Human Biology

By:
Willy Cushwa

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< http://cnx.org/content/col11903/1.3/ >

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Preface[1]

Welcome to *Human Biology*, a textbook created utilizing OpenStax resources. This textbook has been created with several goals in mind: accessibility, customization, and student engagement—all while encouraging students toward high levels of academic scholarship. Students will find that this textbook offers a strong introduction to human biology in an accessible format.

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Cost

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[1] This content is available online at <http://cnx.org/content/m57955/1.5/>.

About Our Team

Concepts of Biology would not be possible if not for the tremendous contributions of the authors and community reviewing team

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Table 2

Chapter 1

Introduction to Human Biology and the Scientific Method

1.1 Introduction[1]

Blood Pressure

Figure 1.1: A basic understanding of medical procedures allows you to better understand information collected by medical professionals. (credit: Bryan Mason/flickr)

[1] This content is available online at <http://cnx.org/content/m57956/1.3/>.

NOTE: After studying this chapter, you will be able to:

- Describe the structure of the body, from simplest to most complex, in terms of the six levels of organization
- List characteristics of human life
- Define homeostasis and explain its importance to normal human functioning

Though you may approach a course in human biology strictly as a requirement for obtaining your degree, the knowledge you gain in this course will serve you well in many aspects of your life. An understanding of your body and how it works can benefit your own health. Familiarity with the human body can help you make healthful choices and prompt you to take appropriate action when signs of illness arise. Your knowledge in this field will help you understand news about nutrition, medications, medical devices, and procedures. This knowledge will also help you understand genetic and infectious diseases. At some point, everyone will have a problem with some aspect of his or her body and your knowledge can help you to be a better parent, spouse, partner, friend, or caregiver.

This chapter begins with an overview of anatomy and physiology. It then covers the characteristics of life and how the body works to maintain stable conditions.

1.2 Structural Organization of the Human Body[2]

Before you begin to study the different structures and functions of the human body, it is helpful to consider its basic architecture; that is, how its smallest parts are assembled into larger structures. It is convenient to consider the structures of the body in terms of fundamental levels of organization that increase in complexity: subatomic particles (e.g. protons, neutrons, and electrons), atoms, molecules, macromolecules (e.g. carbohydrates, lipids, proteins, and nucleic acids) organelles, cells, tissues, organs, organ systems, and organisms (Figure 1.2 (Levels of Structural Organization of the Human Body)).

[2]This content is available online at <http://cnx.org/content/m57957/1.2/>.

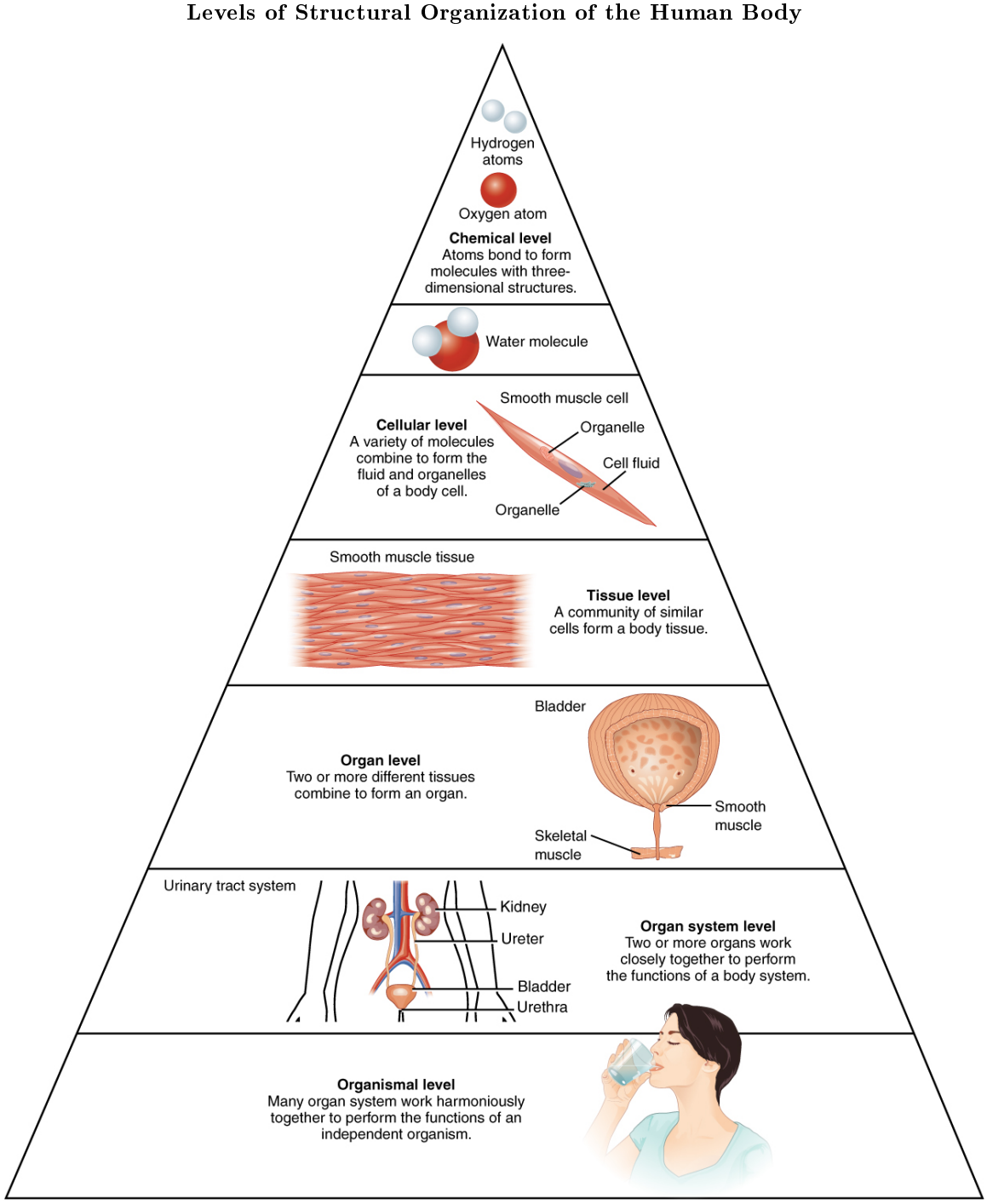


Figure 1.2: The organization of the body often is discussed in terms of six distinct levels of increasing complexity, from the smallest chemical building blocks to a unique human organism. Note: The macromolecule level (which is located between molecules and organelles) isn't shown.

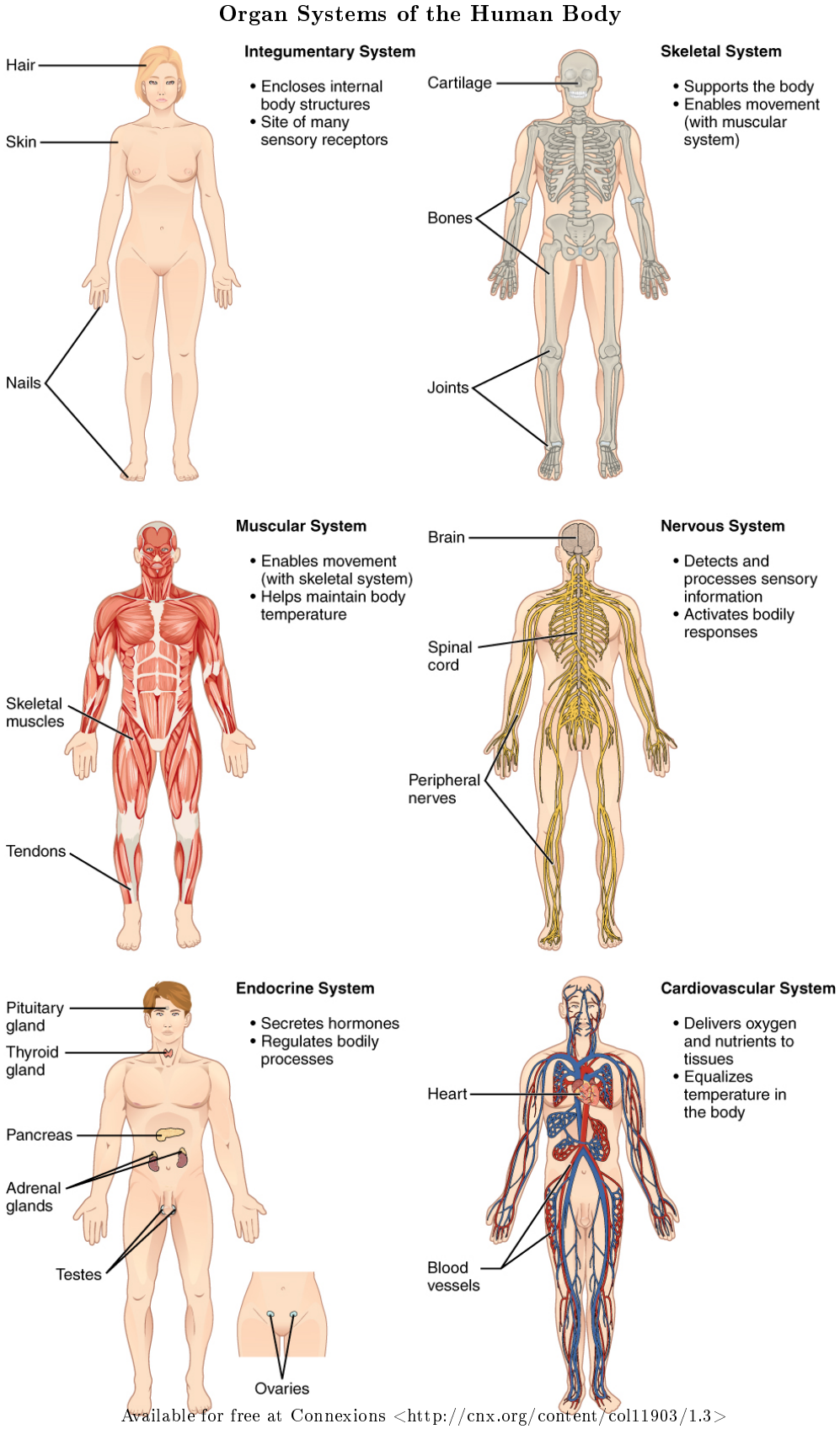
1.2.1 The Levels of Organization

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

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

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

Figures 2 and 3 below show the eleven distinct organ systems in the human body. Assigning organs to organ systems can be imprecise since organs that "belong" to one system can also have functions integral to another system. In fact, most organs contribute to more than one system. In this course, we will discuss some, but not all, of these organ systems.



Available for free at Connexions <http://cnx.org/content/col11903/1.3>

Figure 1.3: Organs that work together are grouped into organ systems.

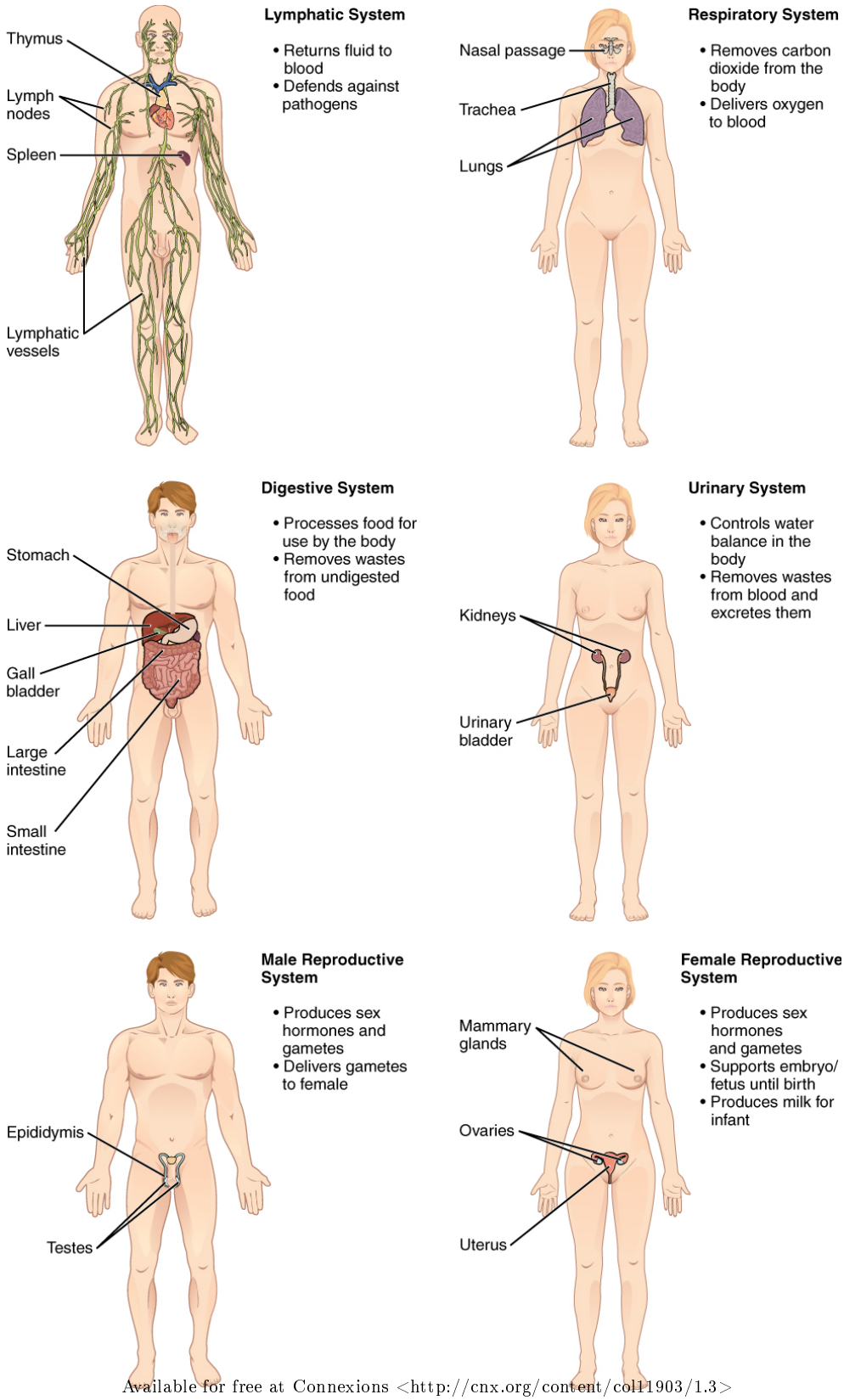


Figure 1.4: Organs that work together are grouped into organ systems.

The organism level is the highest level of organization. An **organism** is a living being that has a cellular structure and that can independently perform all physiologic functions necessary for life. In multicellular organisms, including humans, all cells, tissues, organs, and organ systems of the body work together to maintain the life and health of the organism.

1.2.2 Chapter Review

Life processes of the human body are maintained at several levels of structural organization. These include the chemical, cellular, tissue, organ, organ system, and the organism level. Higher levels of organization are built from lower levels. Therefore, subatomic particles combine to produce atoms, atoms combine to produce molecules, molecules combine to produce macromolecules, macromolecules contribute to the formation of organelles which combine to form cells, cells combine to form tissues, tissues combine to form organs, organs combine to form organ systems, and organ systems combine to form organisms.

1.2.3 Review Questions

Exercise 1.2.1 *(Solution on p. 26.)*

The smallest independently functioning unit of an organism is a(n) _____.

a. cell
b. molecule
c. organ
d. tissue

Exercise 1.2.2 *(Solution on p. 26.)*

A collection of similar tissues that performs a specific function is an _____.

a. organ
b. organelle
c. organism
d. organ system

Exercise 1.2.3 *(Solution on p. 26.)*

The body system responsible for processing food, absorbing nutrients, and expelling wastes is the _____.

a. cardiovascular system
b. endocrine system
c. muscular system
d. digestive system

1.2.4 CRITICAL THINKING QUESTIONS

Exercise 1.2.4 *(Solution on p. 26.)*

Name the six levels of organization of the human body.

Exercise 1.2.5 *(Solution on p. 26.)*

The female ovaries and the male testes are a part of which body system? Can these organs be members of more than one organ system? Why or why not?

1.3 Functions of Human Life[3]

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

1.3.1 Organization

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

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

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

1.3.2 Metabolism

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

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

Taken together, these two processes are called metabolism. **Metabolism** is the sum of all anabolic and catabolic reactions that take place in the body (Figure 1.5 (Metabolism)). Both anabolism and catabolism occur simultaneously and continuously to keep you alive.

[3] This content is available online at <http://cnx.org/content/m57958/1.2/>.

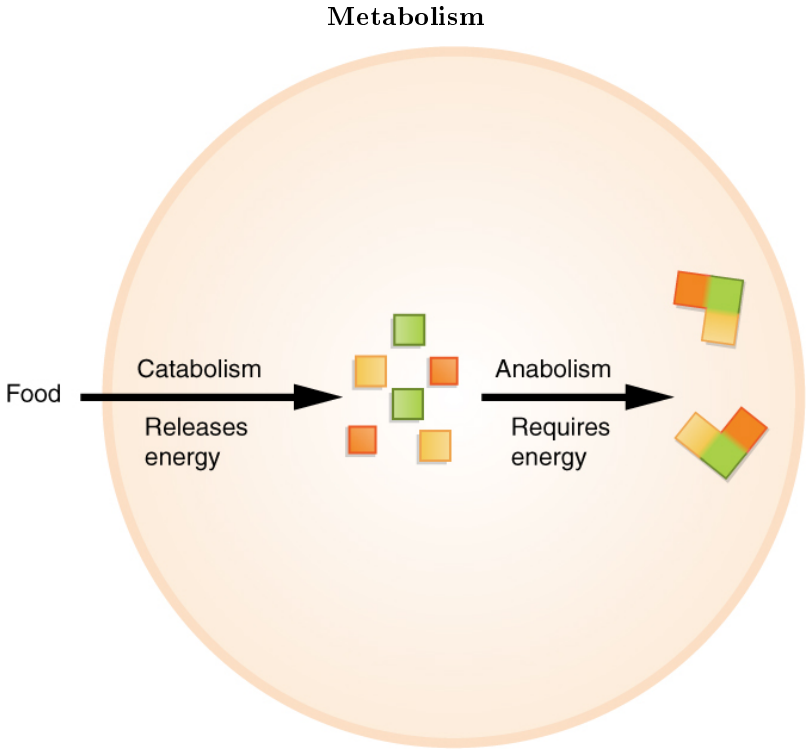


Figure 1.5: Anabolic reactions are building reactions, and they consume energy. Catabolic reactions break materials down and release energy. Metabolism includes both anabolic and catabolic reactions.

Every cell in your body makes use of a chemical compound, **adenosine triphosphate (ATP)**, to store and release energy. Think of ATP as the energy "currency" of the cell. If energy is needed for something to happen in the cell, then ATP is used to "pay the energy bill". The cell stores energy in the synthesis (anabolism) of ATP, then moves the ATP molecules to the location where energy is needed to fuel cellular activities. Then the ATP is broken down (catabolism) and a controlled amount of energy is released, which is used by the cell to perform a particular job.

1.3.3 Responsiveness

Responsiveness is the ability of an organism to adjust to changes in its internal and external environments. An example of responsiveness to external stimuli could include moving toward sources of food and water and away from perceived dangers. Changes in an organism's internal environment, such as increased body temperature, can cause the responses of sweating and the dilation of blood vessels in the skin in order to decrease body temperature, as shown by the runners in Figure 1.6 (Marathon Runners).

1.3.4 Homeostasis

To function properly, cells require appropriate conditions such as proper temperature, pH, and concentrations of diverse chemicals. These conditions may, however, change from one moment to the next. Organisms are able to maintain internal conditions within a narrow range almost constantly, despite environmental changes,

through a process called homeostasis or "steady state"—the ability of an organism to maintain constant internal conditions. For example, many organisms regulate their body temperature in a process known as thermoregulation. Organisms that live in cold climates, such as the polar bear, have body structures that help them withstand low temperatures and conserve body heat. In hot climates, organisms have methods (such as perspiration in humans or panting in dogs) that help them to shed excess body heat. As we discuss organ systems, the concept of homeostasis will be critically important to remember.

1.3.5 Adaptation

All living organisms exhibit a "fit" to their environment. Biologists refer to this fit as adaptation and it is a consequence of evolution by natural selection (i.e. survival of the fittest), which operates in every lineage of reproducing organisms. Examples of adaptations are diverse and unique, from heat-resistant bacteria that live in boiling hot springs to the tongue length of a nectar-feeding moth that matches the size of the flower from which it feeds. All adaptations enhance the reproductive potential of the individual exhibiting them, including their ability to survive to reproduce. Adaptations are not constant. As an environment changes, natural selection causes the characteristics of the individuals in a population to track those changes.

1.3.6 Movement

Human movement includes not only actions at the joints of the body, but also the motion of individual organs and even individual cells. As you read these words, red and white blood cells are moving throughout your body, muscle cells are contracting and relaxing to maintain your posture and to focus your vision, and glands are secreting chemicals to regulate body functions. Your body is coordinating the action of entire muscle groups to enable you to move air into and out of your lungs, to push blood throughout your body, and to propel the food you have eaten through your digestive tract. Consciously, of course, you contract your skeletal muscles to move the bones of your skeleton to get from one place to another (as the runners are doing in Figure 1.6 (Marathon Runners)), and to carry out all of the activities of your daily life.

Marathon Runners

Figure 1.6: Runners demonstrate two characteristics of living humans—responsiveness and movement. Anatomic structures and physiological processes allow runners to coordinate the action of muscle groups and sweat in response to rising internal body temperature. (credit: Phil Roeder/flickr)

1.3.7 Development, growth and reproduction

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

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

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

1.3.8 Chapter Review

Most processes that occur in the human body are not consciously controlled. They occur continuously to build, maintain, and sustain life. These processes include: organization, in terms of the maintenance

of essential body boundaries; metabolism, including energy transfer via anabolic and catabolic reactions; responsiveness; homeostasis; adaptation; movement; and growth, differentiation, reproduction, and renewal.

1.3.9 Interactive Link Questions

Exercise 1.3.1 *(Solution on p. 26.)*

View this animation[4] to learn more about metabolic processes. What kind of catabolism occurs in the heart?

1.3.10 Review Questions

Exercise 1.3.2 *(Solution on p. 26.)*

Metabolism can be defined as the _ _ _ _ _ _ _ _ _.

a. adjustment by an organism to external or internal changes
b. process whereby all unspecialized cells become specialized to perform distinct functions
c. process whereby new cells are formed to replace worn-out cells
d. sum of all chemical reactions in an organism

Exercise 1.3.3 *(Solution on p. 26.)*

Adenosine triphosphate (ATP) is an important molecule because it _ _ _ _ _ _ _ _ _.

a. is the result of catabolism
b. releases energy in uncontrolled bursts
c. provides energy for use by body cells
d. All of the above

Exercise 1.3.4 *(Solution on p. 26.)*

Cancer cells can be characterized as "generic" cells that perform no specialized body function. Thus cancer cells lack _ _ _ _ _ _ _ _ _.

a. differentiation
b. reproduction
c. responsiveness
d. both reproduction and responsiveness

1.3.11 CRITICAL THINKING QUESTIONS

Exercise 1.3.5 *(Solution on p. 26.)*

Explain why the smell of smoke when you are sitting at a campfire does not trigger alarm, but the smell of smoke in your residence hall does.

Exercise 1.3.6 *(Solution on p. 26.)*

Identify three different ways that growth can occur in the human body.

[4] http://openstaxcollege.org/l/metabolic

1.4 Classification of Organisms[5]

1.4.1 The Diversity of Life

In the 18th century, a scientist named Carl Linnaeus first proposed organizing the known species of organisms into a hierarchical taxonomy. In this system, species that are most similar to each other are put together within a grouping known as a genus. Furthermore, similar genera (the plural of genus) are put together within a family. This grouping continues until all organisms are collected together into groups at the highest level. The current taxonomic system now has eight levels in its hierarchy, from lowest to highest: species, genus, family, order, class, phylum, kingdom, domain. Thus species are grouped within genera, genera are grouped within families, families are grouped within orders, and so on (Figure 1.7).

