Therefore macrophages are called antigen-presenting cells as shown in Figure **13.5.2** and Figure **13.5.3**. B lymphocytes can also act as antigen-presenting cells. Helper T cells are more easily activated than killer T cells. Activation of killer T cells is strongly regulated and may require additional stimulation from helper T cells.

HELPER T CELLS

Activated helper T cells do not kill infected or cancerous cells. Instead, their role is to "manage" both innate and adaptive immune responses by directing other cells to perform these tasks. They control other cells by releasing cytokines. These are proteins that can influence the activity of many cell types, including cytotoxic killer T cells (sometimes referred to as only killer T cells), B cells, and macrophages. For example, some cytokines released by helper T cells help activate killer T cells.

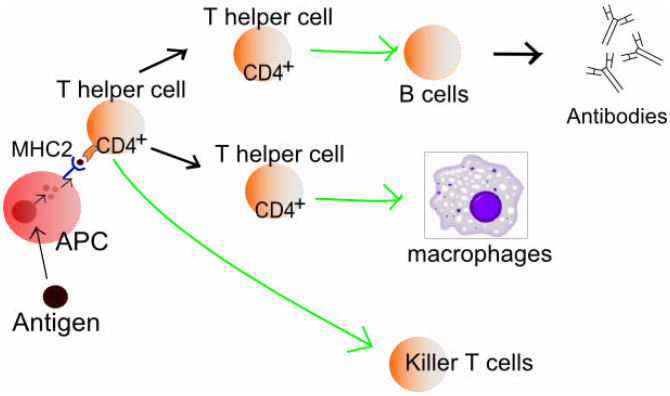


Figure **13.5.2**: After getting activated by an antigen-presenting cell, helper T cells trigger various other cells of the immune system, such as activation of B cells to produce antibodies, recruitment and activation of macrophages, and activation of cytotoxic killer T cells. In this image, APC stands for antigen-presenting cells and $CD4^+$ stands for Cluster Differentiation glycoprotein which is present on the surface of helper T cells.

KILLER T CELLS (CYTOTOXIC T CELLS)

When infected body cells present pathogen antigen to a killer T cell, it gets activated (see lower panel of Figure **13.5.3**). Activated killer T cells induce the death of cells that bear a specific non-self antigen because they are infected with pathogens or are cancerous. The antigen targets the cell for destruction by killer T cells, which travel

through the bloodstream searching for target cells to kill. Killer T cells may use various mechanisms to kill target cells. One way is by releasing toxins in granules that enter and kill infected or cancerous cells (Figure 13.5.3).

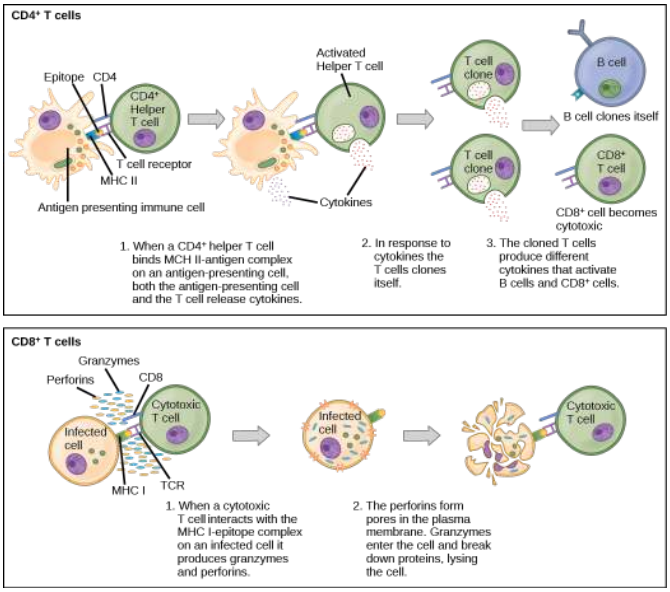


Figure 13.5.3: Naïve CD4+ (Helper) T cells engage MHC II molecules on antigen-presenting cells (APCs) and become activated. Clones of the activated helper T cell, in turn, activate B cells and CD8+ T (killer) cells, which become cytotoxic T cells. Cytotoxic T cells kill infected cells.

B CELLS AND B CELL ACTIVATION

B cells, or B lymphocytes, are the major cells involved in the creation of antibodies that circulate in blood plasma and lymph. Antibodies are large, Y-shaped proteins used by the immune system to identify and neutralize foreign invaders. Besides producing antibodies, B cells may also function as antigen-presenting cells or secrete cytokines that help control other immune cells and responses.

Before B cells can actively function to defend the host, they must be activated. As shown in Figure 13.5.4, B cell activation begins when a B cell engulfs and digests an antigen. The antigen may be either free-floating or on top of the pathogen. B cell internalize antigen and present it on its MHC to a helper T cell. The T cell activates and secretes cytokines that help the B cell to multiply and the daughter cells to mature into plasma cells and memory B cells. Plasma B cells produce antibodies.

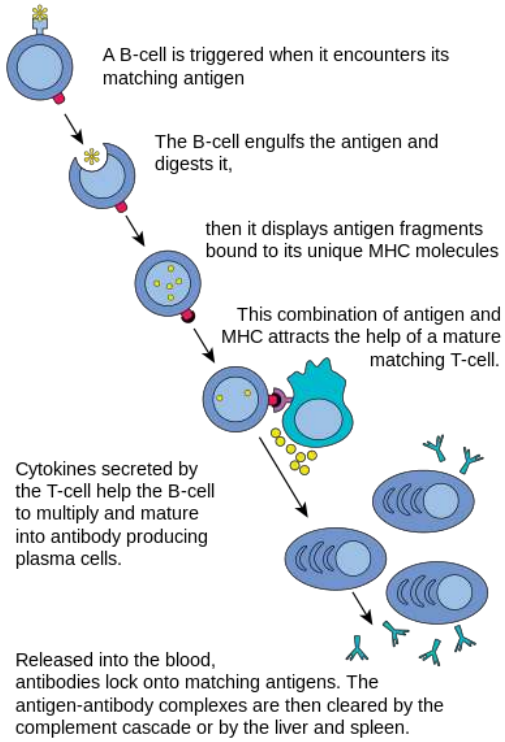


Figure 13.5.4: B cells are activated and become antibody-producing plasma cells with the help of helper T cells.

PLASMA CELLS

Plasma cells are antibody-secreting cells that form from activated B cells. Each plasma cell is like a tiny antibody factory. It may secrete millions of copies of an antibody, each of which can bind to the specific antigen that activated the original B cell. The specificity of an antibody to a specific antigen is illustrated in Figure 13.5.5. When antibodies bind with antigens, it makes the cells bearing them easier targets for phagocytes to find and destroy. Antibody-antigen complexes may also trigger the complement system of the innate immune system, which destroys the cells in a cascade of protein enzymes. In addition, the complexes are likely to clump together (agglutinate). If this occurs, they are filtered out of the blood in the spleen or liver.

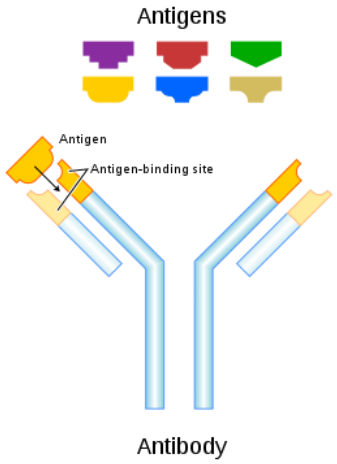


Figure **13.5.5**: Each antibody fits its antigen like a lock fits a key.

IMMUNITY

Most activated T cells and B cells die within a few days once a pathogen has been cleared from the body. However, a few of the cells survive and remain in the body as memory T cells or memory B cells. These memory cells are ready to activate an immediate response if they are exposed to the same antigen again in the future. This is the basis of **immunity.**

The earliest known reference to the concept of immunity relates to the bubonic plague (see Figure **13.5.6**). In 430 B.C., a Greek historian and general named Thucydides noted that people who had recovered from a previous bout of the plague could nurse people sick with the plague without contracting the illness a second time. We now know that this is true of many diseases and it occurs because of active immunity.



Figure **13.5.6**: Dead, blackened tissues at the fingertips and other extremities are a sign of the bubonic plague, giving rise to its other name, the black death.

ACTIVE IMMUNITY

Active immunity is the ability of the adaptive immune system to resist a specific pathogen because it has formed an immunological memory of the pathogen. Active immunity is adaptive because it occurs during the lifetime of an individual as an adaptation to infection with a specific pathogen and prepares the immune system for future challenges from that pathogen. Active immunity can come about naturally or artificially.

NATURALLY ACQUIRED ACTIVE IMMUNITY

Active immunity is acquired naturally when a pathogen invades the body and activates the adaptive immune system. When the initial infection is over, memory B cells and memory T cells remain that provide immunological memory of the pathogen. As long as the memory cells are alive, the immune system is ready to mount an immediate response if the same pathogen tries to infect the body again.