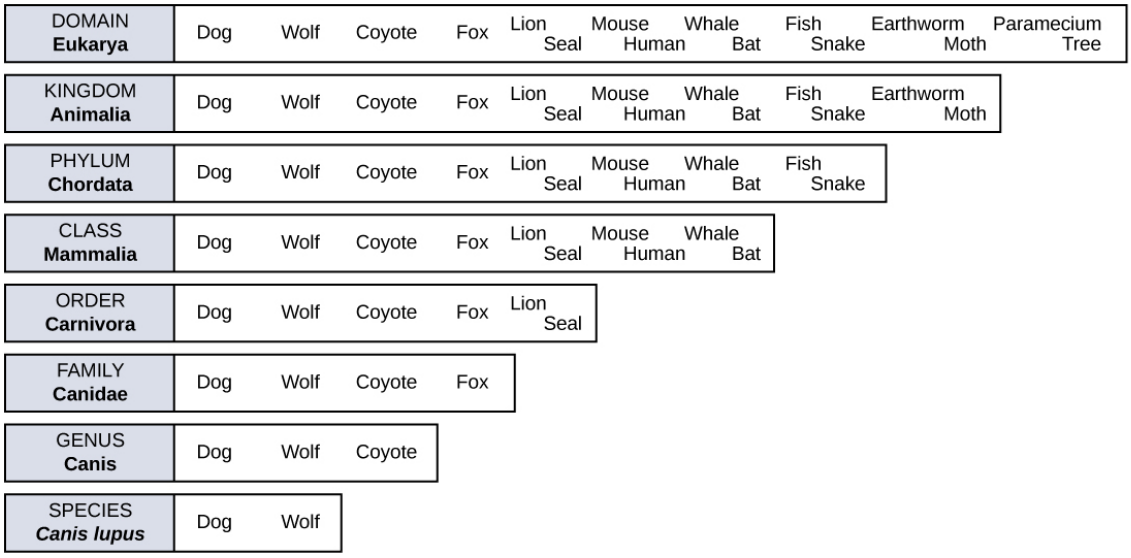


Figure 1.7: This diagram shows the levels of taxonomic hierarchy for a dog, from the broadest category—domain—to the most specific—species. Notice that humans and dogs diverge at the level of order. Humans are classified in the following levels: order-Primates; family-Hominidae; genus: Homo; species- Homo sapiens; scientific/binomial name: Homo sapiens.

In addition to the hierarchical taxonomic system, Linnaeus was the first to name organisms using two unique names, now called the binomial naming system. Before Linnaeus, the use of common names to refer to organisms caused confusion because there were regional differences in these common names. Binomial names (also called scientific names) consist of the genus name (which is capitalized) and the species name (all lower-case). Both names are set in italics when they are printed. Every species is given a unique binomial which is recognized the world over, so that a scientist in any location can know which organism is being referred to. For example, the North American blue jay is known uniquely as *Cyanocitta cristata*. Our own species is *Homo sapiens*.

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[5]This content is available online at <http://cnx.org/content/m57961/1.2/>.

1.5 The Process of Science[6]

Like geology, physics, and chemistry, biology is a science that gathers knowledge about the natural world. Specifically, biology is the study of life. The discoveries of biology are made by a community of researchers who work individually and together using agreed-on methods. In this sense, biology, like all sciences is a social enterprise like politics or the arts. The methods of science include careful observation, record keeping, logical and mathematical reasoning, experimentation, and submitting conclusions to the scrutiny of others. Science also requires considerable imagination and creativity; a well-designed experiment is commonly described as elegant, or beautiful. Like politics, science has considerable practical implications and some science is dedicated to practical applications, such as the prevention of disease (see Figure 1.8). Other science proceeds largely motivated by curiosity. Whatever its goal, there is no doubt that science, including biology, has transformed human existence and will continue to do so.

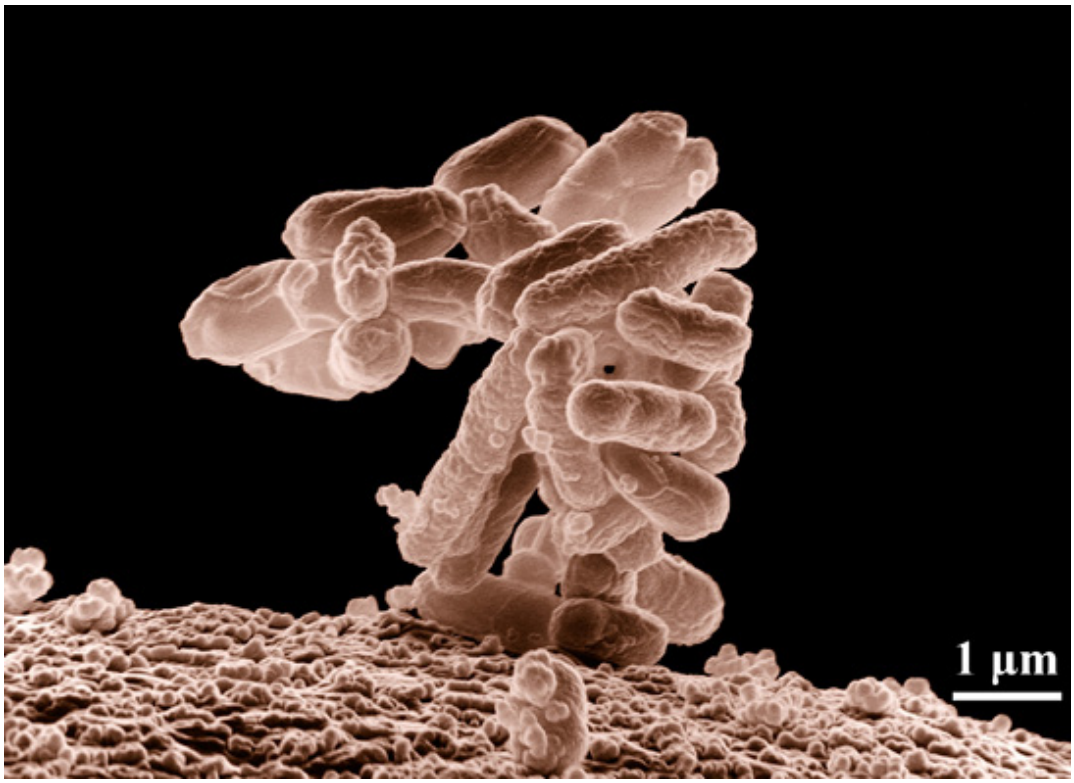

Figure 1.8: Biologists may choose to study *Escherichia coli* (*E. coli*), a bacterium that is a normal resident of our digestive tracts but which is also sometimes responsible for disease outbreaks. In this micrograph, the bacterium is visualized using a scanning electron microscope and digital colorization. (credit: Eric Erbe; digital colorization by Christopher Pooley, USDA-ARS)

[6] This content is available online at <http://cnx.org/content/m57960/1.2/>.

1.5.1 The Nature of Science

Biology is a science, but what exactly is science? What does the study of biology share with other scientific disciplines? **Science** (from the Latin *scientia*, meaning "knowledge") can be defined as knowledge about the natural world.

Science is a very specific way of learning, or knowing, about the world. The history of the past 500 years demonstrates that science is a very powerful way of knowing about the world; it is largely responsible for the technological revolutions that have taken place during this time. There are however, areas of knowledge and human experience that the methods of science cannot be applied to. These include such things as answering purely moral questions, aesthetic questions, or what can be generally categorized as spiritual questions. Science has cannot investigate these areas because they are outside the realm of material phenomena, the phenomena of matter and energy, and cannot be observed and measured.

The **scientific method** is a method of research with defined steps that include experiments and careful observation. The steps of the scientific method will be examined in detail later, but one of the most important aspects of this method is the testing of hypotheses. A **hypothesis** is a suggested explanation for an event, which can be tested. Hypotheses, or tentative explanations, are generally produced within the context of a **scientific theory**. A scientific theory is a generally accepted, thoroughly tested and confirmed explanation for a set of observations or phenomena. Scientific theory is the foundation of scientific knowledge. In addition, in many scientific disciplines (less so in biology) there are **scientific laws**, often expressed in mathematical formulas, which describe how elements of nature will behave under certain specific conditions. There is not an evolution of hypotheses through theories to laws as if they represented some increase in certainty about the world. Hypotheses are the day-to-day material that scientists work with and they are developed within the context of theories. Laws are concise descriptions of parts of the world that are amenable to formulaic or mathematical description.

1.5.1.1 Scientific Inquiry

One thing is common to all forms of science: an ultimate goal "to know." Curiosity and inquiry are the driving forces for the development of science. Scientists seek to understand the world and the way it operates. There are two main pathways of scientific study: descriptive science and hypothesis-based science. **Descriptive** (or discovery) **science** aims to observe, explore, and discover, while **hypothesis-based science** begins with a specific question or problem and a potential answer or solution that can be tested. The boundary between these two forms of study is often blurred, because most scientific endeavors combine both approaches. Observations lead to questions, questions lead to forming a hypothesis as a possible answer to those questions, and then the hypothesis is tested. Thus, descriptive science and hypothesis-based science are in continuous dialogue.

1.5.2 Hypothesis Testing

Biologists study the living world by posing questions about it and seeking science-based responses. This approach is common to other sciences as well and is often referred to as the scientific method. The scientific method was used even in ancient times, but it was first documented by England's Sir Francis Bacon (1561–1626) (Figure 1.9). The scientific method is not exclusively used by biologists but can be applied to almost anything as a logical problem-solving method.

Figure 1.9: Sir Francis Bacon is credited with being the first to document the scientific method.

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

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

Once a hypothesis has been selected, a prediction may be made. A prediction is similar to a hypothesis but it typically has the format "If . . . then . . . ." For example, the prediction for the first hypothesis might be, "*If* the student turns on the air conditioning, *then* the classroom will no longer be too warm. Notice that the portion of the statement after the word "then" indicates what will be observed if the hypothesis is correct.

A hypothesis must be testable to ensure that it is valid. For example, a hypothesis that depends on what a bear thinks is not testable, because it can never be known what a bear thinks. It should also

be **falsifiable**, meaning that it can be shown to be incorrect by experimental results. An example of an unfalsifiable hypothesis is "Botticelli's *Birth of Venus* is beautiful." There is no experiment that might show this statement to be false. To test a hypothesis, a researcher will conduct one or more experiments designed to eliminate one or more of the hypotheses. This is important. A hypothesis can be shown to be incorrect, or eliminated, but it can never be proven. Science does not deal in proofs like mathematics. If an experiment fails to show a hypothesis is incorrect, then we find support for that explanation, but this is not to say that down the road a better explanation will not be found, or a more carefully designed experiment will be found to falsify the hypothesis.

Each experiment will have one or more variables and one or more controls. A **variable** is any part of the experiment that can vary or change during the experiment. There are three types of variables we will discuss: Independent variable(s) of interest, independent variables not of interest (i.e. controlled variables), and dependent variables. Typically, basic experiments will only have one independent variable of interest (i.e. the factor that is being changed in a deliberate manner to determine if it has an impact on the dependent variable). The dependent variable is the one being measured. For example, if an experiment is designed to test the effects of three different brands of plant fertilizer on plant growth, the independent variable of interest is the brand of fertilizer and the dependent variable is plant growth. It is important to realize that independent variables other than the brand of fertilizer could affect plant growth: soil moisture content, amount of sunlight, temperature, etc. In order to prevent these variables from impacting the results, they are "controlled", meaning they are not allowed to change during the experiment. In other words, plants treated with all three brands of fertilizer should have the same amounts of water and sunlight to prevent these variables from interacting with the independent variable of interest. A **control group** is a part of the experiment that does not change and provides a baseline of comparison to determine the effect of the independent variable of interest on the dependent variable. Look for the variables and controls in the example that follows. An experiment is conducted to test the hypothesis that phosphate limits the growth of algae in freshwater ponds. A series of artificial ponds are filled with water and half of them are treated by adding phosphate each week, while the other half are treated by adding a salt that is known not to be used by algae. The independent variable of interest here is the phosphate (or lack of phosphate), the experimental or treatment cases are the ponds with added phosphate and the control ponds are those with something inert added, such as the salt. Just adding something is also a control against the possibility that adding extra matter to the pond has an effect. If the treated ponds show lesser growth of algae, then we have found support for our hypothesis. If they do not, then we reject our hypothesis. Be aware that rejecting one hypothesis does not determine whether or not the other hypotheses can be accepted; it simply eliminates one hypothesis that is not valid (Figure 1.10). Using the scientific method, the hypotheses that are inconsistent with experimental data are rejected. In human drug trials, it is common for the control group to be given a placebo (i.e. "sugar pill") so that individuals both groups (experimental and control) are taking a pill. Otherwise, the act of taking a pill would be a variable that wasn't controlled. It is also common for neither the subjects nor the researchers directly working with them to know which group is receiving the placebo. This feature of experiments, called a double-blind design, is included to prevent any bias from influencing the results.

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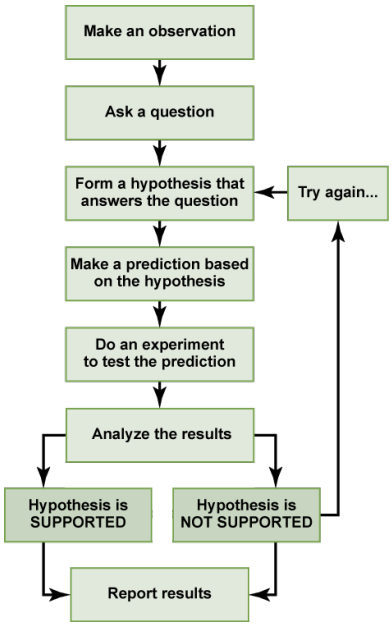

Figure 1.10: The scientific method is a series of defined steps that include experiments and careful observation. If a hypothesis is not supported by data, a new hypothesis can be proposed.

In practice, the scientific method is not as rigid and structured as it might at first appear. Sometimes an experiment leads to conclusions that favor a change in approach; often, an experiment brings entirely new scientific questions to the puzzle. Many times, science does not operate in a linear fashion; instead, scientists continually draw inferences and make generalizations, finding patterns as their research proceeds. Scientific reasoning is more complex than the scientific method alone suggests.

1.5.3 Reporting Scientific Work

Whether scientific research is basic science or applied science, scientists must share their findings for other researchers to expand and build upon their discoveries. Communication and collaboration within and between sub disciplines of science are key to the advancement of knowledge in science. For this reason, an important aspect of a scientist's work is disseminating results and communicating with peers. Scientists can share results by presenting them at a scientific meeting or conference, but this approach can reach only the limited few who are present. Instead, most scientists present their results in peer-reviewed articles that are published in scientific journals. **Peer-reviewed articles** are scientific papers that are reviewed, usually anonymously by a scientist's colleagues, or peers. These colleagues are qualified individuals, often experts in the same research area, who judge whether or not the scientist's work is suitable for publication. The process of peer review helps to ensure that the research described in a scientific paper or grant proposal is original, significant, logical, and thorough. Grant proposals, which are requests for research funding, are also subject to peer review. Scientists publish their work so other scientists can reproduce their experiments under similar or different conditions to expand on the findings. The experimental results must be consistent with the findings of other scientists.

There are many journals and the popular press that do not use a peer-review system. A large number of online open-access journals, journals with articles available without cost, are now available many of which use rigorous peer-review systems, but some of which do not. Results of any studies published in these forums without peer review are not reliable and should not form the basis for other scientific work. In one exception,

journals may allow a researcher to cite a personal communication from another researcher about unpublished results with the cited author's permission.

1.5.4 Section Summary

A hypothesis is a tentative explanation for an observation. A scientific theory is a well-tested and consistently verified explanation for a set of observations or phenomena. A scientific law is a description, often in the form of a mathematical formula, of the behavior of an aspect of nature under certain circumstances. The common thread throughout scientific research is the use of the scientific method. Scientists present their results in peer-reviewed scientific papers published in scientific journals.

1.5.5 Art Connections

Exercise 1.5.1 ***(Solution on p. 26.)***

Figure 1.10 In the example below, the scientific method is used to solve an everyday problem. Which part in the example below is the hypothesis? Which is the prediction? Based on the results of the experiment, is the hypothesis supported? If it is not supported, propose some alternative hypotheses.

1. My toaster doesn't toast my bread.
2. Why doesn't my toaster work?
3. There is something wrong with the electrical outlet.
4. If something is wrong with the outlet, my coffeemaker also won't work when plugged into it.
5. I plug my coffeemaker into the outlet.
6. My coffeemaker works.

1.5.6 Multiple Choice

Exercise 1.5.2 ***(Solution on p. 26.)***

A suggested and testable explanation for an event is called a _____.

a. hypothesis
b. variable
c. theory
d. control

Exercise 1.5.3 ***(Solution on p. 26.)***

Which of the following statements correct describes a double-blind experiment?

a. Both the test subjects and the researchers in direct contact with them know who is in the experimental group and who is in the control group.
b. The test subjects but not the researchers in direct contact with them know who is in the experimental group and who is in the control group.
c. The researchers in direct contact with the test subjects, but not the test subjects, know who is in the experimental group and who is in the control group.
d. Neither the test subjects or the researchers in direct contact with them know who is in the experimental group and who is in the control group.

1.5.7 Free Response

Exercise 1.5.4 *(Solution on p. 26.)*

A research group is testing a new disease vaccine on mice. Which group (experimental or control) should receive the placebo? Explain the rationale for your response.

Solutions to Exercises in Chapter 1

to Exercise 1.2.1 (p. 12)
A
to Exercise 1.2.2 (p. 12)
A
to Exercise 1.2.3 (p. 12)
D
to Exercise 1.2.4 (p. 12)
Chemical, cellular, tissue, organ, organ system, organism.
to Exercise 1.2.5 (p. 12)
The female ovaries and the male testes are parts of the reproductive system. But they also secrete hormones, as does the endocrine system, therefore ovaries and testes function within both the endocrine and reproductive systems.
to Exercise 1.3.1 (p. 17)
Fatty acid catabolism.
to Exercise 1.3.2 (p. 17)
D
to Exercise 1.3.3 (p. 17)
C
to Exercise 1.3.4 (p. 17)
A
to Exercise 1.3.5 (p. 17)
When you are sitting at a campfire, your sense of smell adapts to the smell of smoke. Only if that smell were to suddenly and dramatically intensify would you be likely to notice and respond. In contrast, the smell of even a trace of smoke would be new and highly unusual in your residence hall, and would be perceived as danger.
to Exercise 1.3.6 (p. 17)
Growth can occur by increasing the number of existing cells, increasing the size of existing cells, or increasing the amount of non-cellular material around cells.
to Exercise 1.5.1 (p. 24)
Figure 1.10 The hypothesis is #3 (there is something wrong with the electrical outlet), and the prediction is #4 (if something is wrong with the outlet, then the coffeemaker also won't work when plugged into the outlet). The original hypothesis is not supported, as the coffee maker works when plugged into the outlet. Alternative hypotheses may include (1) the toaster might be broken or (2) the toaster wasn't turned on.
to Exercise 1.5.2 (p. 24)
A
to Exercise 1.5.3 (p. 24)
D
to Exercise 1.5.4 (p. 25)
The control group should receive the placebo, or injection without the active components of the vaccine. The response in the control group will provide a baseline of comparison for interpreting the results of the experimental group.

Chapter 2

Chemistry and Life

2.1 Introduction[1]

Figure 2.1: Foods such as bread, fruit, and cheese are rich sources of biological macromolecules, such as starch, fiber, triglycerides, and polypeptides/proteins. (credit: modification of work by Bengt Nyman)

[1] This content is available online at <http://cnx.org/content/m57962/1.1/>.

The elements carbon, hydrogen, nitrogen, oxygen, sulfur, and phosphorus are the key building blocks of the chemicals found in living things. They form the carbohydrates, nucleic acids, proteins, and lipids (all of which will be defined later in this chapter) that are the fundamental molecular components of all organisms. In this chapter, we will discuss these important building blocks and learn how the unique properties of the atoms of different elements affect their interactions with other atoms to form the molecules of life.

Food provides an organism with nutrients—the matter it needs to survive. Many of these critical nutrients come in the form of biological macromolecules, or large molecules necessary for life. These macromolecules are built from different combinations of smaller organic molecules. What specific types of biological macromolecules do living things require? How are these molecules formed? What functions do they serve? In this chapter, we will explore these questions.

2.2 The Building Blocks of Molecules[2]

At its most fundamental level, life is made up of matter. **Matter** occupies space and has mass. All matter is composed of **elements**, substances that cannot be broken down or transformed chemically into other substances. Each element is made of atoms, each with a constant number of protons and unique properties. A total of 118 elements have been defined; however, only 92 occur naturally, and fewer than 30 are found in living cells. The remaining 26 elements are unstable and, therefore, do not exist for very long or are theoretical and have yet to be detected.

Each element is designated by its chemical symbol (such as H, N, O, C, and Na), and possesses unique properties. These unique properties allow elements to combine and to bond with each other in specific ways.

2.2.1 Atoms

An atom is the smallest component of an element that retains all of the chemical properties of that element. For example, one hydrogen atom has all of the properties of the element hydrogen, such as it exists as a gas at room temperature, and it bonds with oxygen to create a water molecule. Hydrogen atoms cannot be broken down into anything smaller while still retaining the properties of hydrogen. If a hydrogen atom were broken down into subatomic particles (i.e. protons, neutrons, and electrons), it would no longer have the properties of hydrogen.

At the most basic level, all organisms are made of a combination of elements. They contain atoms that combine together to form molecules. In multicellular organisms, such as animals, molecules can interact to form cells that combine to form tissues, which make up organs. These combinations continue until entire multicellular organisms are formed.

All atoms contain protons, electrons, and neutrons (Figure 2.2). The only exception is hydrogen (H), which is made of one proton and one electron. A **proton** is a positively charged particle that resides in the **nucleus** (the core of the atom) of an atom and has a mass of 1 and a charge of +1. An **electron** is a negatively charged particle that travels in the space around the nucleus. In other words, it resides outside of the nucleus. It has a negligible mass (i.e. considered to be zero compared to protons and neutrons) and has a charge of –1.

[2]This content is available online at <http://cnx.org/content/m57963/1.2/>.

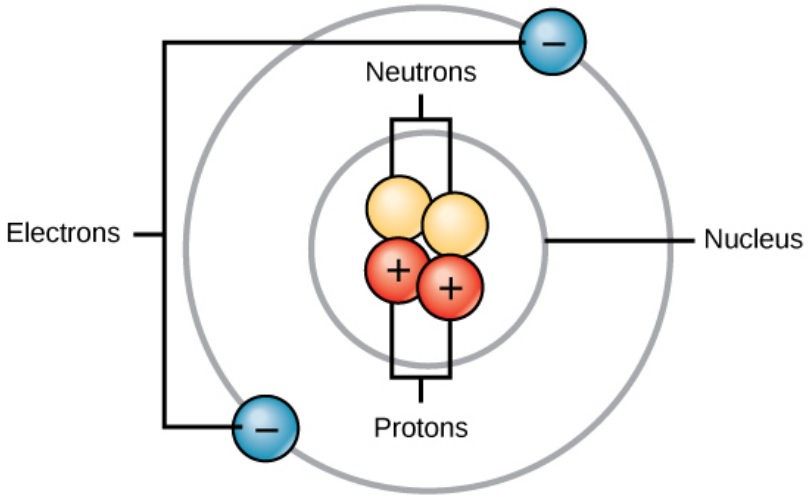

Figure 2.2: Atoms are made up of protons and neutrons located within the nucleus, and electrons surrounding the nucleus.

Neutrons, like protons, reside in the nucleus of an atom. They have a mass of 1 and no charge. The positive (protons) and negative (electrons) charges balance each other in a neutral atom, which has a net zero charge.

Because protons and neutrons each have a mass of 1, the mass of an atom is equal to the combined number of protons and neutrons of that atom. The number of electrons does not factor into the overall mass, because their mass is so small.

As stated earlier, each element has its own unique properties. Each contains a different number of protons and neutrons, giving it its own atomic number and mass number. The **atomic number** of an element is equal to the number of protons that element contains. The **mass number**, or atomic mass, is the number of protons plus the number of neutrons of that element. Therefore, it is possible to determine the number of neutrons by subtracting the atomic number from the mass number. For example, the element phosphorus (P) has an atomic number of 15 and a mass number of 31. Therefore, an atom of phosphorus has 15 protons, 15 electrons, and 16 neutrons (31-15 = 16).

These numbers provide information about the elements and how they will react when combined. Different elements have different melting and boiling points, and are in different states (liquid, solid, or gas) at room temperature. They also combine in different ways. Some form specific types of bonds, whereas others do not. How they combine is based on the number of electrons present. Because of these characteristics, the elements are arranged into the **periodic table of elements**, a chart of the elements that includes the atomic number and relative atomic mass of each element. The periodic table also provides key information about the properties of elements (Figure 2.2)—often indicated by color-coding. The arrangement of the table also shows how the electrons in each element are organized and provides important details about how atoms will react with each other to form molecules.

Isotopes are different forms of the same element that have the same number of protons, but a different number of neutrons. Some elements, such as carbon, potassium, and uranium, have naturally occurring isotopes. Carbon-12, the most common isotope of carbon, contains six protons and six neutrons. Therefore, it has a mass number of 12 (six protons and six neutrons) and an atomic number of 6 (which makes it carbon). Carbon-14 contains six protons and eight neutrons. Therefore, it has a mass number of 14 (six protons and eight neutrons) and an atomic number of 6, meaning it is still the element carbon. These two

alternate forms of carbon are isotopes. Some isotopes are unstable and will lose protons, other subatomic particles, or energy to form more stable elements. These are called **radioactive isotopes** or radioisotopes.

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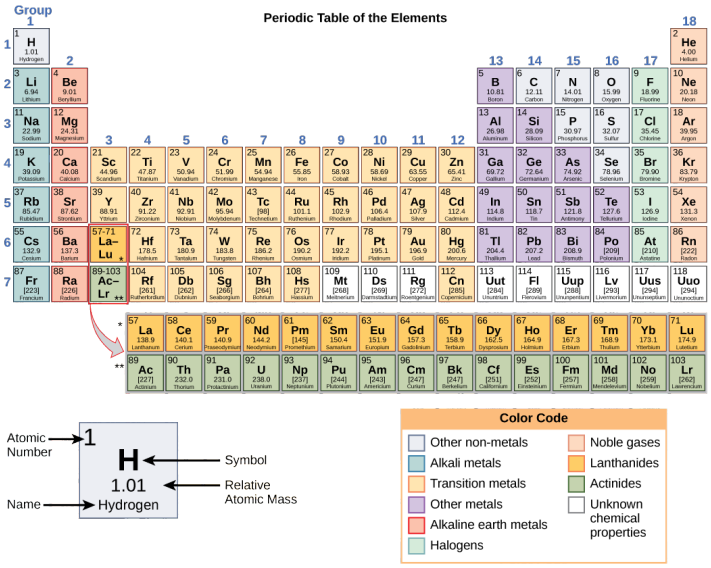


Figure 2.3: Arranged in columns and rows based on the characteristics of the elements, the periodic table provides key information about the elements and how they might interact with each other to form molecules. Most periodic tables provide a key or legend to the information they contain.

: Carbon Dating

Carbon-14 (^{14}C) is a naturally occurring radioisotope that is created in the atmosphere by cosmic rays. This is a continuous process, so more ^{14}C is always being created. As a living organism develops, the relative level of ^{14}C in its body is equal to the concentration of ^{14}C in the atmosphere. When an organism dies, it is no longer ingesting ^{14}C, so the ratio will decline. ^{14}C decays to ^{14}N by a process called beta decay; it gives off energy in this slow process.

After approximately 5,730 years, only one-half of the starting concentration of ^{14}C will have been converted to ^{14}N. The time it takes for half of the original concentration of an isotope to decay to its more stable form is called its half-life. Because the half-life of ^{14}C is long, it is used to age formerly living objects, such as fossils. Using the ratio of the ^{14}C concentration found in an object to the amount of ^{14}C detected in the atmosphere, the amount of the isotope that has not yet decayed can be determined. Based on this amount, the age of the fossil can be calculated to about 50,000 years (Figure 2.4). Isotopes with longer half-lives, such as potassium-40, are used to calculate the ages of older fossils. Through the use of carbon dating, scientists can reconstruct the ecology and biogeography of organisms living within the past 50,000 years.

Figure 2.4: The age of remains that contain carbon and are less than about 50,000 years old, such as this pygmy mammoth, can be determined using carbon dating. (credit: Bill Faulkner/NPS)

: To learn more about atoms and isotopes, and how you can tell one isotope from another, visit this site[3] and run the simulation.

2.2.2 Chemical Bonds

How elements interact with one another depends on how their electrons are arranged and how many openings for electrons exist at the outermost region where electrons are present in an atom. Electrons exist at energy levels that form shells around the nucleus. The closest shell can hold up to two electrons. The closest shell to the nucleus is always filled first, before any other shell can be filled. Hydrogen has one electron; therefore, it has only one spot occupied within the lowest shell. Helium has two electrons; therefore, it can completely

[3] http://openstaxcollege.org/l/isotopes

fill the lowest shell with its two electrons. If you look at the periodic table, you will see that hydrogen and helium are the only two elements in the first row. This is because they only have electrons in their first shell. Hydrogen and helium are the only two elements that have the lowest shell and no other shells.

The second and third energy levels can hold up to eight electrons. The eight electrons are arranged in four pairs and one position in each pair is filled with an electron before any pairs are completed.

Looking at the periodic table again (Figure 2.3), you will notice that there are seven rows. These rows correspond to the number of shells that the elements within that row have. The elements within a particular row have increasing numbers of electrons as the columns proceed from left to right. Although each element has the same number of shells, not all of the shells are completely filled with electrons. If you look at the second row of the periodic table, you will find lithium (Li), beryllium (Be), boron (B), carbon (C), nitrogen (N), oxygen (O), fluorine (F), and neon (Ne). These all have electrons that occupy only the first and second shells. Lithium has only one electron in its outermost shell, beryllium has two electrons, boron has three, and so on, until the entire shell is filled with eight electrons, as is the case with neon.

Not all elements have enough electrons to fill their outermost shells, but an atom is at its most stable when all of the electron positions in the outermost shell are filled. Because of these vacancies in the outermost shells, we see the formation of **chemical bonds**, or interactions between two or more of the same or different elements that result in the formation of molecules. To achieve greater stability, atoms will tend to completely fill their outer shells and will bond with other elements to accomplish this goal by sharing electrons, accepting electrons from another atom, or donating electrons to another atom. Because the outermost shells of the elements with low atomic numbers (up to calcium, with atomic number 20) can hold eight electrons, this is referred to as the **octet rule**. An element can donate, accept, or share electrons with other elements to fill its outer shell and satisfy the octet rule.

When an atom does not contain equal numbers of protons and electrons, it is called an **ion**. Because the number of electrons does not equal the number of protons, each ion has a net charge. Positive ions are formed by losing electrons and are called **cations**. Negative ions are formed by gaining electrons and are called **anions**.

For example, sodium only has one electron in its outermost shell. It takes less energy for sodium to donate that one electron than it does to accept seven more electrons to fill the outer shell. If sodium loses an electron, it now has 11 protons and only 10 electrons, leaving it with an overall charge of +1. It is now called a sodium ion.

The chlorine atom has seven electrons in its outer shell. Again, it is more energy-efficient for chlorine to gain one electron than to lose seven. Therefore, it tends to gain an electron to create an ion with 17 protons and 18 electrons, giving it a net negative (–1) charge. It is now called a chloride ion. This movement of electrons from one element to another is referred to as **electron transfer**. As Figure 2.5 illustrates, a sodium atom (Na) only has one electron in its outermost shell, whereas a chlorine atom (Cl) has seven electrons in its outermost shell. A sodium atom will donate its one electron to empty its shell, and a chlorine atom will accept that electron to fill its shell, becoming chloride. Both ions now satisfy the octet rule and have complete outermost shells. Because the number of electrons is no longer equal to the number of protons, each is now an ion and has a +1 (sodium) or –1 (chloride) charge.

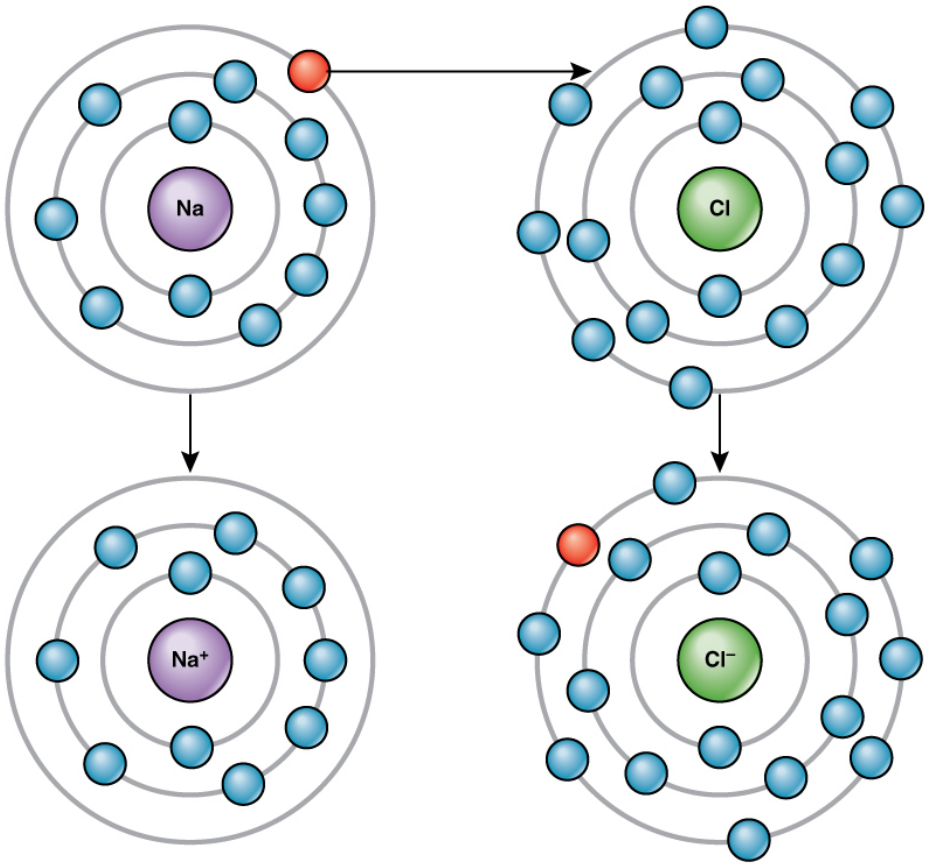


Figure 2.5: Elements tend to fill their outermost shells with electrons. To do this, they can either donate or accept electrons from other elements.

2.2.2.1 Ionic Bonds

We will study three types of bonds or interactions: ionic, covalent, and hydrogen bonds. When an element donates an electron from its outer shell, as in the sodium atom example above, a positive ion is formed. The element accepting the electron is now negatively charged. Because positive and negative charges attract, these ions stay together and form an **ionic bond**, or a bond between ions. The elements bond together with the electron from one element staying predominantly with the other element. When Na^+ and Cl^- ions combine to produce NaCl, an electron from a sodium atom stays with the other seven from the chlorine atom, and the sodium and chloride ions attract each other in a lattice of ions with a net zero charge.

2.2.2.2 Covalent Bonds

Another type of chemical bond between two or more atoms is a **covalent bond**. These bonds form when an electron is shared between two elements and are the strongest and most common form of chemical bond in living organisms. Covalent bonds form between the elements that make up the biological molecules in our cells. Unlike ionic bonds, covalent bonds do not dissociate (i.e. separate) in water.

The hydrogen and oxygen atoms that combine to form water molecules are bound together by covalent bonds. The electron from the hydrogen atom divides its time between the outer shell of the hydrogen atom and the incomplete outer shell of the oxygen atom. To completely fill the outer shell of an oxygen atom, two electrons from two hydrogen atoms are needed, hence the subscript "2" in H_2O. The electrons are shared between the atoms, dividing their time between them to "fill" the outer shell of each. This sharing is a lower energy state for all of the atoms involved than if they existed without their outer shells filled.

There are two types of covalent bonds: polar and nonpolar. **Nonpolar covalent bonds** form between two atoms of the same element or between different elements that share the electrons equally. For example, an oxygen atom can bond with another oxygen atom to fill their outer shells. This association is nonpolar because the electrons will be equally distributed between each oxygen atom. Two covalent bonds form between the two oxygen atoms because oxygen requires two shared electrons to fill its outermost shell. Nitrogen atoms will form three covalent bonds (also called triple covalent) between two atoms of nitrogen because each nitrogen atom needs three electrons to fill its outermost shell. Another example of a nonpolar covalent bond is found in the methane (CH_4) molecule. The carbon atom has four electrons in its outermost shell and needs four more to fill it. It gets these four from four hydrogen atoms, each atom providing one. These elements all share the electrons equally, creating four nonpolar covalent bonds (Figure 2.6).

In a **polar covalent bond**, the electrons shared by the atoms spend more time closer to one nucleus than to the other nucleus. Because of the unequal distribution of electrons between the different nuclei, a slightly positive ($\delta+$) or slightly negative ($\delta-$) charge develops. The covalent bonds between hydrogen and oxygen atoms in water are polar covalent bonds. The shared electrons spend more time near the oxygen nucleus, giving it a small negative charge, than they spend near the hydrogen nuclei, giving these molecules a small positive charge.

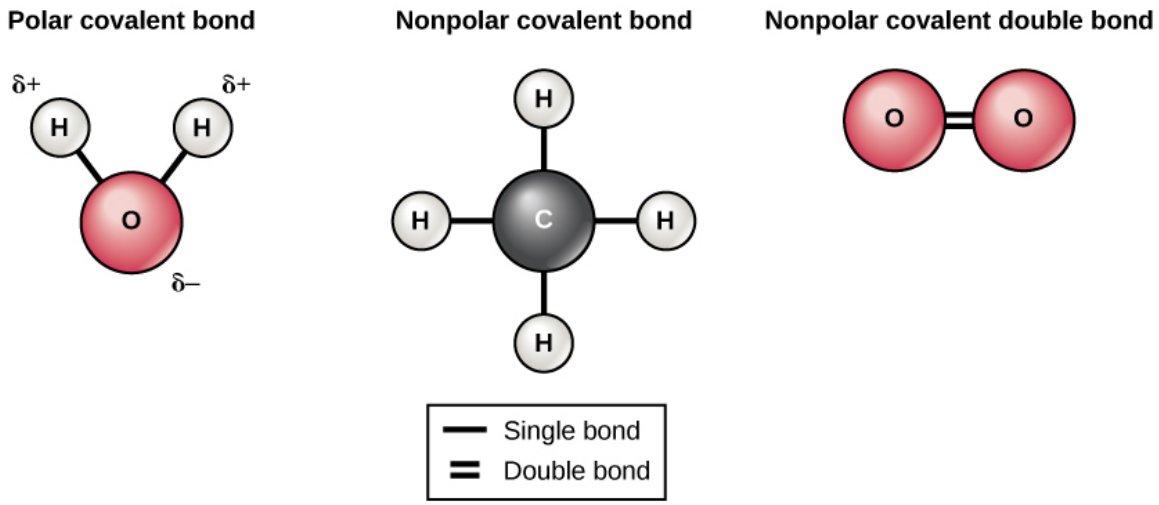


Figure 2.6: The water molecule (left) depicts a polar bond with a slightly positive charge on the hydrogen atoms and a slightly negative charge on the oxygen. Examples of nonpolar bonds include methane (middle) and oxygen (right).

2.2.2.3 Hydrogen Bonds

Ionic and covalent bonds are strong bonds that require considerable energy to break. However, not all bonds between elements are ionic or covalent bonds. Weaker bonds can also form. These are attractions that occur between positive and negative charges that do not require much energy to break. An example of relatively weak bonds that occur frequently is hydrogen bonds. This bond gives rise to the unique properties of water and the unique structures of DNA and proteins.

When polar covalent bonds containing a hydrogen atom form, the hydrogen atom in that bond has a slightly positive charge. This is because the shared electron is pulled more strongly toward the other element and away from the hydrogen nucleus. Because the hydrogen atom is slightly positive ($\delta+$), it will be attracted to neighboring negative partial charges ($\delta-$). When this happens, a weak interaction occurs between the $\delta+$ charge of the hydrogen atom of one molecule and the $\delta-$ charge of the other molecule. This interaction is called a **hydrogen bond**. This type of bond is common; for example, the liquid nature of water is caused by the hydrogen bonds between water molecules (Figure 2.7). Hydrogen bonds give water the unique properties that sustain life. If it were not for hydrogen bonding, water would be a gas rather than a liquid at room temperature.

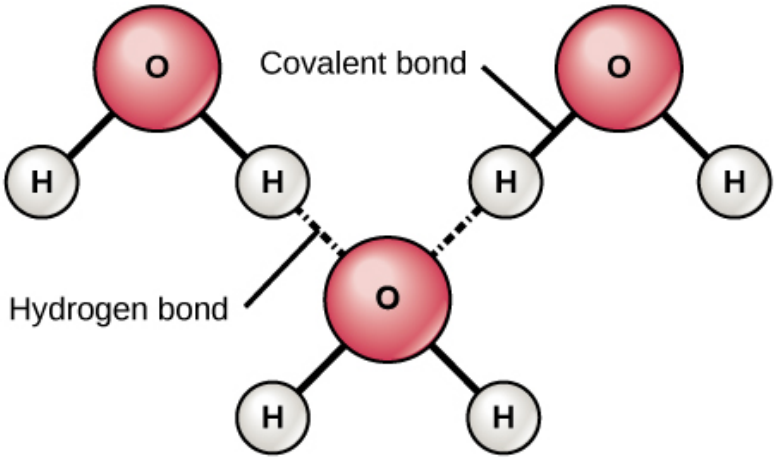


Figure 2.7: Hydrogen bonds form between slightly positive ($\delta+$) and slightly negative ($\delta-$) charges of polar covalent molecules, such as water.

Hydrogen bonds can form between different molecules and they do not always have to include a water molecule. Hydrogen atoms in polar bonds within any molecule can form bonds with other adjacent molecules. For example, hydrogen bonds hold together two long strands of DNA to give the DNA molecule its characteristic double-helix structure. Hydrogen bonds are also responsible for some of the three-dimensional structure of proteins.

2.2.3 Section Summary

Matter is anything that occupies space and has mass. It is made up of atoms of different elements. All of the 92 elements that occur naturally have unique qualities that allow them to combine in various ways to create compounds or molecules. Atoms, which consist of protons, neutrons, and electrons, are the smallest units of an element that retain all of the properties of that element. Electrons can be donated or shared between atoms to create bonds, including ionic, covalent, and hydrogen bonds.

2.2.4 Art Connections

Exercise 2.2.1 *(Solution on p. 60.)*
Figure 2.3 How many neutrons do (K) potassium-39 and potassium-40 have, respectively?

2.2.5 Multiple Choice

Exercise 2.2.2 *(Solution on p. 60.)*
Magnesium has an atomic number of 12. Which of the following statements is true of a neutral magnesium atom?

a. It has 12 protons, 12 electrons, and 12 neutrons.
b. It has 12 protons, 12 electrons, and six neutrons.
c. It has six protons, six electrons, and no neutrons.
d. It has six protons, six electrons, and six neutrons.

Exercise 2.2.3 *(Solution on p. 60.)*
Which type of bond represents a weak chemical bond?

a. hydrogen bond
b. ionic bond
c. covalent bond
d. polar covalent bond

Exercise 2.2.4 *(Solution on p. 60.)*
An isotope of sodium (Na) has a mass number of 22. How many neutrons does it have?

a. 11
b. 12
c. 22
d. 44

2.2.6 Free Response

Exercise 2.2.5 *(Solution on p. 60.)*
Why are hydrogen bonds necessary for cells?

2.3 The Chemical and Physical Properties of Water[4]

Do you ever wonder why scientists spend time looking for water on other planets? It is because water is essential to life; even minute traces of it on another planet can indicate that life could or did exist on that planet. Water is one of the more abundant molecules in living cells and the one most critical to life as we know it. Approximately 60–70 percent of your body is made up of water. Without it, life simply would not exist.

[4]This content is available online at <http://cnx.org/content/m57964/1.2/>.

2.3.1 Water Is Polar

The hydrogen and oxygen atoms within water molecules form polar covalent bonds. The shared electrons spend more time associated with the oxygen atom than they do with hydrogen atoms. There is no overall charge to a water molecule, but there is a slight positive charge on each hydrogen atom and a slight negative charge on the oxygen atom. Because of these charges, the slightly positive hydrogen atoms repel each other. Each water molecule attracts other water molecules because of the positive and negative charges in the different parts of the molecule. Water also attracts other polar molecules (such as sugars), forming hydrogen bonds. When a substance readily forms hydrogen bonds with water, it can dissolve in water and is referred to as **hydrophilic** ("water-loving"). Hydrogen bonds are not readily formed with nonpolar substances like oils and fats (Figure 2.8). These nonpolar compounds are **hydrophobic** ("water-fearing") and will not dissolve in water.

Figure 2.8: As this macroscopic image of oil and water show, oil is a nonpolar compound and, hence, will not dissolve in water. Oil and water do not mix. (credit: Gautam Dogra)

2.3.2 Water Stabilizes Temperature

The hydrogen bonds in water allow it to absorb and release heat energy more slowly than many other substances. **Temperature** is a measure of the motion (kinetic energy) of molecules. As the motion increases, energy is higher and thus temperature is higher. Water absorbs a great deal of energy before its temperature rises. Increased energy disrupts the hydrogen bonds between water molecules. Because these bonds can be created and disrupted rapidly, water absorbs an increase in energy and temperature changes only minimally. This means that water moderates temperature changes within organisms and in their environments. As energy input continues, the balance between hydrogen-bond formation and destruction swings toward the

destruction side. More bonds are broken than are formed. This process results in the release of individual water molecules at the surface of the liquid (such as a body of water, the leaves of a plant, or the skin of an organism) in a process called **evaporation**. Evaporation of sweat, which is 90 percent water, allows for cooling of an organism, because breaking hydrogen bonds requires an input of energy and takes heat away from the body.

2.3.3 Water Is an Excellent Solvent

Because water is polar, with slight positive and negative charges, ionic compounds and polar molecules can readily dissolve in it. Water is, therefore, what is referred to as a **solvent**—a substance capable of dissolving another substance, referred to as the solute, in order to form a solution. The charged particles will form hydrogen bonds with a surrounding layer of water molecules. This is referred to as a sphere of hydration and serves to keep the particles separated or dispersed in the water. In the case of table salt (NaCl) mixed in water (Figure 2.9), the sodium and chloride ions separate, or dissociate, in the water, and spheres of hydration are formed around the ions. A positively charged sodium ion is surrounded by the partially negative charges of oxygen atoms in water molecules. A negatively charged chloride ion is surrounded by the partially positive charges of hydrogen atoms in water molecules. The polarity of the water molecule makes it an effective solvent and is important in its many roles in living systems.

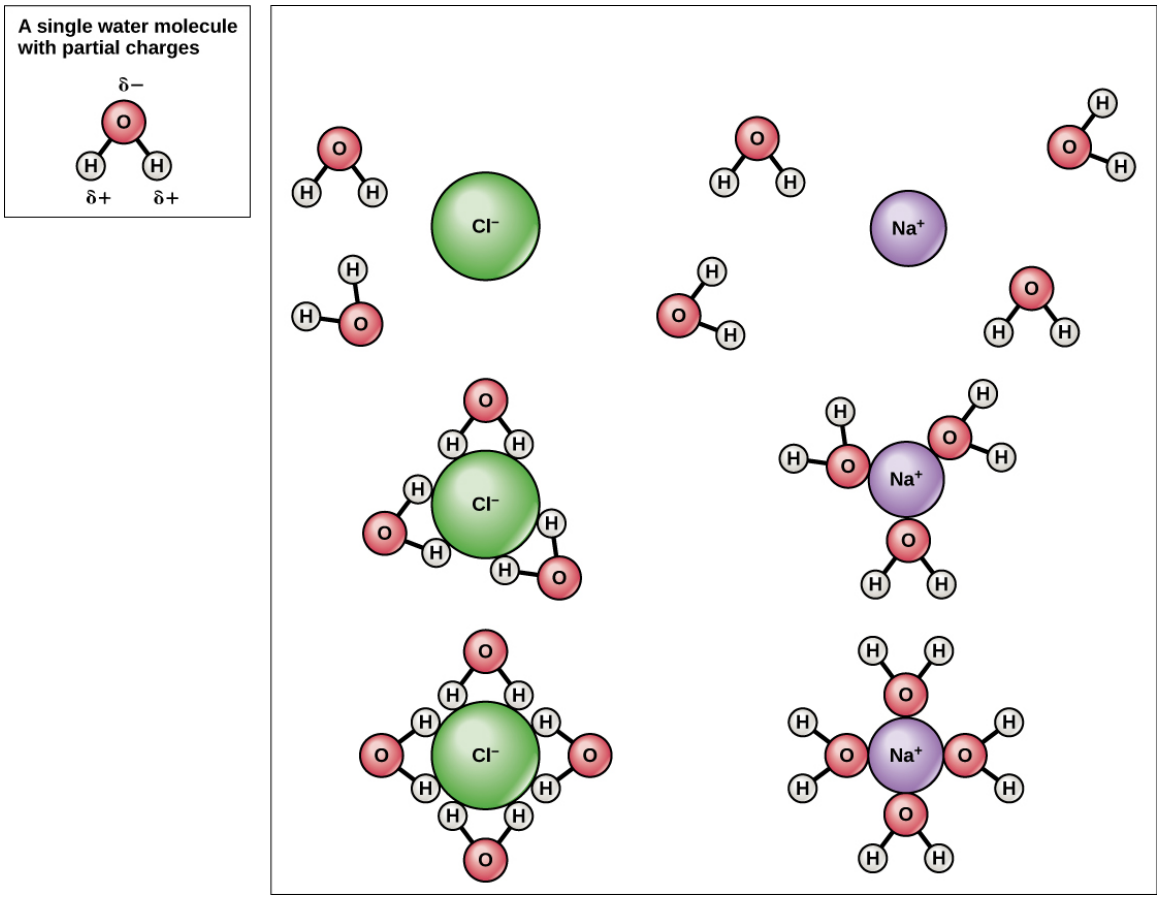


Figure 2.9: When table salt (NaCl) is mixed in water, spheres of hydration form around the ions.