ARTIFICIALLY ACQUIRED ACTIVE IMMUNITY

Active immunity can also be acquired artificially through immunization. **Immunization** is the deliberate exposure of a person to a pathogen in order to provoke an adaptive immune response and the formation of memory cells specific to that pathogen. The pathogen is introduced in a vaccine — usually by injection, sometimes by nose or mouth (Figure **13.5.7**) — so immunization is also called vaccination.



Figure **13.5.7**: This young child is receiving an oral polio vaccine.

In a **vaccine,** only part of a pathogen, a weakened form of the pathogen, or a dead pathogen is typically used. This causes an adaptive immune response without making the immunized person sick. This is how you most likely became immune to diseases such as measles, mumps, and chickenpox. Immunizations may last for a lifetime or require periodic booster shots to maintain immunity. While immunization generally has long-lasting effects, it usually takes several weeks to develop full immunity.

Immunization is the most effective method ever discovered in preventing infectious diseases. As many as 3 million deaths are prevented each year because of vaccinations. Widespread immunity due to vaccinations is largely responsible for the worldwide eradication of smallpox and the near elimination of several other infectious diseases from many populations, including such diseases as polio and measles. Immunization is so successful because it exploits the natural specificity and inducibility of the adaptive immune system.

PASSIVE IMMUNITY

Passive immunity results when pathogen-specific antibodies or activated T cells are transferred to a person who has never been exposed to the pathogen. Passive immunity provides immediate protection from a pathogen, but the adaptive immune system does not develop immunological memory to protect the host from the same pathogen in the future. Unlike active immunity, passive immunity lasts only as long as the transferred antibodies or T cells survive in the blood. This is usually between a few days and a few

months. However, like active immunity, passive immunity can be acquired both naturally and artificially.

NATURALLY ACQUIRED PASSIVE IMMUNITY

Passive immunity is acquired naturally by a fetus through its mother's blood. Antibodies are transported from mother to fetus across the placenta, so babies have high levels of antibodies at birth. Their antibodies have the same range of antigen specificity as their mother's. Passive immunity may also be acquired by an infant through the mother's breast milk. This gives young infants protection from common pathogens in their environment while their own immune system matures.

ARTIFICIALLY ACQUIRED PASSIVE IMMUNITY

Older children and adults can acquire passive immunity artificially through the injection of antibodies or activated T cells. This may be done when there is a high risk of infection and insufficient time for the body to develop active immunity through vaccination. It may also be done to reduce symptoms of ongoing disease or to compensate for immunodeficiency diseases (for the latter, see the concept Disorders of the Immune System).

ADAPTIVE IMMUNE EVASION

Many pathogens have been around for a long time, living with human populations for generations. To persist, some have evolved mechanisms to evade the adaptive immune system of human hosts. One way they have done this is by rapidly changing their non-essential antigens. This is called antigenic variation. An example of a pathogen that takes this approach is the human immunodeficiency virus (HIV). It mutates rapidly so the proteins on its viral envelope are constantly changing. By the time the adaptive immune system responds, the virus's antigens have changed. Antigenic variation is the main reason that efforts to develop a vaccine against HIV have not yet been successful.

Another evasion approach some pathogens may take is to mask pathogen antigens with host molecules so the host's immune system cannot detect the antigens. HIV takes this approach as well. The envelope that covers the virus is formed from the outermost membrane of the host cell.

FEATURE: MY HUMAN BODY

If you think that immunizations are just for kids, think again. There are several vaccines recommended by the CDC for people over the age of 18. This link shows the vaccine schedule recommended for all adults aged 19 years and older. Additional vaccines may be recommended for certain adults based on specific medical conditions or other indications. Are you up to date with your vaccines? You can check with your doctor to be sure.

REVIEW

1. What is the adaptive immune system?
2. Describe the main cells of the adaptive immune system.
3. How are lymphocytes activated?
4. Identify two common types of T cells and their functions.
5. How do activated B cells help defend against pathogens?
6. Define immunity.
7. What are two ways active immunity may come about?
8. How does passive immunity differ from active immunity?
9. How may passive immunity occur?
10. What ways of evading the human adaptive immune system evolved in the human immunodeficiency virus (HIV)?
11. Describe two ways in which B cells and T cells work together to generate adaptive immune responses.
12. Which cells directly kill pathogen-infected or cancerous cells?
    A. A. Plasma cells
    B. B. Killer T cells
    C. C. Helper T cells
    D. D. All of the above
13. Why do vaccinations involve the exposure of a person to a version of a pathogen?
14. *True or False.* Immunization is a form of passive immunity.
15. *True or False.* Antibodies transmitted from mother to child via breast milk cause the formation of memory B cells and long-term immunity.

EXPLORE MORE

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ATTRIBUTIONS

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13.6: DISORDERS OF THE IMMUNE SYSTEM

ALLERGY EYES

Eyes that are red, watery, and itchy are typical of an allergic reaction known as allergic rhinitis. Commonly called hay fever, allergic rhinitis is an immune system reaction typically to the pollen of certain plants. Your immune system usually protects you from pathogens and keeps you well. However, like any other body system, the immune system itself can develop problems. Sometimes it responds to harmless foreign substances as though they were pathogens. That's the basis of allergies such as hay fever.



Figure **13.6.1**: Oedema of the conjunctiva due to hay fever allergy

ALLERGIES

An **allergy** is a disorder in which the immune system makes an inflammatory response to a harmless antigen. It occurs when the immune system is hypersensitive to an antigen in the environment that causes little or no response in most people. Allergies are strongly familial: allergic parents are more likely to have allergic children and those children's allergies are likely to be more severe. This is evidence that there is a heritable tendency to develop allergies. Allergies are more common in children than adults because many children outgrow their allergies by adulthood.

ALLERGENS



Figure **13.6.2**: Common causes of allergies include pollen and poison ivy

Any antigen that causes an allergy is called an **allergen.** Common allergens are plant pollens, dust mites, mold, specific foods (such as peanuts or shellfish), insect stings, and certain common medications (such as aspirin and penicillin). Allergens may be inhaled or ingested, or they may come into contact with the skin or eyes. Symptoms vary depending on the type of exposure and the severity of the immune system response. Two common causes of allergies are ragweed and poison ivy. Inhaling ragweed pollen may cause symptoms of allergic rhinitis, such as sneezing and red itchy eyes. Skin contact with oils in poison ivy may cause an itchy rash. This type of allergy is called contact dermatitis.

PREVALENCE OF ALLERGIES

There has been a significant increase in the prevalence of allergies over the past several decades, especially in the rich nations of the world, where allergies are now very common disorders. In the developed countries, about 20 percent of people have or have had hay fever, another 20 percent have had contact dermatitis, and about 6 percent have food allergies. In the poorer nations of the world, on the other hand, allergies of all types are much less common.

One explanation for the rise in allergies in the developed world is called the hygiene hypothesis. According to this hypothesis, people in developed countries live in relatively sterile environments because of hygienic practices and sanitation systems. As a result, people in these countries are exposed to fewer pathogens than their immune system evolved to cope with. To compensate, their immune system "keeps busy" by attacking harmless antigens in allergic responses.

HOW ALLERGIES OCCUR

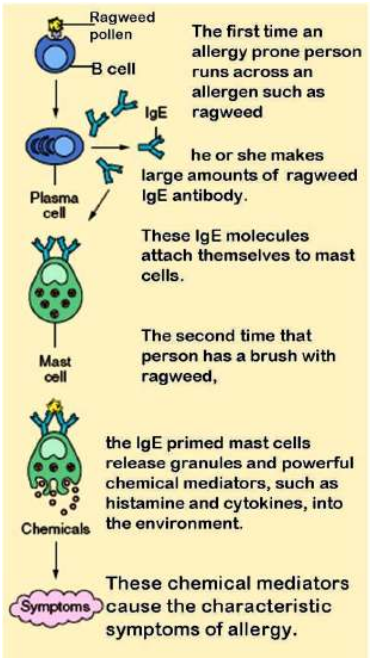


Figure **13.6.3**: This diagram shows how the adaptive immune system is activated by an otherwise harmless antigen on ragweed pollen, responding to the allergen as though it was a pathogen.

The diagram in Figure **13.6.3** shows how an allergic reaction occurs. At the first exposure to an allergen, B cells are activated to form plasma cells that produce large amounts of antibodies to the allergen. These antibodies attach to leukocytes called mast cells. Subsequently, every time the person encounters the allergen again,

the mast cells are already primed and ready to deal with it. The primed mast cells immediately release cytokines and histamines, which in turn cause inflammation and recruitment of leukocytes, among other responses. These responses are responsible for the signs and symptoms of allergies.

TREATING ALLERGIES

The symptoms of allergies can range from mild to life-threatening. Mild allergy symptoms are often treated with antihistamines. These are drugs that reduce or eliminate the effects of the histamines that produce allergy symptoms.