2.3.4 Buffers, pH, Acids, and Bases

The pH of a solution is a measure of its acidity or alkalinity. You have probably used **litmus paper**, paper that has been treated with a natural water-soluble dye so it can be used as a pH indicator, to test how much acid or base (alkalinity) exists in a solution. You might have even used some to make sure the water in an outdoor swimming pool is properly treated. In both cases, this pH test measures the amount of hydrogen ions that exists in a given solution. High concentrations of hydrogen ions yield a low pH, whereas low levels of hydrogen ions result in a high pH. The overall concentration of hydrogen ions is inversely related to its pH and can be measured on the **pH scale** (Figure 2.10). Therefore, the more hydrogen ions present, the lower the pH; conversely, the fewer hydrogen ions, the higher the pH.

The pH scale ranges from 0 to 14. A change of one unit on the pH scale represents a change in the concentration of hydrogen ions by a factor of 10, a change in two units represents a change in the concentration of hydrogen ions by a factor of 100. Thus, small changes in pH represent large changes in the concentrations of hydrogen ions. Pure water is neutral. It is neither acidic nor basic, and has a pH of 7.0. Anything below 7.0 (ranging from 0.0 to 6.9) is acidic, and anything above 7.0 (from 7.1 to 14.0) is alkaline. The blood in

your veins is slightly alkaline (pH = 7.4). The environment in your stomach is highly acidic (pH = 1 to 2). Orange juice is mildly acidic (pH = approximately 3.5), whereas baking soda is basic (pH = 9.0).

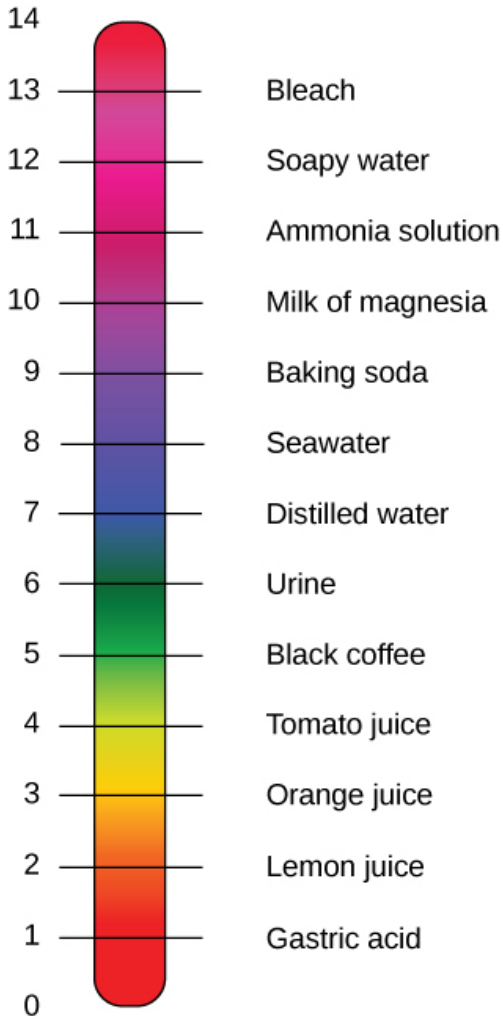


Figure 2.10: The pH scale measures the amount of hydrogen ions (H^+) in a substance. (credit: modification of work by Edward Stevens)

Acids are substances that provide hydrogen ions (H^+) and lower pH, whereas **bases** provide hydroxide ions (OH^-) and raise pH. The stronger the acid, the more readily it donates H^+. For example, hydrochloric acid and lemon juice are very acidic and readily give up H^+ when added to water. Conversely, bases are those substances that readily donate OH^-. The OH^- ions combine with H^+ to produce water, which raises a substance's pH. Sodium hydroxide and many household cleaners are very alkaline and give up OH^- rapidly when placed in water, thereby raising the pH.

Most cells in our bodies operate within a very narrow window of the pH scale, typically ranging only from 7.2 to 7.6. If the pH of the body is outside of this range, the respiratory system malfunctions, as do

other organs in the body. Cells no longer function properly, and proteins will break down. Deviation outside of the pH range can induce coma or even cause death.

So how is it that we can ingest or inhale acidic or basic substances and not die? Buffers are the key. **Buffers** readily absorb excess H^+ or OH^-, keeping the pH of the body carefully maintained in the aforementioned narrow range. Carbon dioxide is part of a prominent buffer system in the human body; it keeps the pH within the proper range. This buffer system involves carbonic acid (H_2CO_3) and bicarbonate (HCO_3^-) anion. If too much H^+ enters the body, bicarbonate will combine with the H^+ to create carbonic acid and limit the decrease in pH. Likewise, if too much OH^- is introduced into the system, carbonic acid will rapidly dissociate into bicarbonate and H^+ ions. The H^+ ions can combine with the OH^- ions, limiting the increase in pH. While carbonic acid is an important product in this reaction, its presence is fleeting because the carbonic acid is released from the body as carbon dioxide gas each time we breathe. Without this buffer system, the pH in our bodies would fluctuate too much and we would fail to survive.

2.3.5 Section Summary

Water has many properties that are critical to maintaining life. It is polar, allowing for the formation of hydrogen bonds, which allow ions and other polar molecules to dissolve in water. Therefore, water is an excellent solvent. The hydrogen bonds between water molecules give water the ability to hold heat better than many other substances. As the temperature rises, the hydrogen bonds between water continually break and reform, allowing for the overall temperature to remain stable, although increased energy is added to the system. All of these unique properties of water are important in the chemistry of living organisms.

The pH of a solution is a measure of the concentration of hydrogen ions in the solution. A solution with a high number of hydrogen ions is acidic and has a low pH value. A solution with a high number of hydroxide ions is basic and has a high pH value. The pH scale ranges from 0 to 14, with a pH of 7 being neutral. Buffers are solutions that moderate pH changes when an acid or base is added to the buffer system. Buffers are important in biological systems because of their ability to maintain constant pH conditions.

2.3.6 Multiple Choice

Exercise 2.3.1 *(Solution on p. 60.)*

Which of the following statements is FALSE?

a. Water is polar.
b. Water stabilizes temperature.
c. Water is essential for life.
d. Water is the most abundant atom in Earth's atmosphere.

Exercise 2.3.2 *(Solution on p. 60.)*

Using a pH meter, you find the pH of an unknown solution to be 8.0. How would you describe this solution?

a. weakly acidic
b. strongly acidic
c. weakly basic
d. strongly basic

Exercise 2.3.3 *(Solution on p. 60.)*

The pH of lemon juice is about 2.0, whereas tomato juice's pH is about 4. Therefore, the concentration of hydrogen ions in the tomato juice is _____ times _____ than the lemon juice.

a. 2; greater
b. 2; less

c. 100; less
d. 100; greater

2.3.7 Free Response

Exercise 2.3.4 *(Solution on p. 60.)*
Explain why water is an excellent solvent.

2.4 Biological Macromolecules[5]

The large molecules necessary for life that are built from smaller organic molecules are called biological **macromolecules**. There are four major classes of biological macromolecules (carbohydrates, lipids, proteins, and nucleic acids), and each is an important component of the cell and performs a wide array of functions. Combined, these molecules make up the majority of a cell's mass. Biological macromolecules are organic, meaning that they contain carbon. In addition, they may contain hydrogen, oxygen, nitrogen, phosphorus, sulfur, and additional minor elements.

2.4.1 Carbon

It is often said that life is "carbon-based." This means that carbon atoms, bonded to other carbon atoms or other elements, form the fundamental components of many, if not most, of the molecules found uniquely in living things. Other elements play important roles in biological molecules, but carbon certainly qualifies as the "foundation" element for molecules in living things. It is the bonding properties of carbon atoms that are responsible for its important role.

2.4.2 Carbon Bonding

Carbon contains four electrons in its outer shell. Therefore, it can form four covalent bonds with other atoms or molecules. The simplest organic carbon molecule is methane (CH_4), in which four hydrogen atoms bind to a carbon atom (Figure 2.11).

[5]This content is available online at <http://cnx.org/content/m57965/1.3/>.

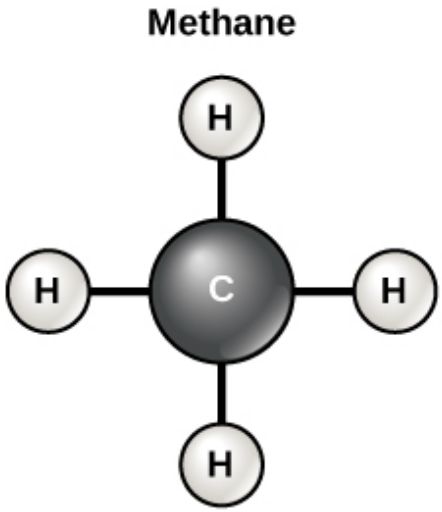
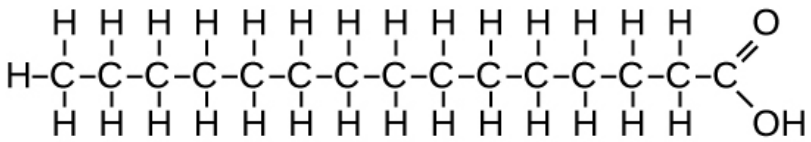
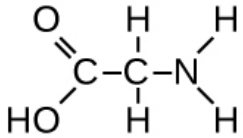


Figure 2.11: Carbon can form four covalent bonds to create an organic molecule. The simplest carbon molecule is methane (CH_4), depicted here.

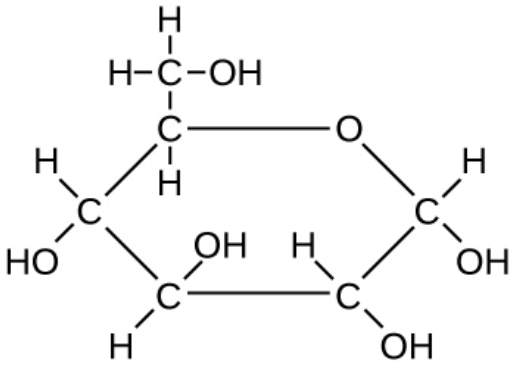
However, structures that are more complex are made using carbon. Any of the hydrogen atoms can be replaced with another carbon atom covalently bonded to the first carbon atom. In this way, long and branching chains of carbon compounds can be made (Figure 2.12**a**). The carbon atoms may bond with atoms of other elements, such as nitrogen, oxygen, and phosphorus (Figure 2.12**b**). The molecules may also form rings, which themselves can link with other rings (Figure 2.12**c**). This diversity of molecular forms accounts for the diversity of functions of the biological macromolecules and is based to a large degree on the ability of carbon to form multiple bonds with itself and other atoms.



(a)



(b)



(c)

Figure 2.12: These examples show three molecules (found in living organisms) that contain carbon atoms bonded in various ways to other carbon atoms and the atoms of other elements. (a) This molecule of stearic acid has a long chain of carbon atoms. (b) Glycine, a component of proteins, contains carbon, nitrogen, oxygen, and hydrogen atoms. (c) Glucose, a sugar, has a ring of five carbon atoms and one oxygen atom. The chemical formula for glucose is $C_6H_{12}O_6$

2.4.3 Carbohydrates

Carbohydrates are macromolecules with which most consumers are somewhat familiar. To lose weight, some individuals adhere to "low-carb" diets. Athletes, in contrast, often "carb-load" before important competitions to ensure that they have sufficient energy to compete at a high level. Carbohydrates are, in fact, an essential part of our diet; grains, fruits, and vegetables are all natural sources of carbohydrates. Carbohydrates provide energy to the body, particularly through glucose, a simple sugar. Carbohydrates also have other important functions in humans, animals, and plants.

Carbohydrates can be represented by the formula $(CH_2O)_n$, where n is the number of carbon atoms in

the molecule. In other words, the ratio of carbon to hydrogen to oxygen is 1:2:1 in carbohydrate molecules. Carbohydrates are classified into three subtypes: monosaccharides, disaccharides, and polysaccharides.

Monosaccharides (mono- = "one"; sacchar- = "sweet") are simple sugars, the most common of which is glucose. In monosaccharides, the number of carbon atoms usually ranges from three to six. Most monosaccharide names end with the suffix -ose. Depending on the number of carbon atoms in the sugar, they may be known as trioses (three carbon atoms), pentoses (five carbon atoms), and hexoses (six carbon atoms).

The chemical formula for glucose is $C_6H_{12}O_6$. In most living species, glucose is an important source of energy. During cellular respiration, energy is released from glucose, and that energy is used to help make adenosine triphosphate (ATP). Plants synthesize glucose using carbon dioxide and water by the process of photosynthesis, and the glucose, in turn, is used for the energy requirements of the plant. The excess synthesized glucose is often stored as starch that is broken down by other organisms that feed on plants.

Galactose (part of lactose, or milk sugar) and fructose (found in fruit) are other common monosaccharides. Although glucose, galactose, and fructose all have the same chemical formula ($C_6H_{12}O_6$), they differ structurally and chemically (and are known as isomers) because of differing arrangements of atoms in the carbon chain (Figure 2.13).

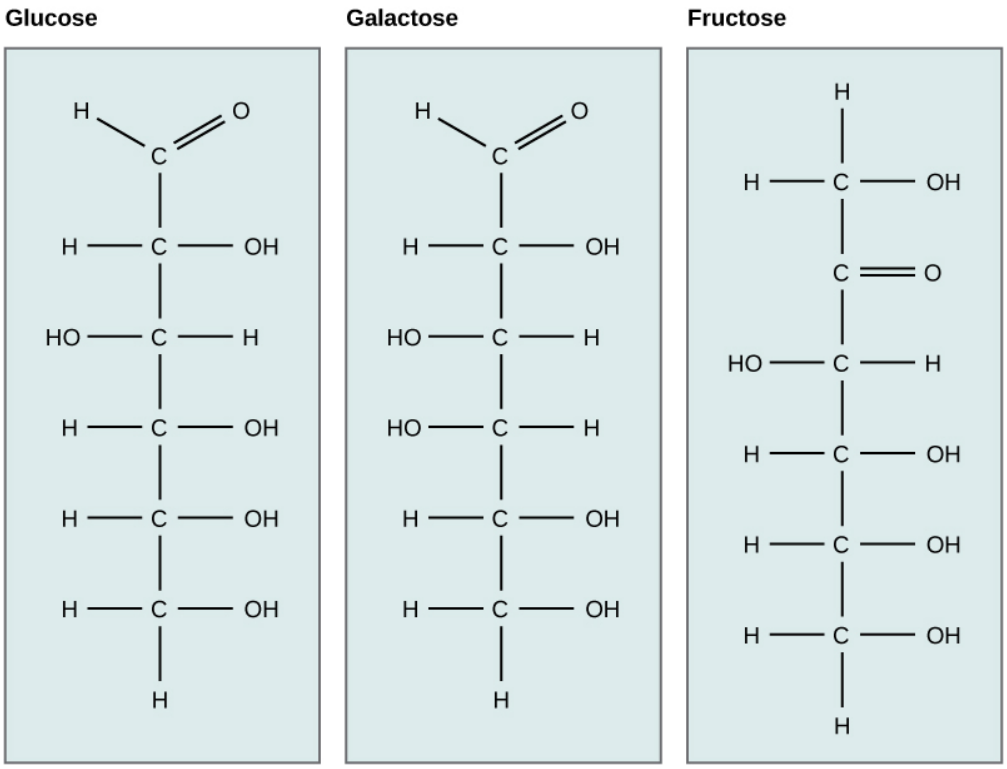


Figure 2.13: Glucose, galactose, and fructose are isomeric monosaccharides, meaning that they have the same chemical formula but slightly different structures.

Disaccharides (di- = "two") form when two monosaccharides undergo a dehydration-synthesis reaction (a reaction in which the removal of a water molecule occurs). During this process, the hydroxyl group (–OH) of one monosaccharide combines with a hydrogen atom of another monosaccharide, releasing a molecule of water (H_2O) and forming a covalent bond between atoms in the two sugar molecules.

Common disaccharides include lactose, maltose, and sucrose. Lactose is a disaccharide consisting of the monomers glucose and galactose. It is found naturally in milk. Maltose, or malt sugar, is a disaccharide formed from a dehydration reaction between two glucose molecules. The most common disaccharide is sucrose, or table sugar, which is composed of the monomers glucose and fructose.

A long chain of monosaccharides linked by covalent bonds is known as a **polysaccharide** (poly- = "many"). The chain may be branched or unbranched, and it may contain different types of monosaccharides. Polysaccharides may be very large molecules. Starch, glycogen, and cellulose are examples of polysaccharides.

Starch is the stored form of sugars in plants and is made up of amylose and amylopectin (both polymers of glucose). Plants are able to synthesize glucose, and the excess glucose is stored as starch in different plant parts, including roots and seeds. The starch that is consumed by animals is broken down into smaller molecules, such as glucose. The cells can then absorb the glucose.

Glycogen is the storage form of glucose in humans and other vertebrates, and is made up of monomers of glucose. Glycogen is the animal equivalent of starch and is a highly branched molecule usually stored in liver and muscle cells as a form of stored energy. Whenever glucose levels decrease, glycogen is broken down to release glucose. In the case of muscle cells, the glucose is used to produce ATP for energy-requiring processes. In the case of the liver, the glucose is released into the circulatory system to maintain blood sugar homeostasis.

Cellulose is one of the most abundant natural biopolymers. The cell walls of plants are mostly made of cellulose, which provides structural support to the cell. Wood and paper are mostly cellulosic in nature. Cellulose is made up of glucose monomers that are linked by bonds between particular carbon atoms in the glucose molecule.

Every other glucose monomer in cellulose is flipped over and packed tightly as extended long chains. This gives cellulose its rigidity and high tensile strength—which is so important to plant cells. Cellulose passing through our digestive system is called dietary fiber. While the glucose-glucose bonds in cellulose cannot be broken down by human digestive enzymes, animals such as cows, buffalos, and horses (examples of ruminants) are able to digest grass that is rich in cellulose and use it as a food source. In these animals, certain species of bacteria reside in the rumen (a part of their digestive system) and secrete the enzyme cellulase. The appendix also contains bacteria that break down cellulose, giving it an important role in the digestive systems of ruminants. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal.

Thus, through differences in molecular structure, carbohydrates are able to serve the very different functions of energy storage (starch and glycogen) and structural support and protection (cellulose) (Figure 2.14).

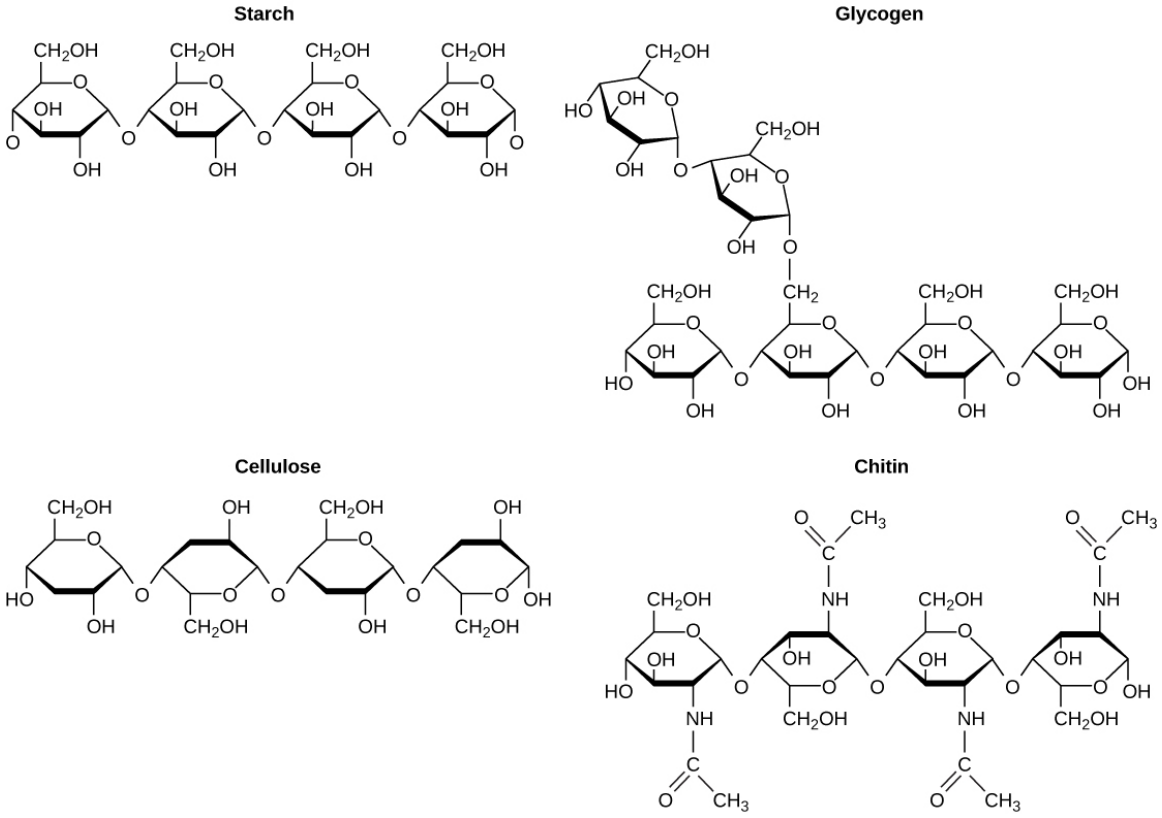


Figure 2.14: Although their structures and functions differ, all polysaccharide carbohydrates are made up of monosaccharides and have the chemical formula $(CH_2O)n$.

: **Registered Dietitian**

Obesity is a worldwide health concern, and many diseases, such as diabetes and heart disease, are becoming more prevalent because of obesity. This is one of the reasons why registered dietitians are increasingly sought after for advice. Registered dietitians help plan food and nutrition programs for individuals in various settings. They often work with patients in health-care facilities, designing nutrition plans to prevent and treat diseases. For example, dietitians may teach a patient with diabetes how to manage blood-sugar levels by eating the correct types and amounts of carbohydrates. Dietitians may also work in nursing homes, schools, and private practices.

To become a registered dietitian, one needs to earn at least a bachelor's degree in dietetics, nutrition, food technology, or a related field. In addition, registered dietitians must complete a supervised internship program and pass a national exam. Those who pursue careers in dietetics take courses in nutrition, chemistry, biochemistry, biology, microbiology, and human physiology. Dietitians must become experts in the chemistry and functions of food (proteins, carbohydrates, and fats).

2.4.4 Lipids

Lipids include a diverse group of compounds that are united by a common feature. **Lipids** are hydrophobic ("water-fearing"), or insoluble in water, because they are nonpolar molecules. This is because they are hydrocarbons that include only nonpolar carbon-carbon or carbon-hydrogen bonds. Lipids perform many different functions in a cell. Cells store energy for long-term use in the form of lipids called fats (or triglycerides). Lipids also provide insulation from the environment for plants and animals (Figure 2.15). For example, they help keep aquatic birds and mammals dry because of their water-repelling nature. Lipids are also the building blocks of many hormones and are an important constituent of the plasma membrane. Lipids include fats, oils, phospholipids, and steroids.