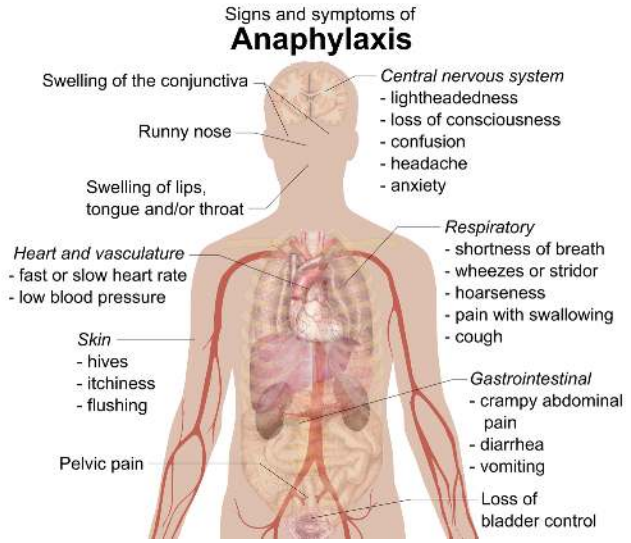


Figure **13.6.4**: Anaphylaxis is a rapid, systemic reaction to allergens that may lead to life-threatening symptoms.

TREATING ANAPHYLAXIS

The most severe allergic reaction is a systemic reaction called **anaphylaxis.** This is a life-threatening response caused by a massive release of histamines. Many of the signs and symptoms of anaphylaxis are shown in Figure **13.6.4**. Some of them include a drop in blood pressure, changes in heart rate, shortness of breath, and swelling of the tongue and throat, which may threaten the patient with suffocation unless emergency treatment is given. People who have had anaphylactic reactions may carry an epinephrine autoinjector (widely known by its brand name EpiPen®) so they can inject themselves with epinephrine if they start to experience an anaphylactic response. The epinephrine helps to control the immune reaction until medical care can be provided. Epinephrine constricts blood vessels to increase blood pressure, relaxes smooth muscles in the lungs to reduce wheezing and improve breathing, modulates heart rate, and works to reduce swelling that may otherwise block the airways.

IMMUNOTHERAPY FOR ALLERGIES

Another way to treat allergies is called **immunotherapy,** commonly called "allergy shots." This approach may actually cure specific allergies, at least for several years if not lifelong. It may be particularly beneficial for allergens such as pollen that are difficult or impossible to avoid. First, however, patients must be tested to identify the specific allergens that are causing their allergies. As shown in Figure **13.6.5**, this may involve scratching tiny amounts of common allergens into the skin and then observing whether there is a localized reaction to any of them. Each allergen is applied in a different numbered location on the skin so if there is a reaction, such as redness or swelling, the responsible allergens can be identified. Then, through periodic injections (usually weekly or monthly), patients are gradually exposed to larger and larger amounts of the allergens. Over time, generally from months to years, the immune system becomes desensitized to the allergens. This method of treating allergies is often effective for allergies to pollen or insect stings, but its usefulness for allergies to food is unclear.



Figure **13.6.5**: Skin testing for common allergens is one way to identify the cause(s) of a patient's allergic symptoms.

AUTOIMMUNE DISEASES

Autoimmune diseases occur when the immune system fails to recognize the body's own molecules as self. As a result, instead of ignoring the body's healthy cells, it attacks them, causing damage to tissues and altered organ growth and function. Most often, it is B cells that are at fault in autoimmune responses. They are generally the cells that lose tolerance for self. Why does this occur? Some autoimmune diseases are thought to be caused by exposure to pathogens that have antigens similar to the body's own molecules. After this exposure, the immune system responds to body cells as though they were pathogens as well.

Certain individuals are genetically susceptible to developing autoimmune diseases. These individuals are also more likely to develop more than one such disease. Gender is also a risk factor for autoimmunity. Females are much more likely than males to develop autoimmune diseases, probably in part because of gender differences in sex hormones.

At a population level, autoimmune diseases are less common where infectious diseases are more common. The hygiene hypothesis has been proposed to explain the inverse relationship between infectious and autoimmune diseases as well as the prevalence of allergies. According to the hypothesis, without infectious diseases to "keep it busy," the immune system may attack the body's own cells instead.

COMMON AUTOIMMUNE DISEASES

An estimated 15 million or more people worldwide have one or more autoimmune diseases. Two of the most common autoimmune diseases are type I diabetes and multiple sclerosis. Both are localized diseases in terms of the specific body cells that are attacked by the immune system. In the case of type I diabetes, the immune system

attacks and destroys insulin-secreting islet cells in the pancreas. In the case of multiple sclerosis, the immune system attacks and destroys the myelin sheaths that normally insulate the axons of neurons and allow rapid transmission of nerve impulses.

Some relatively common autoimmune diseases are systemic, or body-wide, diseases. They include rheumatoid arthritis and systemic lupus erythematosus (SLE). In these diseases, many tissues and organs may be attacked and injured by the immune system. For example, as you can see in Figure **13.6.6**, symptoms of SLE may involve the muscular, skeletal, integumentary, respiratory, and cardiovascular systems.

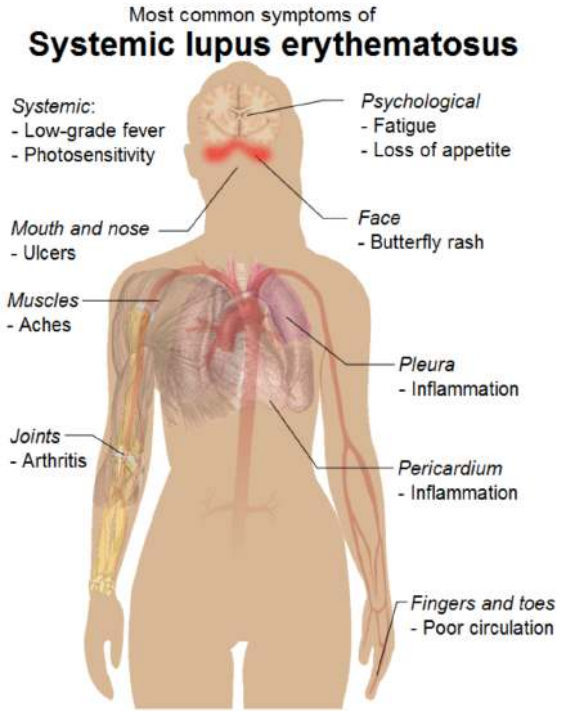


Figure **13.6.6**: Systemic lupus erythematosus is an autoimmune disease that may cause symptoms of body-wide tissue damage. The symptoms listed here are psychological fatigue and loss of appetite, butterfly rash on the face, inflammation of pleura and pericardium, poor circulation to finger and toes, fever, photosensitivity, mouth and nose ulcers, muscle aches, and joint arthritis.

TREATMENT FOR AUTOIMMUNE DISEASES

None of these common autoimmune diseases can be cured, although all of them have treatments that may help relieve symptoms and prevent some of the long-term damage they may cause. Traditional treatments for autoimmune diseases include immunosuppressive drugs to block the immune response and anti-inflammatory drugs to quell inflammation. Hormone replacement may be another option. For example, type I diabetes is treated with injections of the hormone insulin because islet cells in the pancreas can no longer secrete it.

IMMUNODEFICIENCY

Immunodeficiency occurs when the immune system is not working properly, generally because one or more components of the immune system are inactive. As a result, the immune system may be unable to fight off pathogens or cancers that a normal immune system would be able to resist. Immunodeficiency may occur for a variety of reasons.

CAUSES OF IMMUNODEFICIENCY

Dozens of rare genetic diseases can result in a defective immune system. This type of immunodeficiency is called primary immunodeficiency. One is born with one of these diseases rather than acquiring it after birth. Probably the best known of these primary immunodeficiency diseases is severe combined immunodeficiency (SCID). It is also known as “bubble boy disease” because people with this disorder are extremely vulnerable to infectious diseases and some of them have become well known for living inside a bubble that provides a sterile environment. SCID is most often caused by an X-linked recessive mutation that interferes with normal B cell and T cell production.

Other types of immunodeficiency are not present at birth but acquired due to experiences or exposures that occur after birth. Acquired immunodeficiency is called secondary immunodeficiency because it is secondary to some other event or exposure. Secondary immunodeficiency may occur for a number of different reasons:

- The immune system naturally becomes less effective as people get older. This age-related decline, called immunosenescence, generally begins at about age 50 and worsens with increasing age. Immunosenescence is why older people are generally more susceptible to disease than younger people.
- The immune system may be damaged by another disorder, such as obesity, alcoholism, or the abuse of other drugs.
- In developing countries, malnutrition is the most common cause of immune system damage and immunodeficiency. Inadequate protein intake is especially damaging to the immune system. It can lead to impaired complement system activity, phagocyte malfunction, and lower-than-normal production of antibodies and cytokines.
- Surgical removal or disease of the thymus, where T lymphocytes normally mature, results in severe immunodeficiency. People without a functioning thymus are extremely susceptible to infections.
- Certain medications can suppress the immune system. This is the intended effect of immunosuppressant drugs given to people with transplanted organs so they do not reject them. In many cases, however, immunosuppression is an unwanted side effect of drugs used to treat other disorders.
- Some pathogens attack and destroy cells of the immune system. An example is a virus known as HIV, which attacks and destroys T cells.

FOCUS ON HIV

The human immunodeficiency virus (HIV) is the most common cause of immunodeficiency in the world today, so it is the focus of the rest of this concept. It is also covered in the concept HIV and AIDS. HIV infections of human hosts are a relatively recent phenomenon. Scientists think that the virus originally infected

monkeys but then jumped to human populations, probably sometime during the early to mid-1900s. This most likely occurred in West Africa, but the virus soon spread around the world. HIV was first identified by medical researchers in 1981. Since then, HIV has killed almost 40 million people worldwide, and its economic toll has also been enormous. The hardest hit countries are in Africa, where the virus has infected human populations the longest, and medications to control the virus are least available.

HIV TRANSMISSION

HIV is transmitted through direct contact of mucous membranes or body fluids such as blood, semen, or breast milk. As shown in Figure **13.6.7**, the transmission of the virus can occur through sexual contact or the use of contaminated hypodermic needles. It can also be transmitted from an infected mother's blood during late pregnancy or childbirth or through breast milk after birth. In the past, HIV was also transmitted occasionally through blood transfusions. Because donated blood is now screened for HIV, the virus is no longer transmitted this way.

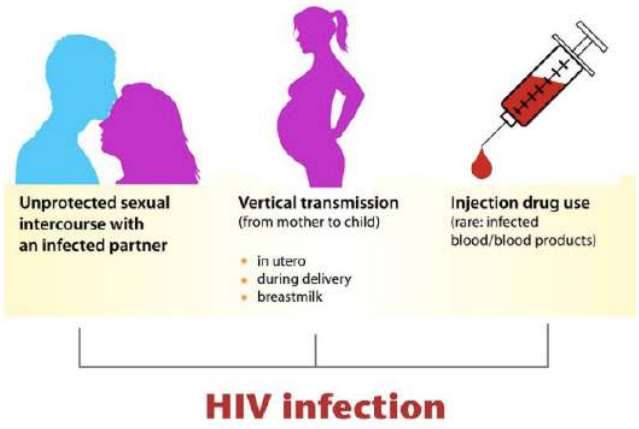


Figure **13.6.7**: HIV may be transmitted in all of the ways shown here.

HIV AND THE IMMUNE SYSTEM

HIV infects and destroys helper T cells, the type of lymphocytes that regulate the immune response. How this occurs is shown in Figure **13.6.8**. The virus injects its own nucleic acid into a helper T cell and uses the T cell's "machinery" to make copies of itself. In the process, the helper T cell is destroyed, and the virus copies go on to infect other helper T cells. HIV is able to evade the immune system and keep destroying helper T cells by mutating frequently so its surface antigens keep changing and by using the host cell's membrane to hide its own antigens.

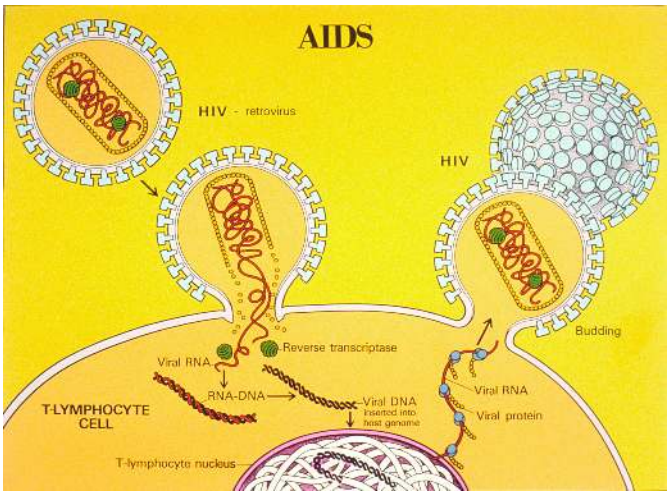


Figure **13.6.8**: The human immunodeficiency virus (HIV-I) enters the T-lymphocyte where the virus loses its outer envelope, releasing its RNA and its reverse transcriptase. The reverse transcriptase builds a complementary DNA strand from the viral RNA template. The DNA helix is inserted into the host genome. When this is transcribed by the infected cell, the new viral RNA and proteins are produced to form new viruses that then bud from the cell membrane, thus completing the life cycle of the virus.

Acquired immunodeficiency syndrome (AIDS) may result from years of damage to the immune system by HIV. It occurs when helper T cells fall to a very low level and opportunistic diseases occur. Opportunistic diseases are infections and tumors that are rare except in people with a damaged immune system. The diseases take advantage of the "opportunity" presented by people whose immune systems cannot fight back. Opportunistic diseases are usually the direct cause of death of people with AIDS.

TREATING HIV/AIDS

For patients who have access to HIV medications, infection with the virus has ceased to be the death sentence that it once was. By 1995, combinations of drugs called "highly active antiretroviral therapy" were developed. For some patients, these drugs can reduce the amount of virus they are carrying to undetectable levels. However, some amount of virus always hides in the body's immune cells and will multiply again if a patient stops taking the medications. Researchers are trying to develop drugs to kill these hidden viruses as well. If their efforts are successful, it could bring an end to AIDS.

FEATURE: HUMAN BIOLOGY IN THE NEWS

EpiPens® and their sole manufacturer, pharmaceutical company Mylan, were featured in the news headlines in 2016 but not for a good reason. A drastic price hike in EpiPens® and Mylan's apparent greed triggered the media outburst.

EpiPens® are auto-injectable syringes preloaded with a measured dose of epinephrine, a drug that can rapidly stop a life-threatening anaphylactic response to an allergen. Using the device is easy and does not require any special training. The injector just needs to be jammed against the thigh, which can be done through clothing or on bare skin. Each year, doctors write millions of prescriptions for EpiPens®. Many people with

severe allergies always carry two of the devices with them just in case they experience anaphylaxis, although most of them never need to use them. Other people with severe allergies have literally had their lives saved multiple times by EpiPens® when they had anaphylactic reactions. Even when the devices haven't been used, they must be replaced each year due to the expiration of the epinephrine.

You might think that EpiPens® would be relatively inexpensive, given their life-saving potential. As recently as 2009, a two-pack of EpiPens® cost about $100. However, in just 7 years, the cost of the same two-pack of EpiPens® skyrocketed by an incredible 400 percent! By 2016, the cost was $600 or more. Mylan apparently raised the price for the sole purpose of increasing profits. The company also raised prices significantly on many other drugs. The price hike in EpiPens® alone was certainly profitable. In 2015, the sale of EpiPens® earned Mylan $1 billion. Mylan's CEO took home almost $19 million the same year, which was an increase of more than 600 percent over her prior salary.

News coverage of the price hike in EpiPens® began in the summer of 2016 after a price increase in May of that year. Both private citizens and elected officials expressed outrage over the price increase, especially when coupled with the gluttonous profits of the company and its CEO. By late August, Mylan responded to the backlash by offering discount coupons for EpiPens®. A few days later, the company promised to introduce a cheaper, generic version of the device. Analysts quickly determined that selling a generic version would allow Mylan to make more money on the product than reducing the price of the name-brand device, which they still declined to do. By September of 2016, Mylan was being investigated for antitrust violations relating to sales of EpiPens® to public schools in New York City.

The Mylan/EpiPen® story may still be making the news. But whatever its outcome, the story has already added fuel to public and private debates about important ethical issues — issues such as the excessive costs of life-saving drugs and the huge profits of big pharma. What is the most recent news on EpiPens® and Mylan? If you are interested, you can check the headlines online to find out. What are your views on the ethical issues they raise?

REVIEW

1. What are allergies? What causes them?
2. Compare the prevalence of allergies in developed and developing countries. How does the hygiene hypothesis explain the differences in prevalence?
3. How do allergies occur?
4. How are mild allergy symptoms treated?
5. What is anaphylaxis, and how is it treated?
6. How does immunotherapy for allergies work?
7. What are autoimmune diseases?
8. Identify two risk factors for autoimmune diseases.
9. Autoimmune diseases may be specific to particular tissues, or they may be systemic. Give an example of each type of autoimmune disease.
10. What is immunodeficiency?
11. Compare and contrast primary and secondary immunodeficiency, and give an example of each.
12. What is the most common cause of immunodeficiency in the world today? How does this cause affect the immune system?
13. Distinguish between HIV and AIDS.
14. *True or False.* Allergies and autoimmune diseases both result from an over-reactive immune system.
15. *True or False.* An anaphylactic reaction can be stopped by administering a shot of histamine.