Figure 2.15: Hydrophobic lipids in the fur of aquatic mammals, such as this river otter, protect them from the elements. (credit: Ken Bosma)

A **fat** molecule, such as a triglyceride, consists of two main components—glycerol and fatty acids. Glycerol is an organic compound with three carbon atoms, five hydrogen atoms, and three hydroxyl (–OH) groups. Fatty acids have a long chain of hydrocarbons to which an acidic carboxyl group (-COOH) is attached, hence the name "fatty acid." The number of carbons in the fatty acid may range from 4 to 36; most common are those containing 12–18 carbons. In a fat molecule, a fatty acid is attached to each of the three oxygen atoms in the –OH groups of the glycerol molecule with a covalent bond (Figure 2.16)created by dehydration-synthesis reactions.

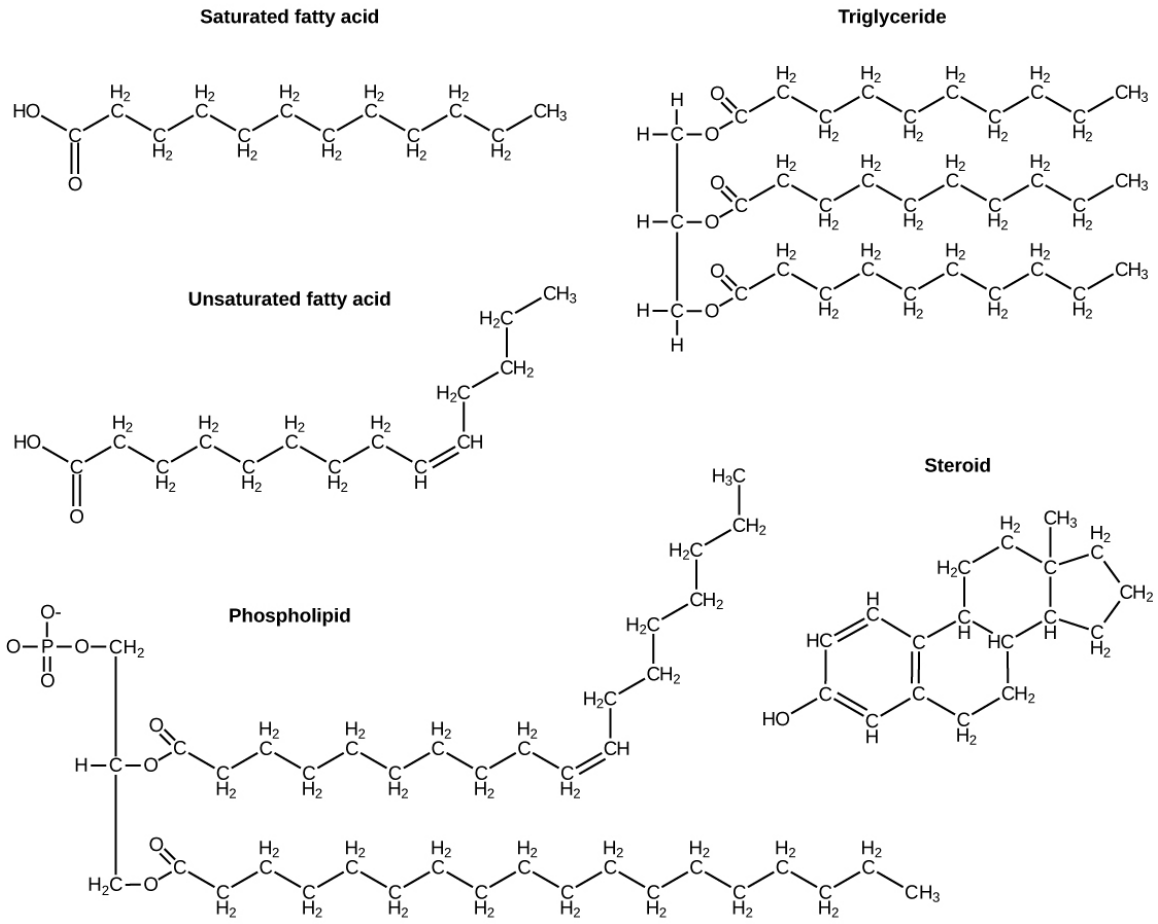


Figure 2.16: Lipids include fats, such as triglycerides, which are made up of fatty acids and glycerol, phospholipids, and steroids.

During this covalent bond formation, three water molecules are released. The three fatty acids in the fat may be similar or dissimilar. These fats are also called **triglycerides** because they have three fatty acids. Some fatty acids have common names that specify their origin. For example, palmitic acid, a saturated fatty acid, is derived from the palm tree. Arachidic acid is derived from *Arachis hypogaea*, the scientific name for peanuts.

Fatty acids may be saturated or unsaturated. In a fatty acid chain, if there are only single bonds between neighboring carbons in the hydrocarbon chain, the fatty acid is saturated. **Saturated fatty acids** are saturated with hydrogen; in other words, the number of hydrogen atoms attached to the carbon skeleton is maximized. When the hydrocarbon chain contains a double bond, the fatty acid is an **unsaturated fatty acid**.

Most unsaturated fats are liquid at room temperature and are called **oils**. If there is only one carbon-carbon double bond in the molecule, then it is known as a monounsaturated fat (e.g. olive oil), and if there is more than one carbon-carbon double bond, then it is known as a polyunsaturated fat (e.g. canola oil).

Saturated fats tend to get packed tightly and are solid at room temperature. Animal fats with stearic

acid and palmitic acid contained in meat, and the fat with butyric acid contained in butter, are examples of saturated fats. Mammals store fats in specialized cells called adipocytes, where globules of fat occupy most of the cell. In plants, fat or oil is stored in seeds and is used as a source of energy during embryonic development.

Unsaturated fats or oils are usually of plant origin and contain unsaturated fatty acids. The double bond causes a bend or a "kink" that prevents the fatty acids from packing tightly, keeping them liquid at room temperature. Olive oil, corn oil, canola oil, and cod liver oil are examples of unsaturated fats. Unsaturated fats help to improve blood cholesterol levels, whereas saturated fats contribute to plaque formation in the arteries, which increases the risk of a heart attack.

In the food industry, oils are artificially hydrogenated to make them semi-solid, leading to less spoilage and increased shelf life. Simply speaking, hydrogen gas is bubbled through oils to solidify them. During this hydrogenation process, double bonds of the *cis*-conformation in the hydrocarbon chain may be converted to double bonds in the *trans*-conformation. This forms a ***trans*-fat** from a *cis*-fat. The orientation of the double bonds affects the chemical properties of the fat (Figure 2.17).

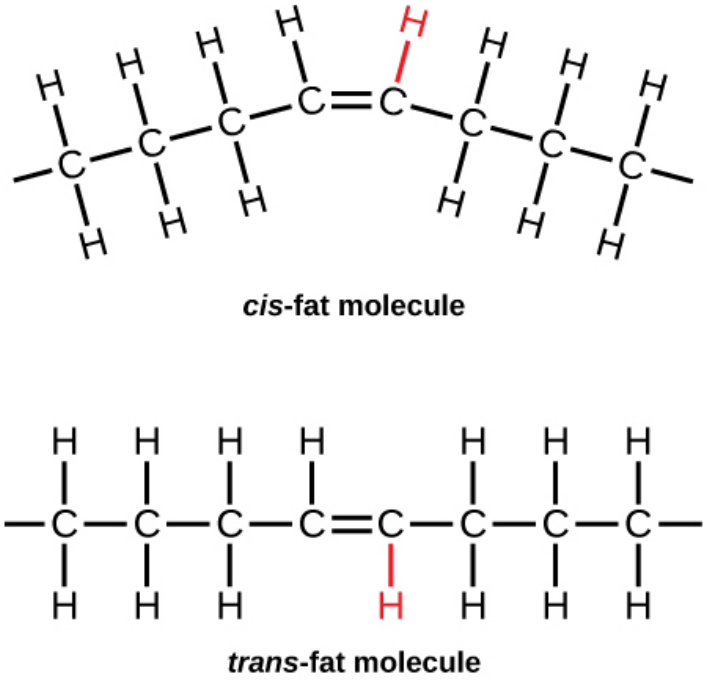


Figure 2.17: During the hydrogenation process, the orientation around the double bonds is changed, making a *trans*-fat from a *cis*-fat. This changes the chemical properties of the molecule.

Margarine, some types of peanut butter, and shortening are examples of artificially hydrogenated *trans*-fats. Recent studies have shown that an increase in *trans*-fats in the human diet may lead to an increase in levels of low-density lipoprotein (LDL), or "bad" cholesterol, which, in turn, may lead to plaque deposition in the arteries, resulting in heart disease. Many fast food restaurants have recently eliminated the use of *trans*-fats, and U.S. food labels are now required to list their *trans*-fat content.

Salmon, trout, and tuna are good sources of omega-3 fatty acids. Omega-3 fatty acids are important in

brain function and normal growth and development. They may also prevent heart disease and reduce the risk of cancer.

Like carbohydrates, fats have received a lot of bad publicity. It is true that eating an excess of fried foods and other "fatty" foods leads to weight gain. However, fats do have important functions. Fats serve as long-term energy storage. They also provide insulation for the body. Therefore, "healthy" unsaturated fats in moderate amounts should be consumed on a regular basis.

Phospholipids are the major constituent of the plasma membrane. Like fats, they are composed of fatty acid chains attached to a glycerol or similar backbone. Instead of three fatty acids attached, however, there are two fatty acids and the third carbon of the glycerol backbone is bound to a phosphate group. The phosphate group is modified by the addition of an alcohol.

A phospholipid has both hydrophobic and hydrophilic regions. The fatty acid chains are hydrophobic and exclude themselves from water, whereas the phosphate is hydrophilic and interacts with water.

Cells are surrounded by a membrane, which has a bilayer of phospholipids. The fatty acids of phospholipids face inside, away from water, whereas the phosphate group can face either the outside environment or the inside of the cell, which are both aqueous.

2.4.4.1 Steroids

Unlike the phospholipids and fats discussed earlier, **steroids** have a ring structure. Although they do not resemble other lipids, they are grouped with them because they are also hydrophobic. All steroids have four, linked carbon rings and several of them, like cholesterol, have a short tail.

Cholesterol is a steroid. Cholesterol is mainly synthesized in the liver and is the precursor of many steroid hormones, such as testosterone and estradiol. It is also the precursor of vitamins E and K. Cholesterol is the precursor of bile salts, which help in the breakdown of fats and their subsequent absorption by cells. Although cholesterol is often spoken of in negative terms, it is necessary for the proper functioning of the body. It is a key component of the plasma membranes of animal cells.

: For an additional perspective on lipids, explore "Biomolecules: The Lipids" through this interactive animation[6] .

2.4.5 Proteins

Proteins are one of the most abundant organic molecules in living systems and have the most diverse range of functions of all macromolecules. Proteins may be structural, regulatory, contractile, or protective; they may serve in transport, storage, or membranes; or they may be toxins or enzymes. Each cell in a living system may contain thousands of different proteins, each with a unique function. Their structures, like their functions, vary greatly. They are all, however, polymers of amino acids, arranged in a linear sequence.

The functions of proteins are very diverse because there are 20 different chemically distinct amino acids that form long chains, and the amino acids can be in any order. For example, proteins can function as enzymes or hormones. **Enzymes**, which are produced by living cells, are catalysts in biochemical reactions (like digestion) and are usually proteins. Catalysts speed up chemical reactions by lowering the amount of

[6] http://openstaxcollege.org/l/lipids

energy required to start them. Each enzyme is specific for the substrate (a reactant that binds to an enzyme) upon which it acts. Enzymes can function to break molecular bonds, to rearrange bonds, or to form new bonds. An example of an enzyme is salivary amylase, which breaks down amylose, a component of starch.

Hormones are chemical signaling molecules, usually proteins or steroids, secreted by an endocrine gland or group of endocrine cells that act to control or regulate specific physiological processes, including growth, development, metabolism, and reproduction. For example, insulin is a protein hormone that maintains blood glucose levels.

Proteins have different shapes and molecular weights; some proteins are globular in shape whereas others are fibrous in nature. For example, hemoglobin is a globular protein, but collagen, found in our skin, is a fibrous protein. Protein shape is critical to its function. Changes in temperature, pH, and exposure to chemicals may lead to permanent changes in the shape of the protein, leading to a loss of function or **denaturation** (to be discussed in more detail later). All proteins are made up of different arrangements of the same 20 kinds of amino acids.

Amino acids are the monomers that make up proteins. Each amino acid has the same fundamental structure, which consists of a central carbon atom bonded to an amino group ($-NH_2$), a carboxyl group ($-COOH$), and a hydrogen atom. Every amino acid also has another variable atom or group of atoms bonded to the central carbon atom known as the R group. The R group is the only difference in structure between the 20 amino acids; otherwise, the amino acids are identical (Figure 2.18).

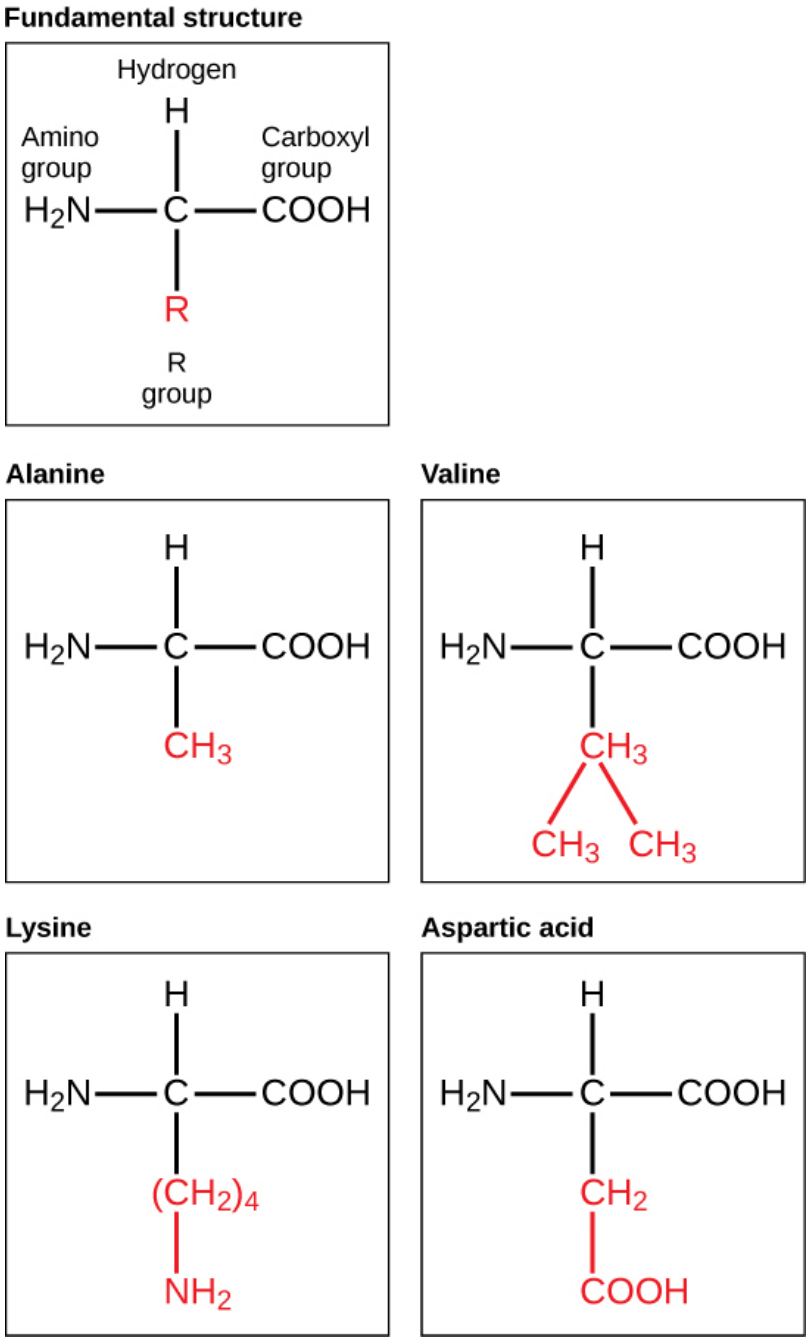


Figure 2.18: Amino acids are made up of a central carbon bonded to an amino group ($-NH_2$), a carboxyl group (–COOH), and a hydrogen atom. The central carbon's fourth bond varies among the different amino acids, as seen in these examples of alanine, valine, lysine, and aspartic acid.

The chemical nature of the R group determines the chemical nature of the amino acid within its protein

(that is, whether it is acidic, basic, polar, or nonpolar).

The sequence and number of amino acids ultimately determine a protein's shape, size, and function. Each amino acid is attached to another amino acid by a covalent bond, known as a peptide bond, which is formed by a dehydration reaction. The carboxyl group of one amino acid and the amino group of a second amino acid combine, releasing a water molecule. The resulting bond is the peptide bond.

The products formed by such a linkage are called polypeptides. While the terms polypeptide and protein are sometimes used interchangeably, a **polypeptide** is technically a polymer of amino acids, whereas the term protein is used for a polypeptide or polypeptides that have combined together, have a distinct shape, and have a unique function.

2.4.5.1 Protein Structure

As discussed earlier, the shape of a protein is critical to its function. To understand how the protein gets its final shape or conformation, we need to understand the four levels of protein structure: primary, secondary, tertiary, and quaternary (Figure 2.19).

The unique sequence and number of amino acids in a polypeptide chain is its primary structure. The unique sequence for every protein is ultimately determined by the gene (i.e. a section of DNA) that encodes (i.e. has the information to make) the protein. Any change in the gene sequence may lead to a different amino acid being added to the polypeptide chain, causing a change in protein structure and function. In sickle cell anemia, the hemoglobin β chain has a single amino acid substitution, causing a change in both the structure and function of the protein. What is most remarkable to consider is that a hemoglobin molecule is made up of two alpha chains and two beta chains that each consist of about 150 amino acids. The molecule, therefore, has about 600 amino acids. The structural difference between a normal hemoglobin molecule and a sickle cell molecule—that dramatically decreases life expectancy in the affected individuals—is a single amino acid of the 600.

Because of this change of one amino acid in the chain, the normally biconcave, or disc-shaped, red blood cells assume a crescent or "sickle" shape, which clogs arteries. This can lead to a myriad of serious health problems, such as breathlessness, dizziness, headaches, and abdominal pain for those who have this disease.

Folding patterns resulting from interactions between the non-R group portions of amino acids give rise to the secondary structure of the protein. The most common are the alpha (α)-helix and beta (β)-pleated sheet structures. Both structures are held in shape by hydrogen bonds. In the alpha helix, the bonds form between every fourth amino acid and cause a twist in the amino acid chain.

In the β-pleated sheet, the "pleats" are formed by hydrogen bonding between atoms on the backbone of the polypeptide chain. The R groups are attached to the carbons, and extend above and below the folds of the pleat. The pleated segments align parallel to each other, and hydrogen bonds form between the same pairs of atoms on each of the aligned amino acids. The α-helix and β-pleated sheet structures are found in many globular and fibrous proteins.

The unique three-dimensional structure of a polypeptide is known as its tertiary structure. This structure is caused by chemical interactions between various amino acids and regions of the polypeptide. Primarily, the interactions among R groups create the complex three-dimensional tertiary structure of a protein. There may be ionic bonds formed between R groups on different amino acids, or hydrogen bonding beyond that involved in the secondary structure. When protein folding takes place, the hydrophobic R groups of nonpolar amino acids lay in the interior of the protein, whereas the hydrophilic R groups lay on the outside. The former types of interactions are also known as hydrophobic interactions.

In nature, some proteins are formed from several polypeptides, also known as subunits, and the interaction of these subunits forms the quaternary structure. Weak interactions between the subunits help to stabilize the overall structure. For example, hemoglobin is a combination of four polypeptide subunits.

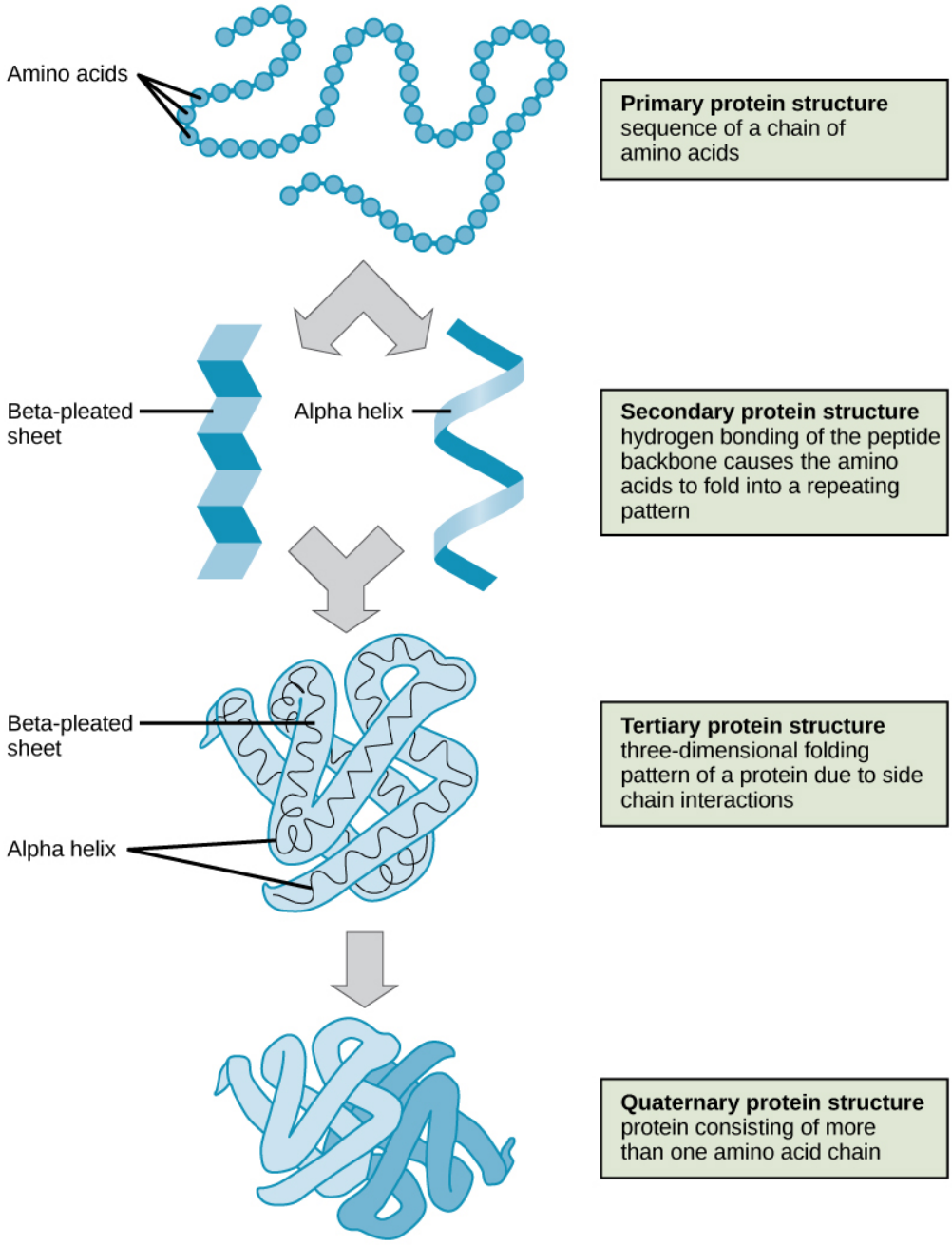


Figure 2.19: The four levels of protein structure can be observed in these illustrations. (credit: modification of work by National Human Genome Research Institute)

Each protein has its own unique sequence and shape held together by chemical interactions. If the protein is subject to changes in temperature, pH, or exposure to chemicals, the protein structure may change, losing

its shape in what is known as denaturation. Denaturation is often reversible because the primary structure is preserved if the denaturing agent is removed, allowing the protein to resume its function. Sometimes denaturation is irreversible, leading to a loss of function. One example of protein denaturation can be seen when an egg is fried or boiled. The albumin protein in the liquid egg white is denatured when placed in a hot pan, changing from a clear substance to an opaque white substance. Not all proteins are denatured at high temperatures; for instance, bacteria that survive in hot springs have proteins that are adapted to function at those temperatures.

: For an additional perspective on proteins, explore "Biomolecules: The Proteins" through this interactive animation[7] .

2.4.6 Nucleic Acids

Nucleic acids are key macromolecules in the continuity of life. They carry the genetic blueprint of a cell and carry instructions for the functioning of the cell.

The two main types of **nucleic acids** are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**. DNA is the genetic material found in all living organisms, ranging from single-celled bacteria to multicellular mammals.

The other type of nucleic acid, RNA, is mostly involved in protein synthesis. The DNA molecules never leave the nucleus, but instead use an RNA intermediary to communicate with the rest of the cell. Other types of RNA are also involved in protein synthesis and its regulation.