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13.7: HUMAN MICROBIOME

BENEFICIAL MICROBES: THE PHARMACY IN THE GUT

While some bacteria can cause disease, others play beneficial roles in human health. We have co-evolved with microbes in and on our body, with everyone having a unique set of microorganisms. The most abundant and well-studied microbiome is found in the gut. It has been estimated that the number of bacteria in the human gut may outnumber the cells in the body by an order of magnitude. Thus, one may consider the gut microbiome as a multicellular organ similar in size to the liver. Indeed, it is sometimes referred to as our "forgotten organ".

Generally, the microbiome within a given body habitat can be defined as the diversity and abundance distribution of distinct types of microorganisms. This microbial composition is highly influenced by individual factors such as diet, age, lifestyle, ethnicity, and host health, among others. Although no taxa are observed to be universally present among all individuals, some microbial patterns demonstrate broad prevalence. Most bacteria belong to the genera *Bacteroides*, *Clostridium*, *Fusobacterium*, *Eubacterium*, *Ruminococcus*, *Peptococcus*, *Peptostreptococcus*, and *Bifidobacterium.*

THE EVOLUTION OF MICROBIOME DURING LIFE

Recent research suggests early in-utero microbial exposure during pregnancy. Following birth, the newborn's digestive tract is quickly colonized by microorganisms from the mother (vaginal, fecal, skin, breast milk, etc.) and the environment in which the delivery takes place. Following birth, the microbiome that enters and evolves in the infant's gut is dependent upon a number of factors, with delivery mode and feeding regime (breastfeeding vs infant formula feeding) of prime importance in the early days and weeks of life. By the age of 2 to 3 years, the microbiome becomes essentially established, having reached a steady state, and remains relatively stable throughout life. However, the gut microbiome continuously changes in response to daily variations in diet, lifestyle, age, and host physiological and immunological health.

HEALTH BENEFITS OF THE MICROBIOME

On the basis of the currently available literature, the gut microbiome is known to contribute to a number of important functions in the host, from protective, immunomodulatory, metabolic to trophic roles. These are promoted via a number of mechanisms. For example, members of the gut microbiome can produce anti-inflammatory factors, pain relieving compounds, antioxidants, and vitamins to protect and nurture the body. Additionally, they may prevent attachment and action of harmful bacteria that can produce toxins causing chronic disease. This close and specific contact with human cells, exchanging nutrients and metabolic wastes, makes symbiotic bacteria essentially a human organ.

GASTROINTESTINAL INFECTION PREVENTION

The indigenous intestinal microbiome serves as a line of resistance to colonization by exogenous microbes such as *Clostridium difficile* and *Helicobacter pylori*, and thus assists in competitive exclusion of pathogens preventing the potential invasion, termed colonization resistance. Indeed, antibiotic-associated diarrhea occurs when antibiotic treatment disturbs the natural balance of the gut microbiome causing harmful bacteria (i.e., *Clostridium difficile*) to proliferate and multiply. Oral probiotics may reduce antibiotic-associated diarrhea significantly.

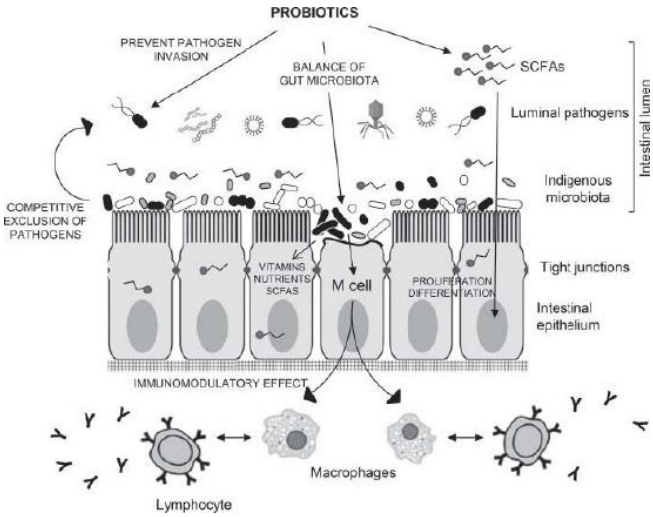


Figure **13.7.1**: Schematic representation of the cross-talk interaction of indigenous microbiome and oral probiotics with the intestinal epithelium. The intestinal microbiome protects the mucosa from invasion by pathogens. These probiotic bacteria may also allow beneficial effects through the release of nutrients (vitamins, SCFAs sugars) which are absorbed in the small intestine. Human microbes and probiotics would also interact with MALT macrophages and naive lymphocyte cells, allowing a mucosal anti-inflammatory response.

IMMUNOMODULATORY EFFECTS

Commensal bacteria can interact with the host immune system in ways that control the host's immune response and counteracts the development of the disease. The complex interactions that may occur between ingested probiotic bacteria, commensals, and the mucosal surface are possible because of the mucosa-associated immune system, typically organized into MALT (Mucosal Associated Lymphoid Tissue, such as Peyer's patches). This cross-talk interaction enhances cellular immune response characterized by activation of macrophages, antigen-specific cytotoxic T-lymphocytes, and the release of various cytokines. Furthermore, some probiotics may be effective in the prevention and/or alleviation of allergies and auto-immune diseases like irritable bowel syndrome and inflammatory bowel diseases (Crohn's disease and ulcerative colitis).

NUTRITIONAL BENEFITS

The metabolic activity of the gut microbiome makes an important contribution to the host's nutritional status via its ability to synthesize certain vitamins and various bioactive metabolites, such as short-chain fatty acids (SCFA), that then become bioavailable to the host. It has been reported that consumption of yogurt containing *Lactobacillus bulgaricus* or *acidophilus* could alleviate lactose intolerance during gastric passage through their enzyme lactase. However, the major metabolic function of the colonic microflora is the fermentation of nondigestible carbohydrates, which are key sources of energy in the colon. These carbohydrates also include large polysaccharides (i.e., resistant starches, pectins, and cellulose) and some oligosaccharides that escape digestion, as well as unabsorbed sugars and alcohols. Other benefits of the gut microbiome on human health, such as a role in supporting the health of the reproductive tract, oral cavity, lungs, skin, and gut-brain axis is currently under investigation.

PROBIOTIC IMBALANCE

When the normal composition of the microbiome is thrown off balance, there is a potential risk of disease. A decrease in microbiome diversity has been linked to cancer, asthma, Parkinson's, obesity, Alzheimer's, type-2 diabetes, cardiovascular disease, and possibly even autism in comparison to healthy subjects. Over-the-counter probiotics can help. In order to arrive alive at their workplace (i.e. the gastrointestinal tract), orally administered probiotics must be able to resist stomach acid, bile, and the effects of digestive enzymes. Certain mechanisms of action (such as the delivery of certain enzymes to the intestine) may not require live cells to play a physiologic benefit. Hence, a probiotic must contain as many live bacteria as claimed on the label. In addition, to survive the stomach and arrive at the intestine in optimal numbers, probiotic strains must be able to adhere to the intestinal epithelium and/or mucus, persist and multiply in the gut to maintain its metabolic activity and confer their probiotic properties in the human body.

RESOURCES

- BIOENGINEERED, 2016, VOL. 7, NO. 1, 11–20: http://dx.doi.org/10.1080/21655979.2015.1126015
- REVIEW: Beneficial Microbes: The pharmacy in the gut, Daniel M. Linares, Paul Ross, and Catherine Stanton, Food Biosciences Department, Teagasc Food Research Center, Moorepark, Fermoy, Cork, Ireland; APC, Microbiome Institute, University College Cork, Cork, Ireland; Biosciences Institute, University College Cork, Cork, Ireland

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13.8: CASE STUDY CONCLUSION- LYMPHOMA AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: DEFENDING YOUR DEFENSES

The person in Figure **13.8.1** is participating in a bike ride to raise funds for leukemia and lymphoma research. Leukemia and lymphoma are blood cancers. About every three minutes, one person in the U.S. is diagnosed with blood cancer. Lymphoma is the most common type of blood cancer. As a lymphoma patient, Wei, whom you learned about in the beginning of this chapter, may eventually benefit from research funded by a bike ride like this one.



Figure **13.8.1**: Fundraising for research

What type of blood cell is affected in lymphoma? As the name implies, lymphoma is cancer that affects lymphocytes, which are a type of white blood cell. As you have learned in this chapter, there are different types of lymphocytes, including the B and T cells of the adaptive immune system. Different types of lymphoma affect different types of lymphocytes in different ways. It is important to correctly identify the type of lymphoma so that patients can be treated appropriately.

You may recall that one of Wei's symptoms was a swollen lymph node, and he was diagnosed with lymphoma after a biopsy of that lymph node. Swollen lymph nodes are a common symptom of lymphoma. As you have learned, lymph nodes are distributed throughout the body along lymphatic vessels as part of the lymphatic system. The lymph nodes filter lymph and store lymphocytes and therefore play an important role in fighting infections. Because of this, they will often swell in response to an infection. In Wei's case, the swelling and other symptoms did not improve after several weeks and a course of antibiotics, which caused Dr. Bouazizi to suspect lymphoma instead. The biopsy showed that Wei did indeed have cancerous lymphocytes in his lymph nodes.

But which type of lymphocytes were affected? Lymphoma most commonly affects B or T lymphocytes. The two major types of lymphoma are called Hodgkin (HL) or non-Hodgkin lymphoma (NHL). NHL is more common than HL. There are more than 70,000 cases of NHL diagnosed in the U.S. each year, compared to about 8,000 for HL. While HL is one distinct type of lymphoma, NHL has about 60 different subtypes, depending on which specific cells are affected and how.

Wei was diagnosed with a type of NHL called diffuse large B-cell lymphoma (DLBCL)—the most common type of NHL. This type of lymphoma affects B cells and causes them to appear large under the microscope. In addition to Wei's symptoms of fatigue, swollen lymph nodes, loss of appetite, and weight loss, common symptoms of this type of lymphoma include fever and night sweats. It is an aggressive and fast-growing type of lymphoma that is fatal if not treated. But the good news is that with early detection and proper treatment, about 70% of patients with DLBCL can be cured.

How do physicians determine the specific type of lymphoma? Tissue obtained from a biopsy can be examined under a microscope to observe physical changes such as abnormal cell size or shape that are characteristic of a particular subtype of lymphoma. Additionally, tests can be performed on the tissue to determine which cell-surface antigens are present. Recall that antigens are molecules that bind to specific antibodies. Antibodies can be produced in the laboratory and labeled with compounds that can be identified by their color under a microscope. When these antibodies are applied to a tissue sample, this color will appear wherever the antigen is present, because it binds to the antibody. For example, this technique was used in the photomicrograph in Figure **13.8.2** to identify the presence of a cell-surface antigen (shown as reddish-brown) in a sample of skin cells. This technique, called **immunohistochemistry**, is also commonly used to identify antigens in tissue samples from lymphoma patients.

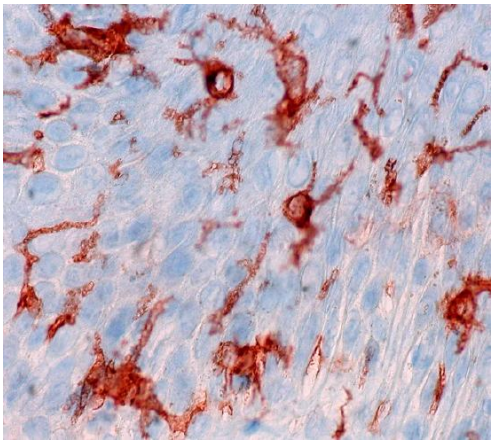


Figure **13.8.2**: Test for lymphoma

Why would identifying cell-surface antigens be important in diagnosing and treating lymphoma? As you have learned, the immune system uses antigens present on the surface of cells or pathogens to distinguish between self and non-self and to launch adaptive immune responses. Cells that become cancerous often change their cell-surface antigens, and this is one way that the immune system can identify and destroy them. Also, different cell types in the body can sometimes be identified by the presence of specific cell-surface antigens. Knowing the types of cell-surface

antigens present in a tissue sample can help physicians identify which cells are cancerous, and possibly the specific subtype of cancer. Knowing this information can be helpful in choosing more tailored and effective treatments.

In fact, one treatment for NHL is the use of medications made from antibodies that bind to cell-surface antigens present on cells affected by the specific subtype of NHL. This is called **immunotherapy**. These drugs can directly bind to and kill the cancerous cells. For patients with DLBCL such as Wei, immunotherapy is often used in conjunction with chemotherapy and radiation as a course of treatment. Although Wei has a difficult road ahead, he and his medical team are optimistic that he may be able to be cured, given the high success rate when DLBCL is caught and treated early. More research into how the immune system functions may lead to even better treatments for lymphoma, and other types of cancers, in the future.

CHAPTER SUMMARY

In this chapter, you learned about the immune system. Specifically, you learned that:

- Any agent that can cause disease is called a pathogen. Most human pathogens are microorganisms such as bacteria and viruses. The immune system is the body system that defends the human host from pathogens and cancerous cells.
- The innate immune system is a subset of the immune system that provides very quick but non-specific responses to pathogens. It includes multiple types of barriers to pathogens, leukocytes that phagocytize pathogens, and several other general responses.
- The adaptive immune system is a subset of the immune system that provides specific responses tailored to particular pathogens. It takes longer to put into effect, but it may lead to immunity to the pathogens.
- Both innate and adaptive immune responses depend on the ability of the immune system to distinguish between self and non-self molecules. Most body cells have major histocompatibility complex (MHC) proteins that identify them as self. Pathogens, infected cells, and tumor cells have non-self proteins called antigens that the immune system recognizes as foreign.
- Antigens are proteins that bind to specific receptors on immune system cells and elicit an adaptive immune response. Some immune cells (B cells) respond to foreign antigens by producing antibodies that bind with antigens and target pathogens for destruction.
- An important role of the immune system is tumor surveillance. Killer T cells of the adaptive immune system find and destroy tumor cells, which they can identify from their abnormal antigens.
- The neuroimmune system that protects the central nervous system is thought to be distinct from the peripheral immune system that protects the rest of the human body. The blood-brain and blood-spinal cord barriers are one type of protection of the neuroimmune system. Glial cells also play role in this system—for example, by carrying out phagocytosis.
- The lymphatic system is a human organ system that is a vital part of the adaptive immune system. It consists of several organs and a system of vessels that transport or filter the fluid called lymph. The main immune function of the lymphatic system is to produce, mature, harbor, and circulate white blood cells called lymphocytes, which are the main cells in the adaptive immune system and are circulated in the lymph.
- The return of lymph to the bloodstream is one of the functions of the lymphatic system. Lymph flows from tissue spaces, where it leaks out of blood vessels, to major veins in the upper chest, where it is returned to the cardiovascular system. Lymph is similar in composition to blood plasma. Its main cellular components are lymphocytes.
- Lymphatic vessels called lacteals are found in villi that line the small intestine. Lacteals absorb fatty acids from the digestion of lipids in the digestive system. The fatty acids are then transported through the network of lymphatic vessels to the bloodstream. Although it plays a role in digestion, the primary function of the lymphatic system is host defense.
- Lymphocytes, which include B cells and T cells, are the subset of white blood cells that are involved in adaptive immune responses. They may create a lasting memory of and immunity to specific pathogens.
- All lymphocytes are produced in the bone marrow and then go through a process of maturation in which they “learn” to distinguish self from non-self. B cells mature in the bone marrow, and T cells mature in the thymus. Both the bone marrow and thymus are considered primary lymphatic organs.
- Secondary lymphatic organs include the tonsils, spleen, and lymph nodes. There are four pairs of tonsils that encircle the throat. The spleen filters blood as well as lymph. There are hundreds of lymph nodes located in clusters along the lymphatic vessels. All of these secondary organs filter lymph and store lymphocytes, so they are sites where pathogens encounter and activate lymphocytes and initiate adaptive immune responses.
- Unlike the adaptive immune system, the innate immune system does not confer immunity. The innate immune system includes surface barriers, inflammation, the complement system, and a variety of cellular responses.
- The body’s first line of defense consists of three different types of barriers that keep most pathogens out of body tissues. The types of barriers are mechanical, chemical, and biological barriers.
- Mechanical barriers—which include the skin, mucous membranes, and fluids such as tears and urine—physically block pathogens from entering the body.
- Chemical barriers—such as enzymes in sweat, saliva, and semen—kill pathogens on body surfaces.
- Biological barriers are harmless bacteria that use up food and space so pathogenic bacteria cannot colonize the body.