DNA and RNA are made up of monomers known as **nucleotides**. The nucleotides combine with each other to form a polynucleotide, DNA or RNA. Each nucleotide is made up of three components: a nitrogenous base, a pentose (five-carbon) sugar, and a phosphate group (Figure 2.20). Each nitrogenous base in a nucleotide is attached to a sugar molecule, which is attached to a phosphate group. DNA nucleotides contain the sugar deoxyribose and one of the four bases adenine (A),thymine (T),guanine (G), or cytosine (C). RNA nucleotides contain the sugar ribose and one of the four bases A,uracil (U),G,or C.

[7] http://openstaxcollege.org/l/proteins

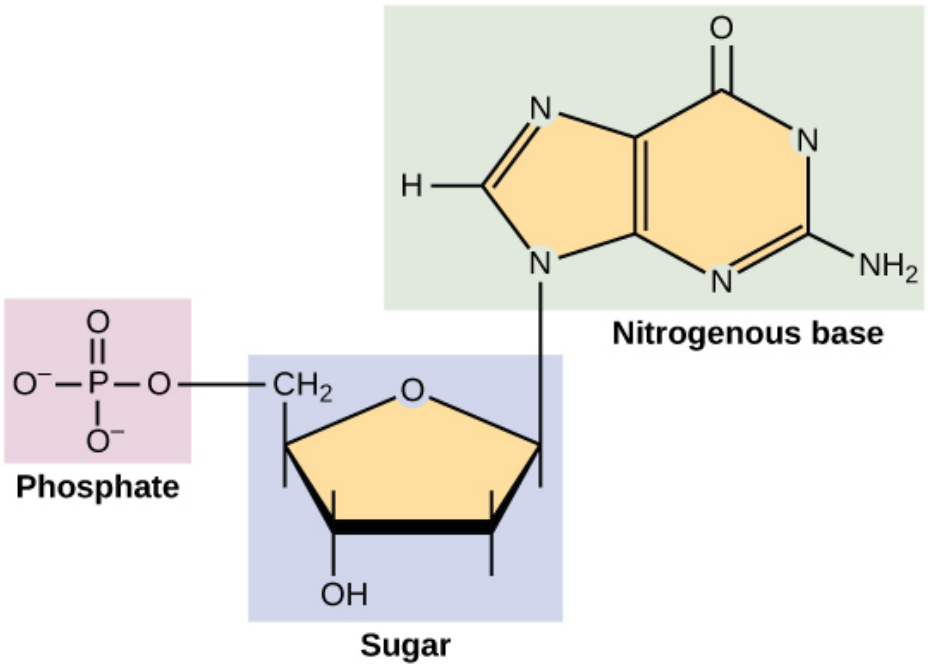


Figure 2.20: A nucleotide is made up of three components: a nitrogenous base, a pentose sugar, and a phosphate group.

2.4.7 DNA Double-Helical Structure

DNA has a double-helical structure (Figure 2.21). It is composed of two strands, or polymers, of nucleotides. Each strand is formed with bonds between phosphate and sugar groups of adjacent nucleotides (called a phosphodiester bond). The two strands are bonded to each other at their bases with hydrogen bonds, and the strands coil about each other along their length, hence the "double helix" description, which means a double spiral.

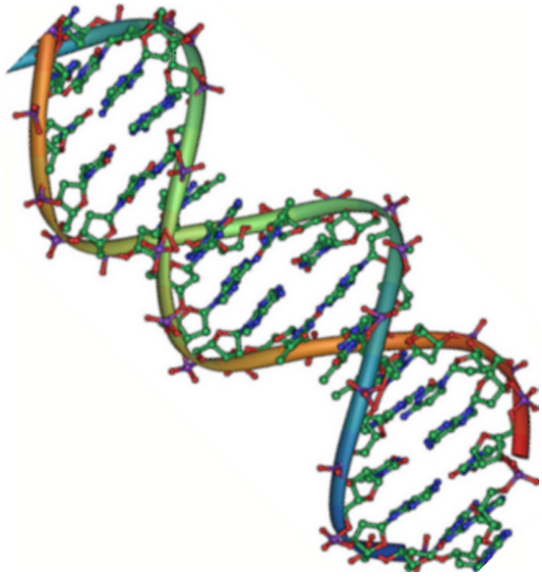


Figure 2.21: The double-helix model shows DNA as two parallel strands of intertwining molecules. (credit: Jerome Walker, Dennis Myts)

The alternating sugar and phosphate groups lie on the outside of each strand, forming the backbone of the DNA. The nitrogenous bases are stacked in the interior, like the steps of a staircase, and these bases pair; the pairs are bound to each other by hydrogen bonds. The bases pair in such a way that the distance between the backbones of the two strands is the same all along the molecule.

2.4.8 Section Summary

Living things are carbon-based because carbon plays such a prominent role in the chemistry of living things. The four covalent bonding positions of the carbon atom can give rise to a wide diversity of compounds with many functions, accounting for the importance of carbon in living things. Carbohydrates are a group of macromolecules that are a vital energy source for the cell, provide structural support to many organisms, and can be found on the surface of the cell as receptors or for cell recognition. Carbohydrates are classified as monosaccharides, disaccharides, and polysaccharides, depending on the number of monomers in the molecule.

Lipids are a class of macromolecules that are nonpolar and hydrophobic in nature. Major types include fats and oils, waxes, phospholipids, and steroids. Fats and oils are a stored form of energy and can include triglycerides. Fats and oils are usually made up of fatty acids and glycerol.

Proteins are a class of macromolecules that can perform a diverse range of functions for the cell. They help in metabolism by providing structural support and by acting as enzymes, carriers or as hormones. The building blocks of proteins are amino acids. Proteins are organized at four levels: primary, secondary, tertiary, and quaternary. Protein shape and function are intricately linked; any change in shape caused by changes in temperature, pH, or chemical exposure may lead to protein denaturation and a loss of function.

Nucleic acids are molecules made up of repeating units of nucleotides that direct cellular activities such as cell division and protein synthesis. Each nucleotide is made up of a pentose sugar, a nitrogenous base, and a phosphate group. There are two types of nucleic acids: DNA and RNA.

2.4.9 Multiple Choice

Exercise 2.4.1 *(Solution on p. 60.)*
An example of a monosaccharide is _____.

a. fructose
b. glucose
c. galactose
d. all of the above

Exercise 2.4.2 *(Solution on p. 60.)*
Cellulose and starch are examples of _____.

a. monosaccharides
b. disaccharides
c. lipids
d. polysaccharides

Exercise 2.4.3 *(Solution on p. 60.)*
Phospholipids are important components of _____.

a. the plasma membrane of cells
b. the ring structure of steroids
c. the waxy covering on leaves
d. the double bond in hydrocarbon chains

Exercise 2.4.4 *(Solution on p. 60.)*
The monomers that make up proteins are called _____.

a. nucleotides
b. disaccharides
c. amino acids
d. chaperones

2.4.10 Free Response

Exercise 2.4.5 *(Solution on p. 60.)*
Explain at least three functions that lipids serve in plants and/or animals.

Exercise 2.4.6 *(Solution on p. 60.)*
Explain what happens if even one amino acid is substituted for another in a polypeptide chain. Provide a specific example.

Solutions to Exercises in Chapter 2

to Exercise 2.2.1 (p. 36)
Figure 2.3 Potassium-39 has twenty neutrons. Potassium-40 has twenty one neutrons.
to Exercise 2.2.2 (p. 36)
A
to Exercise 2.2.3 (p. 36)
A
to Exercise 2.2.4 (p. 36)
A
to Exercise 2.2.5 (p. 36)
Hydrogen bonds form weak associations between different molecules. They provide the structure and shape necessary for proteins and DNA within cells so that they function properly. Hydrogen bonds also give water its unique properties, which are necessary for life.
to Exercise 2.3.1 (p. 41)
D
to Exercise 2.3.2 (p. 41)
C
to Exercise 2.3.3 (p. 41)
C
to Exercise 2.3.4 (p. 42)
Water molecules are polar, meaning they have separated partial positive and negative charges. Because of these charges, water molecules are able to surround charged particles created when a substance dissociates. The surrounding layer of water molecules stabilizes the ion and keeps differently charged ions from reassociating, so the substance stays dissolved.
to Exercise 2.4.1 (p. 59)
D
to Exercise 2.4.2 (p. 59)
D
to Exercise 2.4.3 (p. 59)
A
to Exercise 2.4.4 (p. 59)
C
to Exercise 2.4.5 (p. 59)
Fat serves as a valuable way for animals to store energy. It can also provide insulation. Phospholipids and steroids are important components of cell membranes.
to Exercise 2.4.6 (p. 59)
A change in gene sequence can lead to a different amino acid being added to a polypeptide chain instead of the normal one. This causes a change in protein structure and function. For example, in sickle cell anemia, the hemoglobin β chain has a single amino acid substitution. Because of this change, the disc-shaped red blood cells assume a crescent shape, which can result in serious health problems.

Chapter 3

Cells

3.1 Introduction[1]

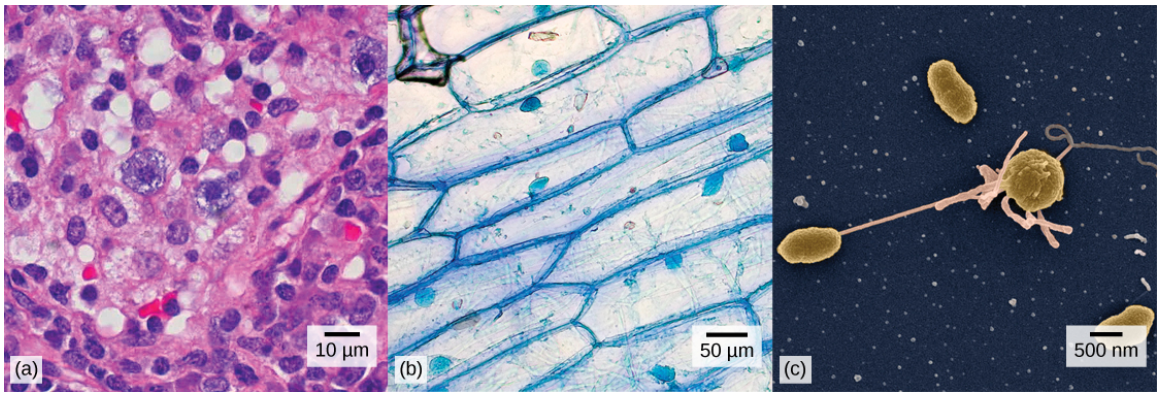


Figure 3.1: (a) Nasal sinus cells (viewed with a light microscope), (b) onion cells (viewed with a light microscope), and (c) *Vibrio tasmaniensis* bacterial cells (viewed using a scanning electron microscope) are from very different organisms, yet all share certain characteristics of basic cell structure. (credit a: modification of work by Ed Uthman, MD; credit b: modification of work by Umberto Salvagnin; credit c: modification of work by Anthony D'Onofrio; scale-bar data from Matt Russell)

Close your eyes and picture a brick wall. What is the basic building block of that wall? It is a single brick, of course. Like a brick wall, your body is composed of basic building blocks, and the building blocks of your body are cells.

Your body has many kinds of cells, each specialized for a specific purpose. Just as a home is made from a variety of building materials, the human body is constructed from many cell types. For example, epithelial cells protect the surface of the body and cover the organs and body cavities within. Bone cells help to support and protect the body. Cells of the immune system fight invading bacteria. Additionally, red blood cells carry oxygen throughout the body. Each of these cell types plays a vital role during the growth, development, and day-to-day maintenance of the body. In spite of their enormous variety, however, all cells

[1] This content is available online at <http://cnx.org/content/m57967/1.1/>.

share certain fundamental characteristics. In this chapter, these characteristics will be examined in greater detail.

3.2 Prokaryotic and Eukaryotic Cells[2]

Cells fall into one of two broad categories: prokaryotic and eukaryotic. The predominantly single-celled organisms of the domains Bacteria and Archaea are classified as prokaryotes (*pro-* = before; *-karyon-* = nucleus). Animal cells, plant cells, fungi, and protists are eukaryotes (*eu-* = true).

3.2.1 Components of Prokaryotic Cells

All cells share four common components: 1) a plasma membrane, an outer covering that separates the cell's interior from its surrounding environment; 2) cytoplasm, consisting of a jelly-like region within the cell in which other cellular components are found; 3) DNA, the genetic material of the cell; and 4) ribosomes, particles that synthesize proteins. However, prokaryotes differ from eukaryotic cells in several ways.

A **prokaryotic cell** is a simple, single-celled (unicellular) organism that lacks a nucleus, or any other membrane-bound organelle. We will shortly come to see that this is significantly different in eukaryotes. Prokaryotic DNA is found in the central part of the cell: a darkened region called the nucleoid (Figure 3.2).

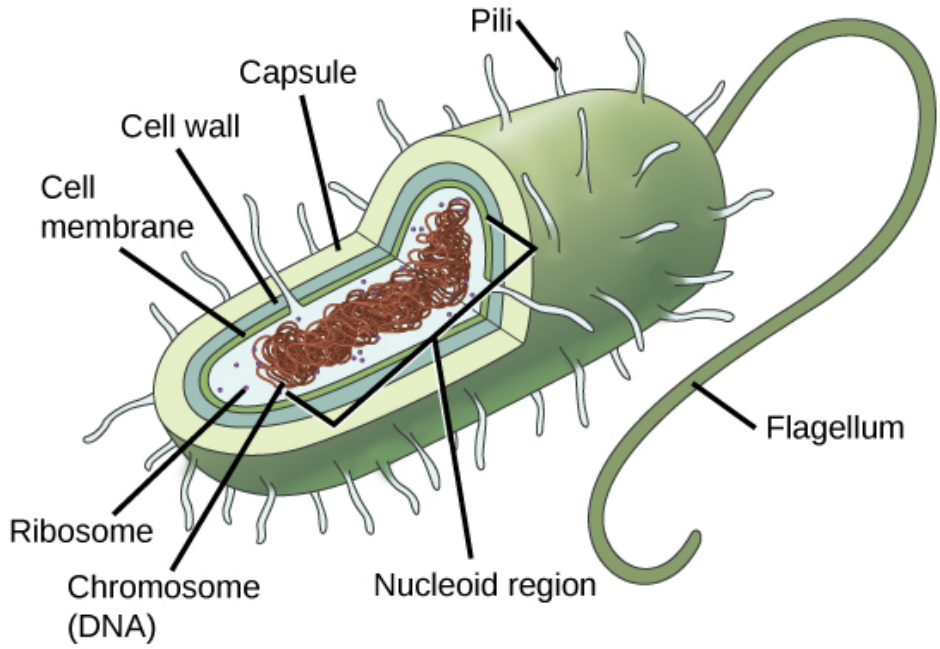


Figure 3.2: This figure shows the generalized structure of a prokaryotic cell.

[2]This content is available online at <http://cnx.org/content/m57968/1.1/>.

3.2.2 Eukaryotic Cells

In nature, the relationship between form and function is apparent at all levels, including the level of the cell, and this will become clear as we explore eukaryotic cells. The principle "form follows function" is found in many contexts. For example, birds and fish have streamlined bodies that allow them to move quickly through the medium in which they live, be it air or water. It means that, in general, one can deduce the function of a structure by looking at its form, because the two are matched.

A **eukaryotic cell** is a cell that has a membrane-bound nucleus and other membrane-bound compartments or sacs, called **organelles**, which have specialized functions. The word eukaryotic means "true kernel" or "true nucleus," alluding to the presence of the membrane-bound nucleus in these cells. The word "organelle" means "little organ," and, as already mentioned, organelles have specialized cellular functions, just as the organs of your body have specialized functions.

3.2.3 Cell Size

At 0.1–5.0 micrometers (μm; 1/1,000,000 of a meter) in diameter, prokaryotic cells are significantly smaller than eukaryotic cells, which have diameters ranging from 10–100 μm (Figure 3.3). The small size of prokaryotes allows ions and organic molecules that enter them to quickly spread to other parts of the cell. Similarly, any wastes produced within a prokaryotic cell can quickly move out. However, larger eukaryotic cells have evolved different structural adaptations to enhance cellular transport. Indeed, the large size of these cells would not be possible without these adaptations. In general, cell size is limited because volume increases much more quickly than does cell surface area. This is because volume is a cubic dimension and surface area is a squared dimension. For example, if X=2, then the surface area (x squared) is 4 and the volume (x cubed) is 8. If x =3, then the surface area is 9 and the volume is 27. As a cell becomes larger, it becomes more and more difficult for the cell to acquire sufficient materials to support the processes inside the cell, because the relative size of the surface area across which materials must be transported declines.

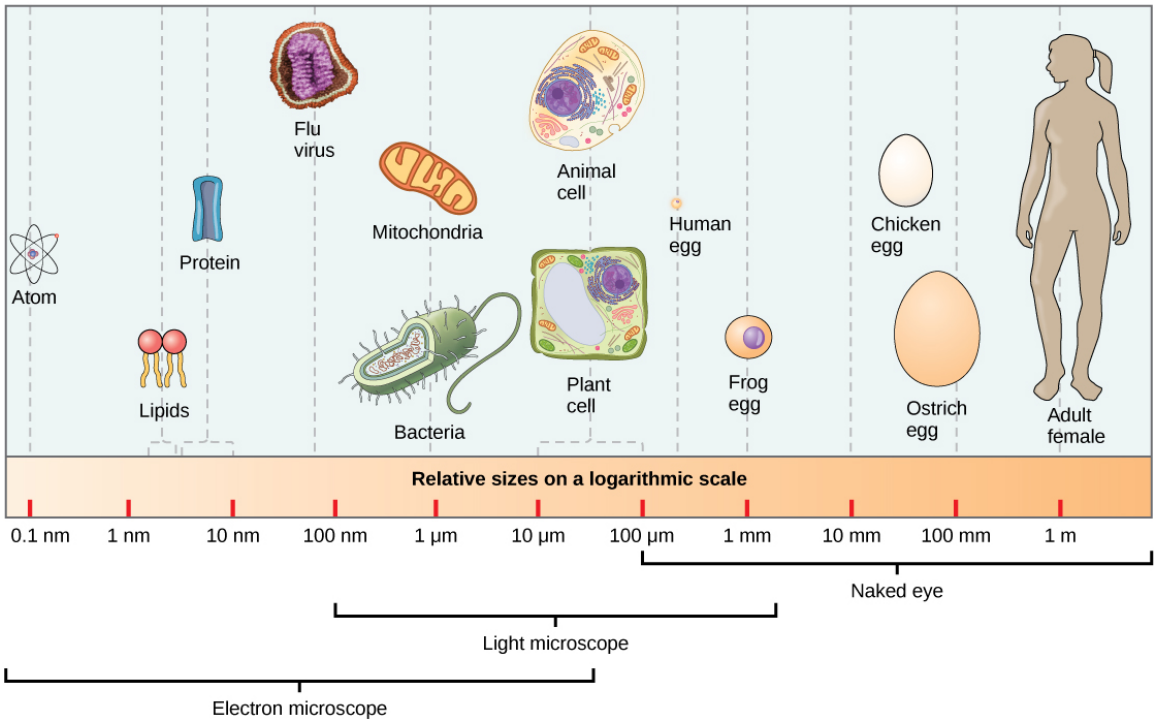


Figure 3.3: This figure shows the relative sizes of different kinds of cells and cellular components. An adult human is shown for comparison. Note that a light microscope is required to view both prokaryotic and eukaryotic cells. Note: 1000 nanometers equals 1 micrometer, 1000 micrometers equals 1 millimeter, and 1000 millimeters equals one meter.

3.2.4 Section Summary

Prokaryotes are predominantly single-celled organisms of the domains Bacteria and Archaea. All prokaryotes have plasma membranes, cytoplasm, ribosomes, a cell wall, DNA, and lack membrane-bound organelles. Many also have polysaccharide capsules. Prokaryotic cells range in diameter from 0.1–5.0 μm.

Like a prokaryotic cell, a eukaryotic cell has a plasma membrane, cytoplasm, and ribosomes, but a eukaryotic cell is typically larger than a prokaryotic cell, has a true nucleus (meaning its DNA is surrounded by a membrane), and has other membrane-bound organelles that allow for compartmentalization of functions. Eukaryotic cells tend to be 10 to 100 times the size of prokaryotic cells.

3.2.5 Multiple Choice

Exercise 3.2.1 *(Solution on p. 88.)*

Which of these do all prokaryotes and eukaryotes share?

a. nuclear envelope
b. cell walls
c. organelles

d. plasma membrane

Exercise 3.2.2 *(Solution on p. 88.)*
A typical prokaryotic cell _____ compared to a eukaryotic cell.

a. is smaller in size by a factor of 100
b. is similar in size
c. is smaller in size by a factor of one million
d. is larger in size by a factor of 10

3.2.6 Free Response

Exercise 3.2.3 *(Solution on p. 88.)*
What are organelles and which type of cells (prokaryotic or eukaryotic) contains them?

3.3 A More Detailed Look at Eukaryotic Cells[3]

At this point, it should be clear that eukaryotic cells have a more complex structure than do prokaryotic cells. Organelles and other cellular components allow for various functions to occur in the cell at the same time. Before discussing the functions of organelles within a eukaryotic cell, let us first examine two important components of the cell: the plasma membrane and the cytoplasm.

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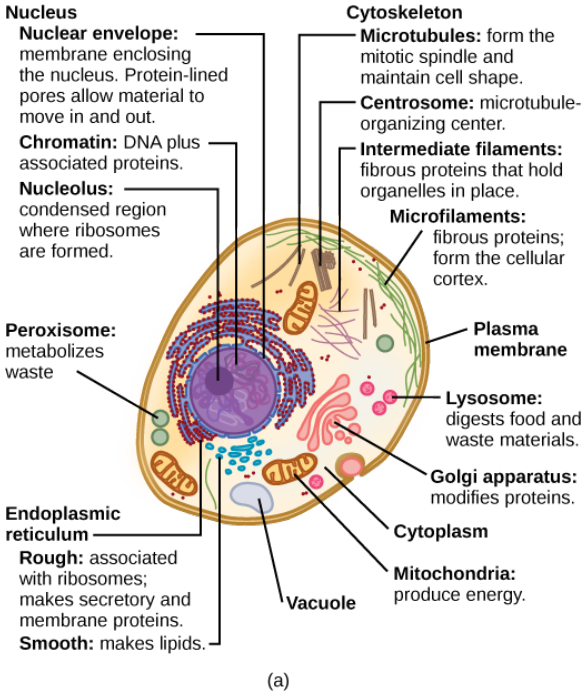
[3]This content is available online at <http://cnx.org/content/m57969/1.2/>.



3.4: This figure shows a typical animal cell.

3.3.1 The Plasma Membrane

Like prokaryotes, eukaryotic cells have a **plasma membrane** (Figure 3.5) made up of a phospholipid bilayer with embedded proteins that separates the internal contents of the cell from its surrounding environment. A phospholipid is a lipid molecule composed of two fatty acid chains, a glycerol backbone, and a phosphate group. The plasma membrane regulates the passage of some substances, such as organic molecules, ions, and water, preventing the passage of some to maintain internal conditions, while actively bringing in or removing others. Other compounds move passively across the membrane.

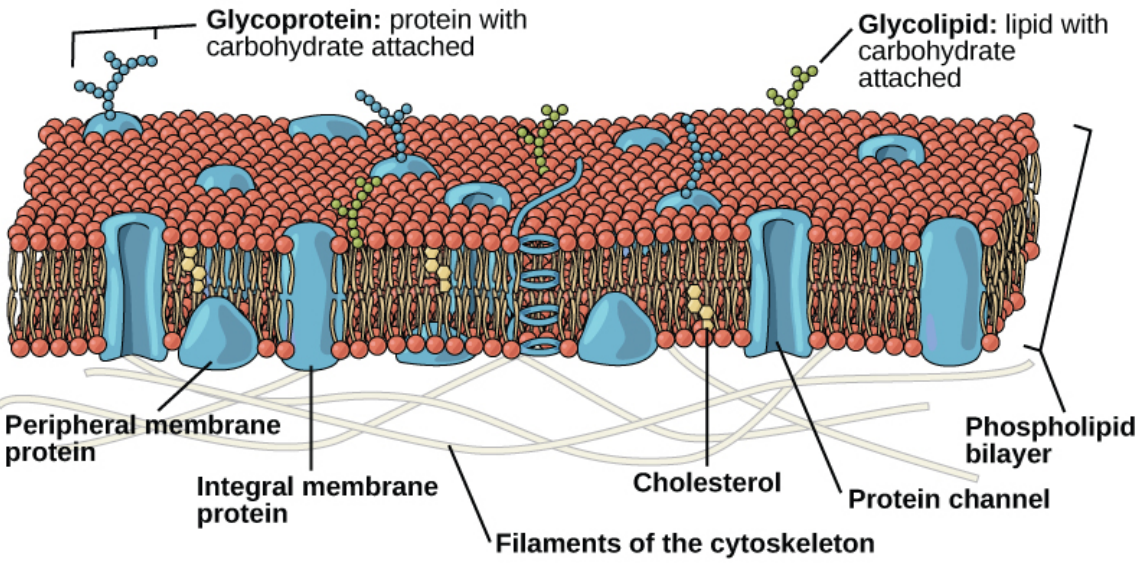


Figure 3.5: The plasma membrane is a phospholipid bilayer with embedded proteins. There are other components, such as cholesterol and carbohydrates, which can be found in the membrane in addition to phospholipids and protein. The phrase "fluid mosaic" is used to describe the structure of the plasma membrane because it is dynamic and contains numerous components.