- If pathogens breach the protective barriers, inflammation occurs. This creates a physical barrier against the spread of infection and repairs tissue damage. Inflammation is triggered by chemicals such as cytokines and histamines, and it causes swelling, redness, and warmth.
- The complement system is a complex biochemical mechanism that helps antibodies kill pathogens. Once activated, the complement system consists of more than two dozen proteins that lead to disruption of the cell membrane of pathogens and bursting of the cells.
- Cellular responses of the innate immune system involve various types of leukocytes (white blood cells). For example, neutrophils, macrophages, and dendritic cells phagocytize pathogens. Basophils and mast cells release chemicals that trigger inflammation. Natural killer cells destroy cancerous or virus-infected cells, and eosinophils kill parasites.
- Many pathogens have evolved mechanisms that help them evade the innate immune system. For example, some pathogens form a protective capsule around themselves, and some mimic host cells so the immune system does not recognize them as foreign.
- The main cells of the adaptive immune system are lymphocytes. There are two major types of lymphocytes: T cells and B cells. Both types must be activated by foreign antigens to become functioning immune cells.
- Most activated T cells become either killer T cells or helper T cells. Killer T cells destroy cells that are infected with pathogens or are cancerous. Helper T cells manage immune responses by releasing cytokines that control other types of leukocytes.
- Activated B cells form plasma cells that secrete antibodies, which bind to specific antigens on pathogens or infected cells. The antibody-antigen complexes generally lead to the destruction of the cells, for example, by attracting phagocytes or triggering the complement system.
- After an adaptive immune response occurs, long-lasting memory B cells and memory T cells may remain to confer immunity to the specific pathogen that caused the adaptive immune response. These memory cells are ready to activate an immediate response if they are exposed to the same antigen again in the future.
- Immunity may be active or passive. Active immunity occurs when the immune system has been presented with antigens that elicit an adaptive immune response. This may occur naturally as the result of an infection or artificially as the result of immunization. Active immunity may last for years or even for life.
- Passive immunity occurs without an adaptive immune response by the transfer of antibodies or activated T cells. This may occur naturally between a mother and her fetus or her nursing infant, or it may occur artificially by injection. Passive immunity lasts only as long as the antibodies or activated T cells remain alive in the body, generally just weeks or months.
- Many pathogens have evolved mechanisms to evade the adaptive immune system. For example, human immunodeficiency virus (HIV) evades the adaptive immune system by frequently changing its antigens and by forming its outer envelope from the host's cell membrane.
- An allergy is a disorder in which the immune system makes an inflammatory response to a harmless antigen. Any antigen that causes allergies is called an allergen. Common allergens include pollen, dust mites, mold, specific foods such as peanuts, insect stings, and certain medications such as aspirin.
- The prevalence of allergies has been increasing for decades, especially in developed countries where they are much more common than in developing countries. The hygiene hypothesis posits that this has occurred because humans evolved to cope with more pathogens than we now typically face in our relatively sterile environments in developed countries. As a result, the immune system "keeps busy" by attacking harmless antigens.
- Allergies occur when B cells are first activated to produce large amounts of antibodies to an otherwise harmless allergen and the antibodies attach to mast cells. On subsequent exposures to the allergen, the mast cells immediately release cytokines and histamines that cause inflammation.
- Mild allergy symptoms are frequently treated with antihistamines that counter histamines and reduce allergy symptoms. A severe systemic allergic reaction, called anaphylaxis, is a medical emergency that is usually treated with injections of epinephrine. Immunotherapy for allergies involves injecting increasing amounts of allergens to desensitize the immune system to them.
- Autoimmune diseases occur when the immune system fails to recognize the body's own molecules as self and attacks them, causing damage to tissues and organs. A family history of autoimmunity and female sex are risk factors for autoimmune diseases.
- In some autoimmune diseases, such as type I diabetes, the immune system attacks, and damages, specific body cells. In other autoimmune diseases, such as systemic lupus erythematosus, many different tissues and organs may be attacked and injured. Autoimmune diseases generally cannot be cured, but their symptoms can often be managed with drugs or other treatments.
- Immunodeficiency occurs when the immune system is not working properly, generally because one or more of its components are inactive. As a result, the immune system is unable to fight off pathogens or cancers that a normal immune system would be able to resist.
- Primarily immunodeficiency is present at birth and caused by rare genetic diseases. An example is severe combined immunodeficiency. Secondary immunodeficiency occurs because of some event or exposure experienced after birth. Possible causes include substance abuse, obesity, and malnutrition, among others.
- The most common cause of immunodeficiency in the world today is the human immunodeficiency virus (HIV), which infects and destroys helper T cells. HIV is transmitted through mucous membranes or body fluids. The virus may eventually lead to such low levels of helper T cells that opportunistic infections occur.

When this happens, the patient is diagnosed with acquired immunodeficiency syndrome (AIDS). Medications can control the multiplication of HIV in the human body but not eliminate the virus completely.

Up to this point, this book has covered body systems that carry out processes within individuals, such as the digestive, muscular, and immune systems. Read the next chapter to learn about the body system that allows humans to produce new individuals—the reproductive system.

CHAPTER SUMMARY REVIEW

1. The skin plays a role in establishing mechanical, chemical, and biological barriers that protect the body against pathogens. Give one example of how the skin contributes to each type of barrier.
2. Compare and contrast a pathogen and an allergen.
3. Describe three ways in which pathogens can enter the body.
4. For each of the following immune responses, state whether it is an innate or adaptive immune response.
   A. Inflammation
   B. Lymphocyte activation
   C. Phagocytosis by leukocytes
   D. Plasma cell maturation
5. The complement system involves the activation of several proteins to kill pathogens. Why do you think this is considered part of the innate immune system instead of the adaptive immune system?
6. Why are innate immune responses generally faster than adaptive immune responses?
7. *Rrue or False.* There is more than one type of immune system cell that can carry out phagocytosis.
8. *True or False.* Semen can act as a chemical barrier against pathogens.
9. *True or False.* Leukocytes in the innate immune system are all phagocytic.
10. Which type of immunity is triggered by vaccination?
    A. Artificially acquired active immunity
    B. Artificially acquired natural immunity
    C. Artificially acquired passive immunity
    D. Innate immunity
11. Explain how an autoimmune disease could be triggered by a pathogen.
12. What is an opportunistic infection? Name two diseases or conditions that could result in opportunistic infections. Explain your answer.
13. Match each description below with the cell type that best fits it from the list provided. Each cell type is used only once. Cell types: mast cells; B cells; killer T cells
    A. Directly destroys body cells that are cancerous or infected with a pathogen
    B. Secretes histamines and are involved in allergies
    C. Once activated, these cells multiply and their daughter cells mature into plasma cells
14. Which cell type in the immune system can be considered an "antibody factory"?
15. Besides foreign pathogens, what is one other thing that the immune system protects the body against?
16. What cell type in the immune system is infected and killed by HIV?
17. What is the difference between primary lymphoid organs and secondary lymphoid organs? Give one example of each in your answer.
18. Name two types of cells that produce cytokines in the immune system. What are two functions of cytokines in the immune system?
19. Many pathogens evade the immune system by altering their outer surface in some way. Based on what you know about the functioning of the immune system, why is this often a successful approach?
20. Major histocompatibility complex proteins:
    A. are involved in antigen-presentation by B cells
    B. help distinguish cells as self
    C. produce histamines
    D. A and B
21. What is "missing self" and how does this condition arise?
22. *True or False.* Sometimes only part of a pathogen is used to create a vaccine.
23. *True or False.* An antigen is the same thing as an allergen.

ATTRIBUTIONS

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5.8: Case Study Conclusion- Pressure and Chapter Summary
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1.2: Shared Traits of All Living Things
3.2: Discovery of Cells and Cell Theory
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6.3: Neurons
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3.3: Variation in Cells
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3.2: Discovery of Cells and Cell Theory
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3.1: Case Study- The Importance of Cells
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3.9: Cellular Respiration
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2.5: Carbohydrates
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6.5: Central Nervous System
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3.6: Cell Organelles
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5.5: Human Body Cavities
5.8: Case Study Conclusion- Pressure and Chapter Summary
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2.3: Chemical Bonding
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2.9: Energy in Chemical Reactions
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2.9: Energy in Chemical Reactions
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3.9: Cellular Respiration
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2.1: Case Study- Chemistry and Your Life
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2.5: Carbohydrates
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10.4: Disorders of the Respiratory System
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3.4: Plasma Membrane
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3.6: Cell Organelles
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4.3: Evidence for Evolution
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11.5: Blood
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2.11: Biochemical Properties of Water
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5.3: Human Cells and Tissues
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4.3: Evidence for Evolution
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4.3: Evidence for Evolution
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13.4: Innate Immune System
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2.7: Proteins
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5.3: Human Cells and Tissues
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6.3: Neurons
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5.3: Human Cells and Tissues
dense irregular connective tissue
5.3: Human Cells and Tissues
dense regular connective tissue
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1.5: Scientific Investigations
desmin
3.5: Cytoplasm and Cytoskeleton
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3.7: Cell Transport
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5.4: Human Organs and Organ Systems
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4.4: Microevolution
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1.3: Diversity of Life
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1.3: Diversity of Life
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2.8: Nucleic Acids
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3.7: Cell Transport

E

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5.3: Human Cells and Tissues
elastic connective tissue
5.3: Human Cells and Tissues
elastic fiber
5.3: Human Cells and Tissues
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3.9: Cellular Respiration
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2.2: Elements and Compounds
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2.2: Elements and Compounds
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3.9: Cellular Respiration
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2.3: Chemical Bonding
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2.9: Energy in Chemical Reactions

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7.3: Endocrine Hormones
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7.1: Case Study- Hormones and Health
7.2: Introduction to the Endocrine System
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9.3: Types of Muscle Tissue
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9.3: Types of Muscle Tissue
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5.3: Human Cells and Tissues
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3.3: Variation in Cells
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3.3: Variation in Cells
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2.9: Energy in Chemical Reactions
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7.2: Introduction to the Endocrine System
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3.8: Active Transport and Homeostasis

F

facilitated diffusion
3.7: Cell Transport
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2.6: Lipids
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3.10: Fermentation
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5.3: Human Cells and Tissues
fibrocartilage
5.3: Human Cells and Tissues
fibrous joint
8.6: Joints
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3.4: Plasma Membrane
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9.5: Physical Exercise
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4.1: Case Study- Everyday Evolution
4.8: Case Study Conclusion- Flu and Chapter Summary
follicle
7.5: Thyroid Gland
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4.4: Microevolution
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fossil record
4.6: Tools for Studying Evolution
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6.5: Central Nervous System

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4.4: Microevolution
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7.5: Thyroid Gland
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5.3: Human Cells and Tissues
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2.8: Nucleic Acids

H

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7.5: Thyroid Gland
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11.3: Heart
heart failure
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3.9: Cellular Respiration
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1.2: Shared Traits of All Living Things
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Homo
1.4: The Human Animal
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Homo sapiens
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hypotonic
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I

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immune system
13: Immune System
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13.5: Adaptive Immune System
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13.6: Disorders of the Immune System
immunotherapy
13.6: Disorders of the Immune System
13.8: Case Study Conclusion- Lymphoma and Chapter Summary

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infundibulum
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innate immune system
13.4: Innate Immune System
insulin
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integumentary
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ion
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isotonic
3.7: Cell Transport
9.4: Muscle Contraction

J

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8.6: Joints
joints
8.6: Joints

K

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3.9: Cellular Respiration

L

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Lactase persistence
4.7: Adaptation in Humans
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13.3: Lymphatic System
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M

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4.5: Macroevolution
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8.3: Divisions of the Skeletal System
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2.2: Elements and Compounds
maxillae
8.3: Divisions of the Skeletal System
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6.5: Central Nervous System
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3.7: Cell Transport
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5.5: Human Body Cavities
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2.10: Chemical Reactions in Living Things
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13.7: Human Microbiome
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4.4: Microevolution
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3.5: Cytoplasm and Cytoskeleton
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6.6: Peripheral Nervous System
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2.2: Elements and Compounds
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2.4: Biochemical Compounds
Monosaccharide
2.4: Biochemical Compounds
2.5: Carbohydrates
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1.3: Diversity of Life
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6.6: Peripheral Nervous System
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6.3: Neurons
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5.3: Human Cells and Tissues
mucus
5.3: Human Cells and Tissues
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9.1: Case Study- Muscles and Movement
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9.4: Muscle Contraction
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5.3: Human Cells and Tissues
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9.6: Disorders of the Muscular System
muscular system
5.4: Human Organs and Organ Systems
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9.6: Disorders of the Muscular System
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9.6: Disorders of the Muscular System
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6.3: Neurons
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9.2: Introduction to the Muscular System
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myofibril
9.4: Muscle Contraction
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9.5: Physical Exercise

N

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10.2: Structure and Function of the Respiratory System
natural selection
4.2: Darwin, Wallace, and the Theory of Evolution by Natural Selection
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6.4: Nerve Impulses
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5.3: Human Cells and Tissues

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5.4: Human Organs and Organ Systems
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neuroimmune system
13.2: Introduction to the Immune System
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9.6: Disorders of the Muscular System
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9.4: Muscle Contraction
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6.3: Neurons
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neutron
2.2: Elements and Compounds
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10.5: Smoking and Health
nitrogenous base
2.8: Nucleic Acids
nodes of Ranvier
6.3: Neurons
nuclear force
2.2: Elements and Compounds
nucleic acids
2.4: Biochemical Compounds
2.8: Nucleic Acids
nucleoplasm
3.5: Cytoplasm and Cytoskeleton
nucleotide
2.8: Nucleic Acids
nucleus
3.6: Cell Organelles

O

occipital lobe
6.5: Central Nervous System
organ system
5.6: Interaction of Organ Systems
5.8: Case Study Conclusion- Pressure and Chapter Summary
organelle
3.3: Variation in Cells
3.6: Cell Organelles
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3.2: Discovery of Cells and Cell Theory
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5.2: Organization of the Body
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3.7: Cell Transport
ossification
8.5: Bone Growth, Remodeling, and Repair
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8.7: Disorders of the Skeletal System
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8.2: Introduction to the Skeletal System
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osteocyte
8.4: Structure of Bone
osteogenic cells
8.4: Structure of Bone
osteon
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Oxydative phosphorylation
3.9: Cellular Respiration
oxytocin
7.4: Pituitary Gland

P

pacemaker
11.3: Heart
paleontologist
4.3: Evidence for Evolution
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7.7: Pancreas
pancreatic islet
7.7: Pancreas
Pancreatitis
7.7: Pancreas
paralysis
6.5: Central Nervous System
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6.5: Central Nervous System
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9.6: Disorders of the Muscular System
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13.5: Adaptive Immune System
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3.7: Cell Transport
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9.3: Types of Muscle Tissue
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11.7: Cardiovascular Disease
peripheral immune system
13.2: Introduction to the Immune System
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6.2: Introduction to the Nervous System
6.6: Peripheral Nervous System
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9.2: Introduction to the Muscular System
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3.8: Active Transport and Homeostasis
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10.2: Structure and Function of the Respiratory System
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2.8: Nucleic Acids
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2.6: Lipids
phospholipid bilayer
2.6: Lipids
3.4: Plasma Membrane
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3.4: Plasma Membrane
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3.9: Cellular Respiration
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1.3: Diversity of Life
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1.3: Diversity of Life
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5.2: Organization of the Body
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7.4: Pituitary Gland
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plasma membrane
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3.4: Plasma Membrane
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2.3: Chemical Bonding
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2.11: Biochemical Properties of Water
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polynucleotide
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polysaccharide
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4.4: Microevolution
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punctuated equilibrium
4.5: Macroevolution

Q

qualitative data
1.5: Scientific Investigations
quantitative data
1.5: Scientific Investigations

R

reactant
2.9: Energy in Chemical Reactions
2.10: Chemical Reactions in Living Things
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reticular fibers
5.3: Human Cells and Tissues
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rib cage
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ribose sugar
2.8: Nucleic Acids
ribosome
3.2: Discovery of Cells and Cell Theory
ribosomes
3.6: Cell Organelles
RNA
2.8: Nucleic Acids
rough endoplasmic reticulum
3.6: Cell Organelles

S

sarcomere
9.3: Types of Muscle Tissue
Saturated fatty acid
2.6: Lipids
Schistosoma
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scientific investigation
1.5: Scientific Investigations
scientific method
1.5: Scientific Investigations
secondary active transport
3.8: Active Transport and Homeostasis
secondhand smoke
10.5: Smoking and Health
sensory nerves
6.6: Peripheral Nervous System
sensory neurons
6.3: Neurons
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4.4: Microevolution
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3.7: Cell Transport
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11.3: Heart
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smooth endoplasmic reticulum
3.6: Cell Organelles
smooth muscle
5.3: Human Cells and Tissues
sodium potassium pump
3.8: Active Transport and Homeostasis
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3.7: Cell Transport
solution
2.12: Acids and Bases
3.7: Cell Transport
solvent
3.7: Cell Transport
somatic nervous system
6.6: Peripheral Nervous System
somatostatin
7.7: Pancreas
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4.5: Macroevolution
species
1.3: Diversity of Life
1.6: Case Study Conclusion- Inhabitants and Chapter Summary
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5.5: Human Body Cavities
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spongy bone tissue
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3.9: Cellular Respiration
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2.5: Carbohydrates
steroid hormone
7.3: Endocrine Hormones
steroids
2.6: Lipids
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6.5: Central Nervous System
9.4: Muscle Contraction
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synapse
6.4: Nerve Impulses
synovial joint
8.6: Joints
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11.3: Heart

T

T cell
13.5: Adaptive Immune System

target cell
7.3: Endocrine Hormones
taxa
1.3: Diversity of Life
1.6: Case Study Conclusion- Inhabitants and Chapter Summary
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1.3: Diversity of Life
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6.5: Central Nervous System
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7.5: Thyroid Gland
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3.9: Cellular Respiration
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9.4: Muscle Contraction
triglyceride
2.6: Lipids
triiodothyronine
7.5: Thyroid Gland
tubulin
3.6: Cell Organelles
type 2 diabetes
7.7: Pancreas
type I diabetes mellitus
7.7: Pancreas

U

underdraining
5.8: Case Study Conclusion- Pressure and Chapter Summary
unsaturated fatty acid
2.6: Lipids
uracil
2.8: Nucleic Acids
urinary system
5.4: Human Organs and Organ Systems

V

vacuole
3.6: Cell Organelles
varicose veins
11.4: Blood Vessels
vasodilation
11.4: Blood Vessels
vasopressin
7.4: Pituitary Gland
ventilation
10.3: Breathing
ventral cavity
5.5: Human Body Cavities
ventricle
11.3: Heart
vertebrae
8.3: Divisions of the Skeletal System
vesicle
3.6: Cell Organelles
vesicular transport
3.8: Active Transport and Homeostasis
vestigial structure
4.3: Evidence for Evolution
vimentin
3.5: Cytoplasm and Cytoskeleton
vital organ
5.4: Human Organs and Organ Systems

W

white blood cell
11.5: Blood
white matter
5.3: Human Cells and Tissues

Glossary

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