The plasma membranes of cells that specialize in absorption are folded into fingerlike projections called microvilli (singular = microvillus). This folding increases the surface area of the plasma membrane. Such cells are typically found lining the small intestine, the organ that absorbs nutrients from digested food. This is an excellent example of form matching the function of a structure.

People with celiac disease have an immune response to gluten, which is a protein found in wheat, barley, and rye. The immune response damages microvilli, and thus, afflicted individuals cannot absorb nutrients. This leads to malnutrition, cramping, and diarrhea. Patients suffering from celiac disease must follow a gluten-free diet.

3.3.2 The Cytoplasm

The **cytoplasm** comprises the contents of a cell between the plasma membrane and the nuclear envelope (a structure to be discussed shortly). It is made up of organelles suspended in the gel-like **cytosol**, the cytoskeleton, and various chemicals. Even though the cytoplasm consists of 70 to 80 percent water, it has a semi-solid consistency, which comes from the proteins within it. However, proteins are not the only organic molecules found in the cytoplasm. Glucose and other simple sugars, polysaccharides, amino acids, nucleic acids, fatty acids, and derivatives of glycerol are found there too. Ions of sodium, potassium, calcium, and many other elements are also dissolved in the cytoplasm. Many metabolic reactions, including protein synthesis, take place in the cytoplasm.

3.3.3 The Endomembrane System

The **endomembrane system** (*endo* = within) is a group of membranes and organelles (Figure 3.9) in eukaryotic cells that work together to modify, package, and transport lipids and proteins. It includes the

nuclear envelope, lysosomes, and vesicles, the endoplasmic reticulum and Golgi apparatus, which we will cover shortly. Although not technically *within* the cell, the plasma membrane is included in the endomembrane system because, as you will see, it interacts with the other endomembranous organelles.

3.3.3.1 The Nucleus

Typically, the nucleus is the most prominent organelle in a cell. The **nucleus** (plural = nuclei) houses the cell's DNA in the form of chromatin and directs the synthesis of ribosomes and proteins. Let us look at it in more detail (Figure 3.6).

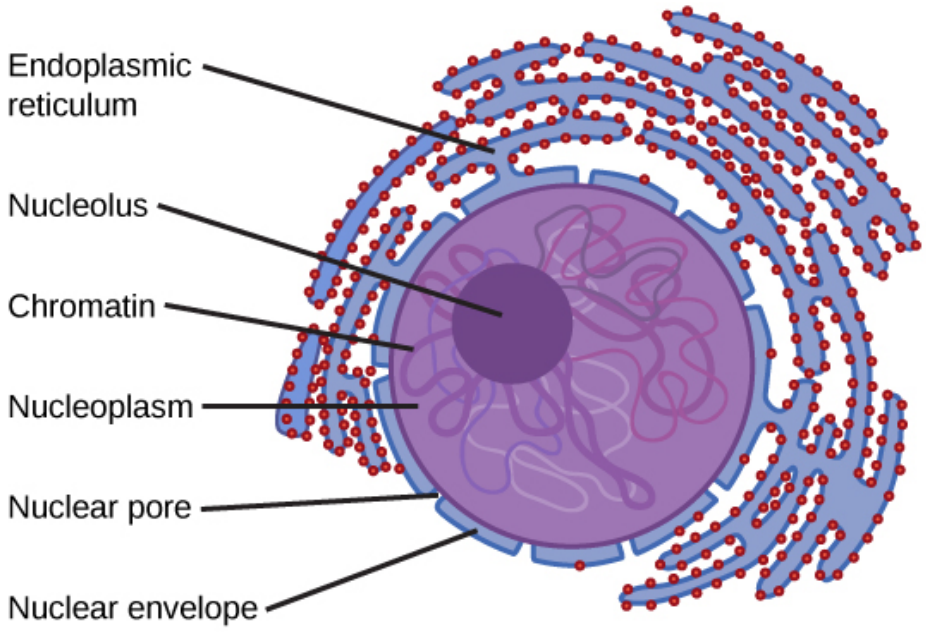


Figure 3.6: The outermost boundary of the nucleus is the nuclear envelope. Notice that the nuclear envelope consists of two phospholipid bilayers (membranes)—an outer membrane and an inner membrane—in contrast to the plasma membrane (Figure 3.5), which consists of only one phospholipid bilayer. (credit: modification of work by NIGMS, NIH)

The **nuclear envelope** is a double-membrane structure that constitutes the outermost portion of the nucleus (Figure 3.6). Both the inner and outer membranes of the nuclear envelope are phospholipid bilayers.

The nuclear envelope is punctuated with pores that control the passage of ions, molecules, and RNA between the nucleoplasm and the cytoplasm. The DNA in the nucleus is too large to fit through the pores.

To understand chromatin, it is helpful to first consider chromosomes. Chromosomes are structures within the nucleus that are made up of DNA (the hereditary material) and proteins. This combination of DNA and proteins is called chromatin. In eukaryotes, chromosomes are linear structures. Every species has a specific number of chromosomes in the nucleus of its body cells. For example, in humans, the chromosome number is 46, whereas in fruit flies, the chromosome number is eight.

Chromosomes are only visible and distinguishable from one another when the cell is getting ready to divide. This is because the DNA condenses or compacts in preparation for cell division. When the cell is in

the growth and maintenance phases of its life cycle, the chromosomes resemble an unwound, jumbled bunch of threads and the DNA is more accessible to be used to make proteins.

We already know that the nucleus directs the synthesis of ribosomes, but how does it do this? Some chromosomes have sections of DNA that encode ribosomal RNA. A darkly staining area within the nucleus, called the **nucleolus** (plural = nucleoli), aggregates the ribosomal RNA with associated proteins to assemble the ribosomal subunits that are then transported through the nuclear pores into the cytoplasm.

3.3.3.2 The Endoplasmic Reticulum

The **endoplasmic reticulum (ER)** (Figure 3.9) is a series of interconnected membranous tubules that collectively modify proteins and synthesize lipids. However, these two functions are performed in separate areas of the endoplasmic reticulum: the rough endoplasmic reticulum and the smooth endoplasmic reticulum, respectively.

The **rough endoplasmic reticulum (RER)** is so named because the ribosomes attached to its cytoplasmic surface give it a studded appearance when viewed through an electron microscope.

The ribosomes synthesize proteins while attached to the ER, resulting in transfer of their newly synthesized proteins into the lumen of the RER where they undergo modifications such as folding or addition of sugars. The RER also makes phospholipids for cell membranes.

If the phospholipids or modified proteins are not destined to stay in the RER, they will be packaged within vesicles and transported from the RER by budding from the membrane (Figure 3.9). Since the RER is engaged in modifying proteins that will be secreted from the cell, it is abundant in cells that secrete proteins, such as the liver.

The **smooth endoplasmic reticulum (SER)** is continuous with the RER but has few or no ribosomes on its cytoplasmic surface (see 3.4). The SER's functions include synthesis of carbohydrates, lipids (including phospholipids), and steroid hormones; detoxification of medications and poisons; alcohol metabolism; and storage of calcium ions.

3.3.3.3 The Golgi Apparatus

We have already mentioned that vesicles can bud from the ER, but where do the vesicles go? Before reaching their final destination, the lipids or proteins within the transport vesicles need to be sorted, packaged, and tagged so that they wind up in the right place. The sorting, tagging, packaging, and distribution of lipids and proteins take place in the **Golgi apparatus** (also called the Golgi body), a series of flattened membranous sacs (Figure 3.7).

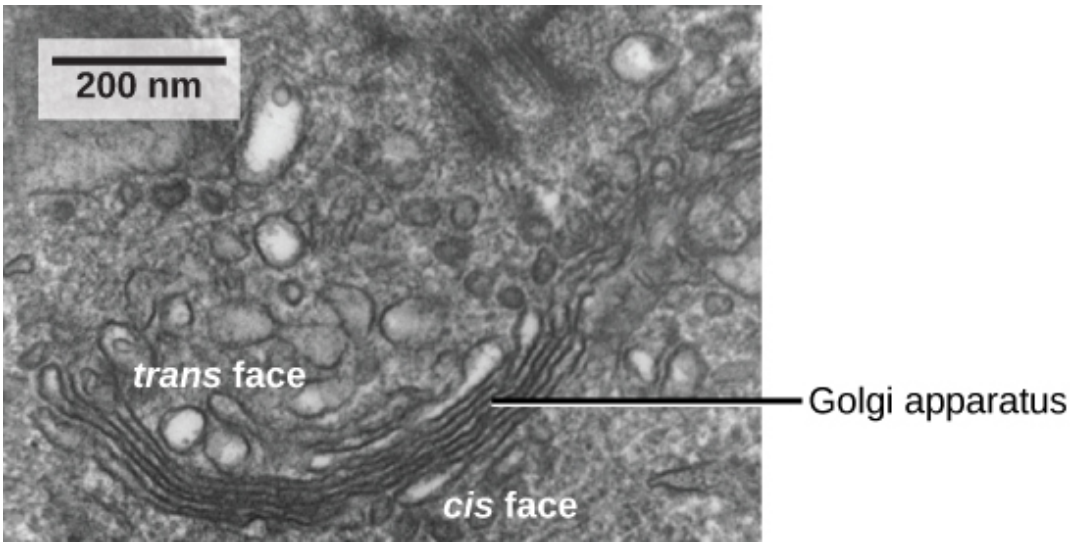


Figure 3.7: The Golgi apparatus in this transmission electron micrograph of a white blood cell is visible as a stack of semicircular flattened rings in the lower portion of this image. Several vesicles can be seen near the Golgi apparatus. (credit: modification of work by Louisa Howard; scale-bar data from Matt Russell)

The Golgi apparatus has a receiving face near the endoplasmic reticulum and a releasing face on the side away from the ER, toward the cell membrane. The transport vesicles that form from the ER travel to the receiving face, fuse with it, and empty their contents into the lumen of the Golgi apparatus. As the proteins and lipids travel through the Golgi, they undergo further modifications. The most frequent modification is the addition of short chains of sugar molecules. The newly modified proteins and lipids are then tagged with small molecular groups to enable them to be routed to their proper destinations.

Finally, the modified and tagged proteins are packaged into vesicles that bud from the opposite face of the Golgi. While some of these vesicles, transport vesicles, deposit their contents into other parts of the cell where they will be used, others, secretory vesicles, fuse with the plasma membrane and release their contents outside the cell.

The amount of Golgi in different cell types again illustrates that form follows function within cells. Cells that engage in a great deal of secretory activity (such as cells of the salivary glands that secrete digestive enzymes or cells of the immune system that secrete antibodies) have an abundant number of Golgi.

3.3.3.4 Lysosomes

In animal cells, the **lysosomes** are the cell's "garbage disposal." Digestive enzymes within the lysosomes aid the breakdown of proteins, polysaccharides, lipids, nucleic acids, and even worn-out organelles. In single-celled eukaryotes, lysosomes are important for digestion of the food they ingest and the recycling of organelles. These enzymes are active at a much lower pH (more acidic) than those located in the cytoplasm. Many reactions that take place in the cytoplasm could not occur at a low pH, thus the advantage of compartmentalizing the eukaryotic cell into organelles is apparent.

Lysosomes also use their hydrolytic enzymes to destroy disease-causing organisms that might enter the cell. A good example of this occurs in a group of white blood cells called macrophages, which are part of your body's immune system. In a process known as phagocytosis, a section of the plasma membrane of

the macrophage invaginates (folds in) and engulfs a pathogen. The invaginated section, with the pathogen inside, then pinches itself off from the plasma membrane and becomes a vesicle. The vesicle fuses with a lysosome. The lysosome's hydrolytic enzymes then destroy the pathogen (Figure 3.8).

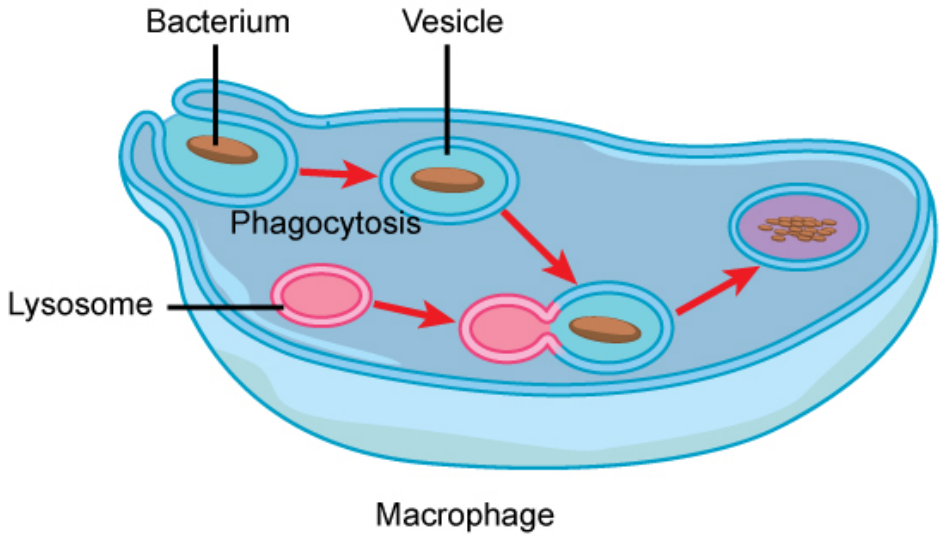


Figure 3.8: A macrophage has phagocytized a potentially pathogenic bacterium into a vesicle, which then fuses with a lysosome within the cell so that the pathogen can be destroyed. Other organelles are present in the cell, but for simplicity, are not shown.

3.3.3.5 Vesicles

Vesicles are membrane-bound sacs that function in storage and transport. Vesicles can fuse with other membranes within the cell system.

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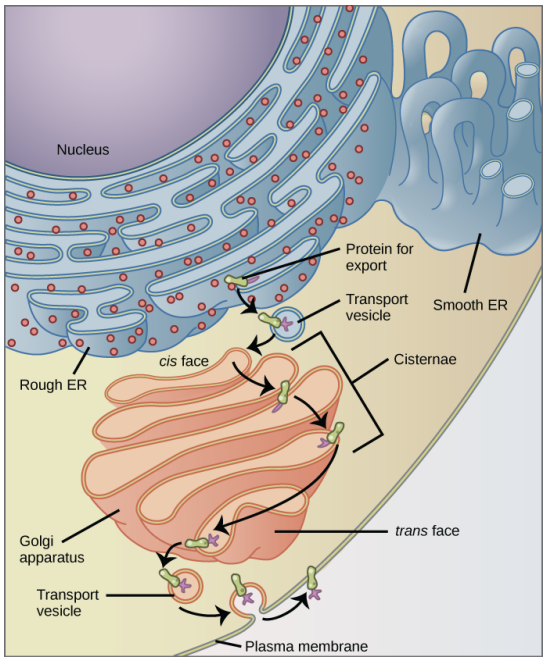

Figure 3.9: The endomembrane system works to modify, package, and transport lipids and proteins. (credit: modification of work by Magnus Manske)

3.3.4 Ribosomes

Ribosomes are the cellular structures responsible for protein synthesis. When viewed through an electron microscope, free ribosomes appear as either clusters or single tiny dots floating freely in the cytoplasm. Ribosomes may be attached to either the cytoplasmic side of the plasma membrane or the cytoplasmic side of the endoplasmic reticulum. Electron microscopy has shown that ribosomes consist of large and small subunits. Ribosomes are enzyme complexes that are responsible for protein synthesis.

Because protein synthesis is essential for all cells, ribosomes are found in practically every cell, although they are smaller in prokaryotic cells. They are particularly abundant in immature red blood cells for the synthesis of hemoglobin, which functions in the transport of oxygen throughout the body.

3.3.5 Mitochondria

Mitochondria (singular = mitochondrion) are often called the "powerhouses" or "energy factories" of a cell because they are responsible for making adenosine triphosphate (ATP), the cell's main energy-carrying molecule. The formation of ATP from the breakdown of glucose is known as cellular respiration. Mitochondria are oval-shaped, double-membrane organelles (Figure 3.10) that have their own ribosomes and DNA. Each membrane is a phospholipid bilayer embedded with proteins. The inner layer has folds called cristae, which increase the surface area of the inner membrane. The area surrounded by the folds is called the mitochondrial matrix. The cristae and the matrix have different roles in cellular respiration.

In keeping with our theme of form following function, it is important to point out that muscle cells have a very high concentration of mitochondria because muscle cells need a lot of energy to contract.

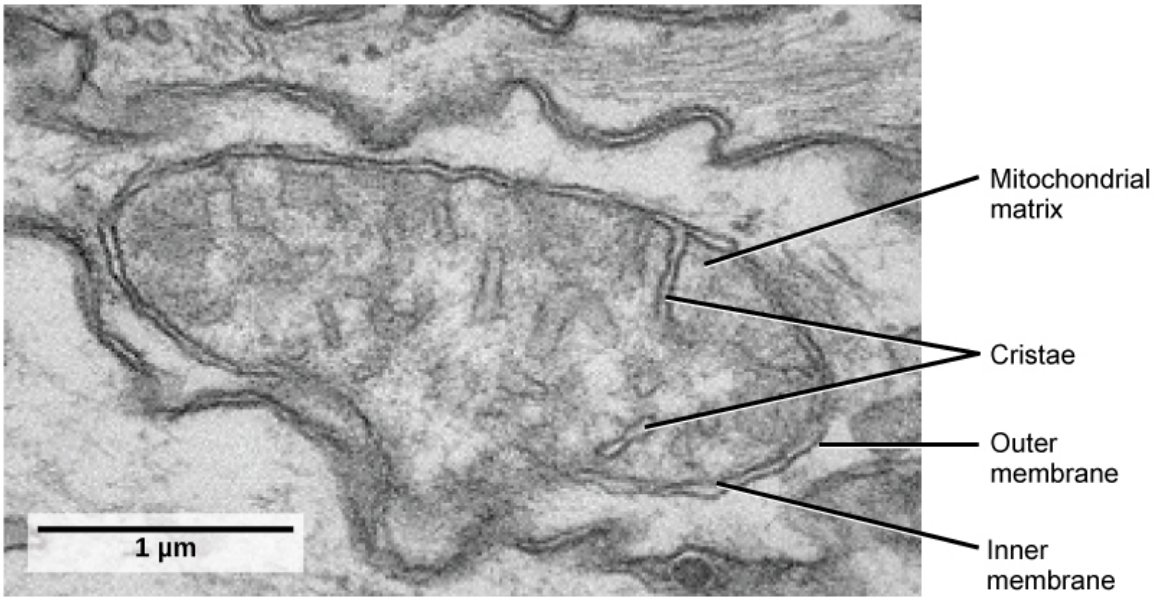

Figure 3.10: This transmission electron micrograph shows a mitochondrion as viewed with an electron microscope. Notice the inner and outer membranes, the cristae, and the mitochondrial matrix. (credit: modification of work by Matthew Britton; scale-bar data from Matt Russell)

3.3.6 Section Summary

Like a prokaryotic cell, a eukaryotic cell has a plasma membrane, cytoplasm, and ribosomes, but a eukaryotic cell is typically larger than a prokaryotic cell, has a true nucleus (meaning its DNA is surrounded by a membrane), and has other membrane-bound organelles that allow for compartmentalization of functions. The plasma membrane is a phospholipid bilayer embedded with proteins. The nucleolus within the nucleus is the site for ribosome assembly. Ribosomes are found in the cytoplasm or are attached to the cytoplasmic side of the plasma membrane or endoplasmic reticulum. They perform protein synthesis. Mitochondria perform cellular respiration and produce ATP. Vesicles are storage and transport compartments.

The endomembrane system includes the nuclear envelope, the endoplasmic reticulum, Golgi apparatus, lysosomes, vesicles, as well as the plasma membrane. These cellular components work together to modify, package, tag, and transport membrane lipids and proteins.

3.3.7 Art Connections

Exercise 3.3.1 ***(Solution on p. 88.)***

Figure 3.9 Why does the *cis* face of the Golgi not face the plasma membrane?

3.3.8 Multiple Choice

Exercise 3.3.2 ***(Solution on p. 88.)***

Which of the following is found both in eukaryotic and prokaryotic cells?

a. nucleus
b. mitochondrion
c. vessicle
d. ribosome

Exercise 3.3.3 *(Solution on p. 88.)*
Which of the following is not a component of the endomembrane system?

a. mitochondrion
b. Golgi apparatus
c. endoplasmic reticulum
d. lysosome

3.3.9 Free Response

Exercise 3.3.4 *(Solution on p. 88.)*
In the context of cell biology, what do we mean by form follows function? What are at least two examples of this concept?

3.4 A More Detailed Look At The Cell Membrane[4]

A cell's plasma membrane defines the boundary of the cell and determines the nature of its contact with the environment. Cells exclude some substances, take in others, and excrete still others, all in controlled quantities. Plasma membranes enclose the borders of cells, but rather than being a static bag, they are dynamic and constantly in flux. The plasma membrane must be sufficiently flexible to allow certain cells, such as red blood cells and white blood cells, to change shape as they pass through narrow capillaries. These are the more obvious functions of a plasma membrane. In addition, the surface of the plasma membrane carries markers that allow cells to recognize one another, which is vital as tissues and organs form during early development, and which later plays a role in the "self" versus "non-self" distinction of the immune response.

The plasma membrane also carries receptors, which are attachment sites for specific substances that interact with the cell. Each receptor is structured to bind with a specific substance. For example, surface receptors of the membrane create changes in the interior, such as changes in enzymes of metabolic pathways. These metabolic pathways might be vital for providing the cell with energy, making specific substances for the cell, or breaking down cellular waste or toxins for disposal. Receptors on the plasma membrane's exterior surface interact with hormones or neurotransmitters, and allow their messages to be transmitted into the cell. Some recognition sites are used by viruses as attachment points. Although they are highly specific, pathogens like viruses may evolve to exploit receptors to gain entry to a cell by mimicking the specific substance that the receptor is meant to bind. This specificity helps to explain why human immunodeficiency virus (HIV) or any of the five types of hepatitis viruses invade only specific cells.

3.4.1 Fluid Mosaic Model

In 1972, S. J. Singer and Garth L. Nicolson proposed a new model of the plasma membrane that, compared to earlier understanding, better explained both microscopic observations and the function of the plasma membrane. This was called the **fluid mosaic model**. The model has evolved somewhat over time, but still best accounts for the structure and functions of the plasma membrane as we now understand them. The

[4]This content is available online at <http://cnx.org/content/m57970/1.2/>.

fluid mosaic model describes the structure of the plasma membrane as a mosaic of components—including phospholipids, cholesterol, proteins, and carbohydrates—in which the components are able to flow and change position, while maintaining the basic integrity of the membrane. Both phospholipid molecules and embedded proteins are able to diffuse rapidly and laterally in the membrane. The fluidity of the plasma membrane is necessary for the activities of certain enzymes and transport molecules within the membrane. Plasma membranes range from 5–10 nanometers (nm) thick. As a comparison, human red blood cells, visible via light microscopy, are approximately 8 micrometers (μm) thick, or approximately 1,000 times thicker than a plasma membrane. (Figure 3.11)

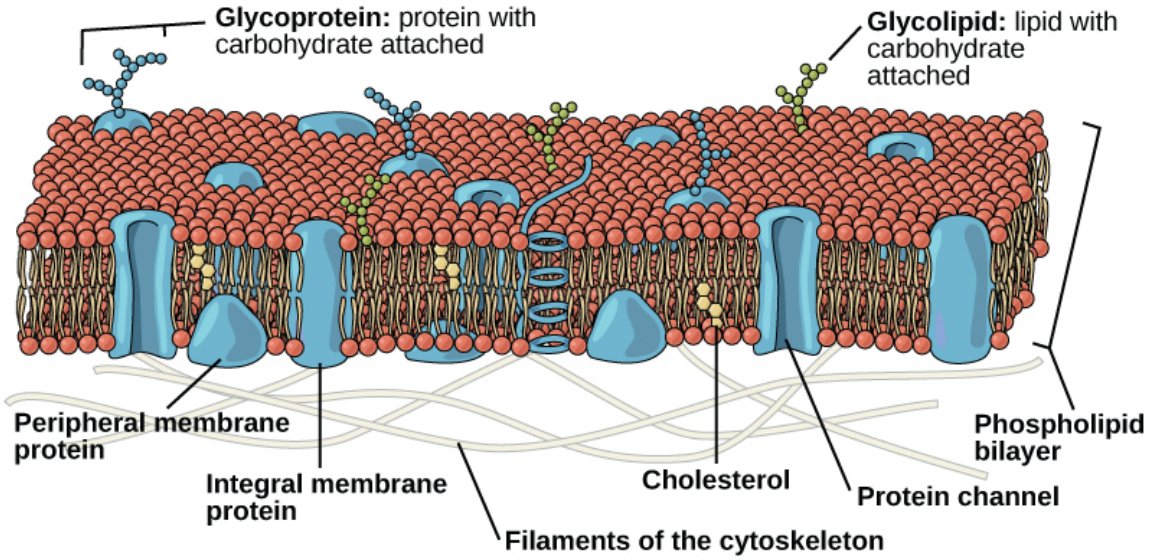

Figure 3.11: The fluid mosaic model of the plasma membrane structure describes the plasma membrane as a fluid combination of phospholipids, cholesterol, proteins, and carbohydrates.

The plasma membrane is made up primarily of a bilayer of phospholipids with embedded proteins, carbohydrates, glycolipids, and glycoproteins, and, in animal cells, cholesterol. The amount of cholesterol in animal plasma membranes regulates the fluidity of the membrane and changes based on the temperature of the cell's environment. In other words, cholesterol acts as antifreeze in the cell membrane and is more abundant in animals that live in cold climates.

The main fabric of the membrane is composed of two layers of phospholipid molecules, and the polar ends of these molecules (which look like a collection of balls in an artist's rendition of the model) (Figure 3.11) are in contact with aqueous fluid both inside and outside the cell. Thus, both surfaces of the plasma membrane are hydrophilic. In contrast, the interior of the membrane, between its two surfaces, is a hydrophobic or nonpolar region because of the fatty acid tails. This region has no attraction for water or other polar molecules.

Proteins make up the second major chemical component of plasma membranes. Integral proteins are embedded in the plasma membrane and may span all or part of the membrane. Integral proteins may serve as channels or pumps to move materials into or out of the cell. Peripheral proteins are found on the exterior or interior surfaces of membranes, attached either to integral proteins or to phospholipid molecules. Both integral and peripheral proteins may serve as enzymes, as structural attachments for the fibers of the cytoskeleton, or as part of the cell's recognition sites.

Carbohydrates are the third major component of plasma membranes. They are always found on the exterior surface of cells and are bound either to proteins (forming glycoproteins) or to lipids (forming glycolipids). These carbohydrate chains may consist of 2–60 monosaccharide units and may be either straight or branched. Along with peripheral proteins, carbohydrates form specialized sites on the cell surface that allow cells to recognize each other.

: **How Viruses Infect Specific Organs**

Specific glycoprotein molecules exposed on the surface of the cell membranes of host cells are exploited by many viruses to infect specific organs. For example, HIV is able to penetrate the plasma membranes of specific kinds of white blood cells called T-helper cells and monocytes, as well as some cells of the central nervous system. The hepatitis virus attacks only liver cells.

These viruses are able to invade these cells, because the cells have binding sites on their surfaces that the viruses have exploited with equally specific glycoproteins in their coats. (Figure 3.12). The cell is tricked by the mimicry of the virus coat molecules, and the virus is able to enter the cell. Other recognition sites on the virus's surface interact with the human immune system, prompting the body to produce antibodies. Antibodies are made in response to the antigens (or proteins associated with invasive pathogens). These same sites serve as places for antibodies to attach, and either destroy or inhibit the activity of the virus. Unfortunately, these sites on HIV are encoded by genes that change quickly, making the production of an effective vaccine against the virus very difficult. The virus population within an infected individual quickly evolves through mutation into different populations, or variants, distinguished by differences in these recognition sites. This rapid change of viral surface markers decreases the effectiveness of the person's immune system in attacking the virus, because the antibodies will not recognize the new variations of the surface patterns.

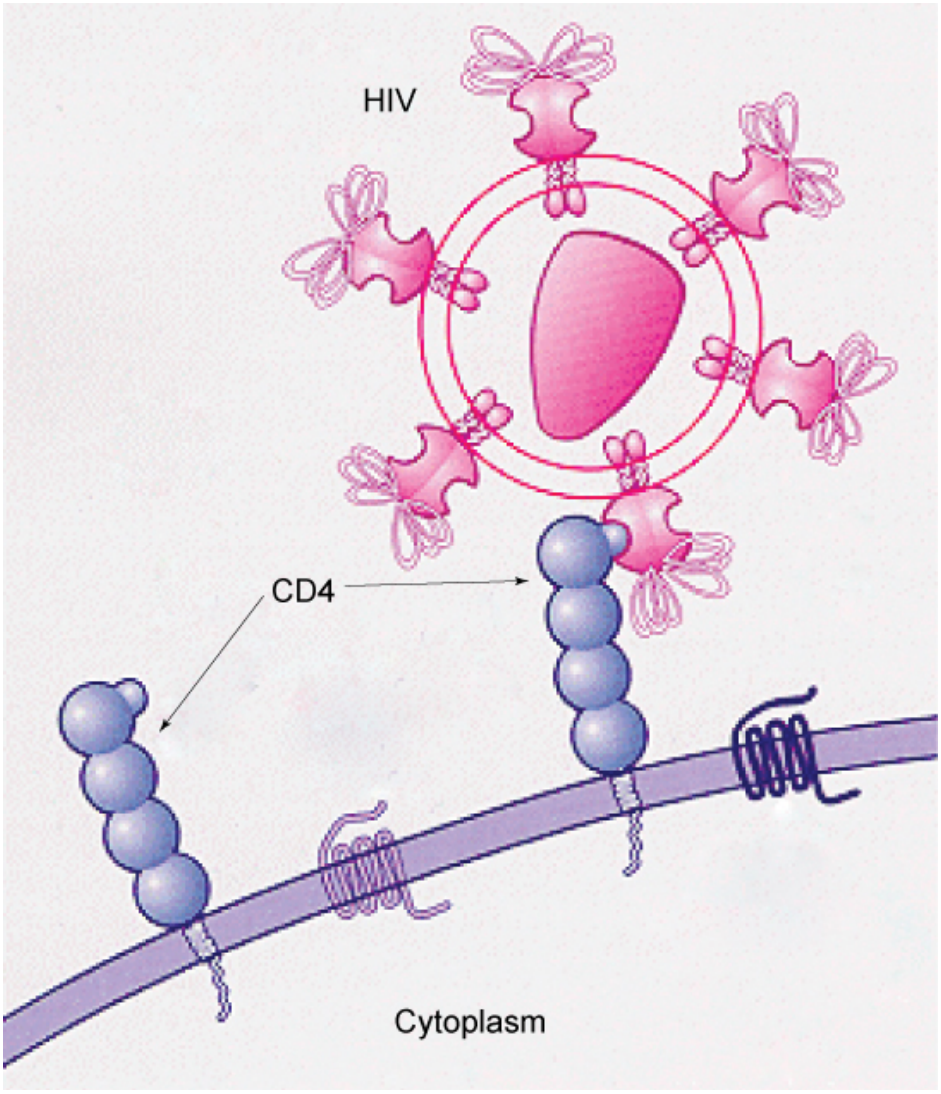

Figure 3.12: HIV docks at and binds to the CD4 receptor, a glycoprotein on the surface of T cells, before entering, or infecting, the cell. (credit: modification of work by US National Institutes of Health/National Institute of Allergy and Infectious Diseases)

3.4.2 Section Summary

The modern understanding of the plasma membrane is referred to as the fluid mosaic model. The plasma membrane is composed of a bilayer of phospholipids, with their hydrophobic, fatty acid tails in contact with each other. The landscape of the membrane is studded with proteins, some of which span the membrane. Some of these proteins serve to transport materials into or out of the cell. Carbohydrates are attached to some of the proteins and lipids on the outward-facing surface of the membrane. These form complexes that function to identify the cell to other cells. The fluid nature of the membrane owes itself to the configuration of the fatty acid tails, the presence of cholesterol embedded in the membrane (in animal cells), and the mosaic

nature of the proteins and protein-carbohydrate complexes, which are not firmly fixed in place. Plasma membranes enclose the borders of cells, but rather than being a static bag, they are dynamic and constantly in flux.

3.4.3 Multiple Choice

Exercise 3.4.1 *(Solution on p. 88.)*
Which plasma membrane component can be either found on its surface or embedded in the membrane structure?

a. protein
b. cholesterol
c. carbohydrate
d. phospholipid

Exercise 3.4.2 *(Solution on p. 88.)*
The tails of the phospholipids of the plasma membrane are composed of _____ and are _____.

a. phosphate groups; hydrophobic
b. fatty acid groups; hydrophilic
c. phosphate groups; hydrophilic
d. fatty acid groups; hydrophobic

3.4.4 Free Response

Exercise 3.4.3 *(Solution on p. 88.)*
Why is it advantageous for the cell membrane to be fluid in nature?

3.5 Passive Transport Mechanisms[5]

Plasma membranes must allow certain substances to enter and leave a cell, while preventing harmful material from entering and essential material from leaving. In other words, plasma membranes are **selectively permeable**—they allow some substances through but not others. If they were to lose this selectivity, the cell would no longer be able to sustain itself, and it would be destroyed. Some cells require larger amounts of specific substances than do other cells; they must have a way of obtaining these materials from the extracellular fluids. This may happen passively, as certain materials move back and forth, or the cell may have special mechanisms that ensure transport. Most cells expend most of their energy, in the form of adenosine triphosphate (ATP), to create and maintain an uneven distribution of ions on the opposite sides of their membranes. The structure of the plasma membrane contributes to these functions, but it also presents some problems.

The most direct forms of membrane transport are passive. **Passive transport** is a naturally occurring phenomenon and does not require the cell to expend energy to accomplish the movement. In passive transport, substances move from an area of higher concentration to an area of lower concentration in a process called diffusion. Concentration refers to the amount of a solute in a volume of solution. The greater the amount of solute in the volume, the higher the concentration. A physical space in which there is a different concentration of a single substance is said to have a **concentration gradient**. For example, if a drop of food

[5]This content is available online at <http://cnx.org/content/m57971/1.2/>.

coloring is added to a glass of water, the place where the dye lands represents a high solute concentration and the rest of the water represents a low solute concentration. Over time, the dye will passively move via diffusion until the concentration is equal throughout the water.

3.5.1 Selective Permeability

Recall that plasma membranes have hydrophilic and hydrophobic regions. This characteristic helps the movement of certain materials through the membrane and hinders the movement of others. Lipid-soluble material can easily slip through the hydrophobic lipid core of the membrane. Substances such as the fat-soluble vitamins A, D, E, and K readily pass through the plasma membranes in the digestive tract and other tissues. Fat-soluble drugs also gain easy entry into cells and are readily transported into the body's tissues and organs. Molecules of oxygen and carbon dioxide, which are relative small and nonpolar, pass through by simple diffusion.

Polar substances, with the exception of water, present problems for the membrane. While some polar molecules connect easily with the outside of a cell, they cannot readily pass through the lipid core of the plasma membrane. Additionally, whereas small ions could easily slip through the spaces in the mosaic of the membrane, their charge prevents them from doing so. Ions such as sodium, potassium, calcium, and chloride must have a special means of penetrating plasma membranes. Simple sugars and amino acids also need help with transport across plasma membranes.

3.5.2 Diffusion

Diffusion is a passive process of transport. A single substance tends to move from an area of high concentration to an area of low concentration until the concentration is equal across the space. You are familiar with diffusion of substances through the air. For example, think about someone opening a bottle of perfume in a room filled with people. The perfume is at its highest concentration in the bottle and is at its lowest at the edges of the room. The perfume vapor will diffuse, or spread away, from the bottle, and gradually, more and more people will smell the perfume as it spreads. Materials move within the cell's cytosol by diffusion, and certain materials move through the plasma membrane by diffusion (Figure 3.13). Diffusion expends no energy. Rather the different concentrations of materials in different areas are a form of potential energy, and diffusion is the dissipation of that potential energy as materials move down their concentration gradients, from high to low.

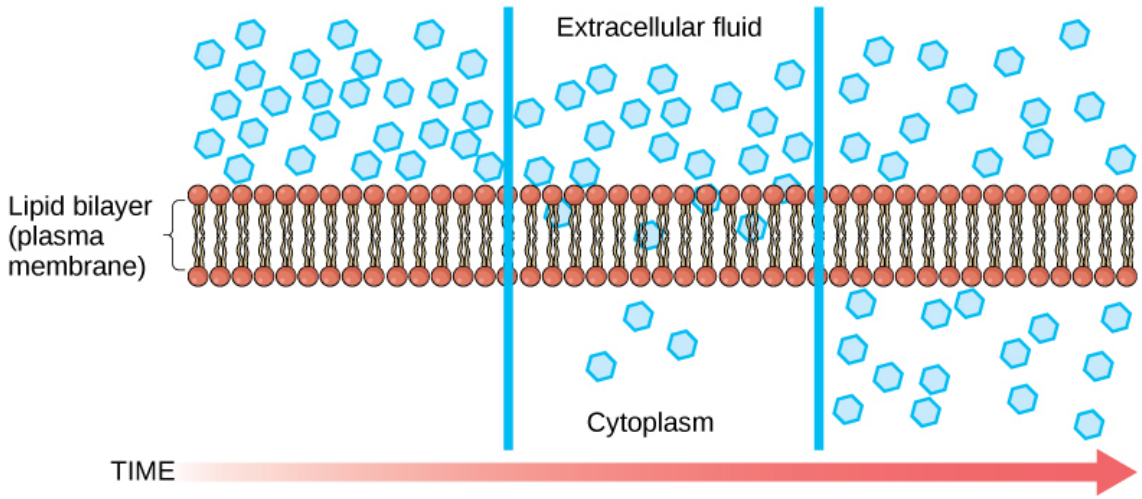

Figure 3.13: Diffusion through a permeable membrane follows the concentration gradient of a substance, moving the substance from an area of high concentration to one of low concentration. When the concentrations are equal on both sides of the membrane, a concentration gradient no longer exists and there is no longer net movement of solution in either direction.(credit: modification of work by Mariana Ruiz Villarreal)

Each separate substance in a medium, such as the extracellular fluid, has its own concentration gradient, independent of the concentration gradients of other materials. Additionally, each substance will diffuse according to that gradient.

Several factors affect the rate of diffusion:

- Extent of the concentration gradient: The greater the difference in concentration, the more rapid the diffusion. The closer the distribution of the material gets to equal on both sides, the slower the rate of diffusion becomes.
- Mass of the molecules diffusing: More massive molecules move more slowly, because it is more difficult for them to move between the molecules of the substance they are moving through; therefore, they diffuse more slowly.
- Temperature: Higher temperatures increase the energy and therefore the movement of the molecules, increasing the rate of diffusion.

: For an animation of the diffusion process in action, view this short

video[6] on cell membrane transport.

3.5.3 Facilitated transport

In **facilitated transport**, also called facilitated diffusion, material moves across the plasma membrane with the assistance of transmembrane proteins down a concentration gradient (from high to low concentration) without the expenditure of cellular energy. However, the substances that undergo facilitated transport would otherwise not diffuse easily or quickly across the plasma membrane. The solution to moving polar substances and other substances across the plasma membrane rests in the proteins that span its surface. The material being transported is first attached to protein or glycoprotein receptors on the exterior surface of the plasma membrane. This allows the material that is needed by the cell to be removed from the extracellular fluid. The substances are then passed to specific integral proteins that facilitate their passage, because they form channels or pores that allow certain substances to pass through the membrane. The integral proteins involved in facilitated transport are collectively referred to as transport proteins, and they function as either channels for the material or carriers.

3.5.4 Osmosis

Osmosis is the diffusion of water through a semipermeable membrane according to the concentration gradient of water across the membrane. Whereas diffusion transports material across membranes and within cells, osmosis transports *only water* across a membrane and the membrane limits the diffusion of solutes in the water. Osmosis is a special case of diffusion. Water, like other substances, moves from an area of higher concentration to one of lower concentration. Imagine a beaker with a semipermeable membrane, separating the two sides or halves (Figure 3.14). On both sides of the membrane, the water level is the same, but there are different concentrations on each side of a dissolved substance, or **solute**, that cannot cross the membrane. If the volume of the water is the same, but the concentrations of solute are different, then there are also different concentrations of water, the solvent, on either side of the membrane.

[6] http://openstaxcollege.org/l/passive_trnsprt

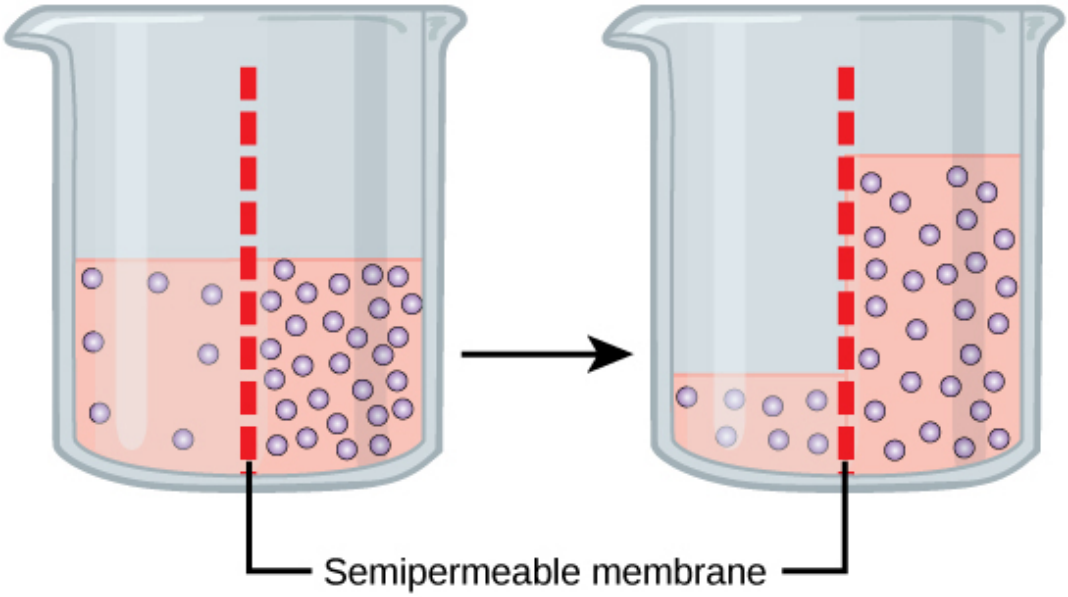

Figure 3.14: In osmosis, water always moves from an area of higher concentration (of water) to one of lower concentration (of water). In this system, the solute cannot pass through the selectively permeable membrane due to its size.

A principle of diffusion is that the molecules move around and will spread evenly throughout the medium if they can. However, only the material capable of getting through the membrane will diffuse through it. In this example, the solute cannot diffuse through the membrane, but the water can. Water has a concentration gradient in this system. Therefore, water will diffuse down its concentration gradient, crossing the membrane to the side where it is less concentrated. This diffusion of water through the membrane—osmosis—will continue until the concentration gradient of water goes to zero. Osmosis proceeds constantly in living systems.

: Watch this video[7] that illustrates diffusion in hot versus cold solutions.

[7] http://openstaxcollege.org/l/passive_trnsprt

3.5.5 Tonicity

Tonicity describes the amount of solute in a solution. Three terms—hypotonic, isotonic, and hypertonic—are used to relate the concentration of solutes inside of a cell compared to the concentration of solutes in the fluid that contains the cells. In a **hypotonic** solution, such as tap water, the extracellular fluid has a lower concentration of solutes than the fluid inside the cell, and water enters the cell. (In living systems, the point of reference is always the cytoplasm, so the prefix *hypo-* means that the extracellular fluid has a lower concentration of solutes, than the cell cytoplasm.) It also means that the extracellular fluid has a higher concentration of water than does the cell. In this situation, water will follow its concentration gradient and enter the cell. This may cause an animal cell to burst, or lyse. Note in these cases that there is always a net movement of water (the solvent) towards the hypertonic solution by the process of osmosis. That is because the hypertonic solution has a lower concentration of water and the solute can't pass through the membrane.

In a **hypertonic** solution (the prefix *hyper-* refers to the extracellular fluid having a higher concentration of solutes than the cell's cytoplasm), the fluid contains less water than the cell does, such as seawater. Because the cell has a lower concentration of solutes, the water will leave the cell. In effect, the solute is drawing the water out of the cell. This may cause an animal cell to shrivel, or crenate.

In an **isotonic** solution, the extracellular fluid has the same osmolarity as the cell. If the concentration of solutes of the cell matches that of the extracellular fluid, there will be no net movement of water into or out of the cell. Blood cells in hypertonic, isotonic, and hypotonic solutions take on characteristic appearances (Figure 3.15).

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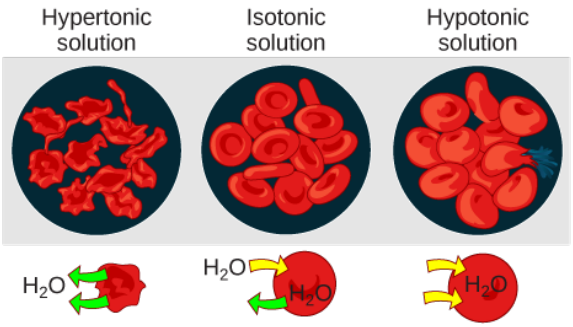

Figure 3.15: Osmotic pressure changes the shape of red blood cells in hypertonic, isotonic, and hypotonic solutions. Note the tonicity terms refer to the solution containing the cells versus the solution inside the cell. If a cell is immersed in a hypotonic solution, then the contents of the cell are hypertonic and there is a net movement of water into the cell.(credit: modification of work by Mariana Ruiz Villarreal)

3.5.6 Section Summary

The passive forms of transport, diffusion and osmosis, move material of small molecular weight. Substances diffuse from areas of high concentration to areas of low concentration, and this process continues until the substance is evenly distributed in a system. In solutions of more than one substance, each type of molecule diffuses according to its own concentration gradient. Many factors can affect the rate of diffusion, including concentration gradient, the sizes of the particles that are diffusing, and the temperature of the system.

In living systems, diffusion of substances into and out of cells is mediated by the plasma membrane. Some materials diffuse readily through the membrane, but others are hindered, and their passage is only made possible by protein channels and carriers. The chemistry of living things occurs in aqueous solutions,

and balancing the concentrations of those solutions is an ongoing problem. In living systems, diffusion of some substances would be slow or difficult without membrane proteins.

3.5.7 Art Connections

Exercise 3.5.1 *(Solution on p. 88.)*

Figure 3.15 A doctor injects a patient with what he thinks is isotonic saline solution. The patient dies, and autopsy reveals that many red blood cells have been destroyed. Do you think the solution the doctor injected was really isotonic?

3.5.8 Multiple Choice

Exercise 3.5.2 *(Solution on p. 88.)*

Water moves via osmosis _____.

a. throughout the cytoplasm
b. from an area with a high concentration of other solutes to a lower one
c. from an area with a low concentration of solutes to an area with a higher one
d. from an area with a low concentration of water to one of higher concentration

Exercise 3.5.3

The principal force driving movement in diffusion is _____.

a. temperature
b. particle size
c. concentration gradient
d. membrane surface area

3.5.9 Free Response

Exercise 3.5.4 *(Solution on p. 88.)*

Why does osmosis occur?

3.6 Active Transport Mechanisms[8]

Active transport mechanisms require the use of the cell's energy, usually in the form of adenosine triphosphate (ATP). If a substance must move into the cell against its concentration gradient, that is, if the concentration of the substance inside the cell must be greater than its concentration in the extracellular fluid, the cell must use energy to move the substance. Some active transport mechanisms move small-molecular weight material, such as ions, through the membrane.

In addition to moving small ions and molecules through the membrane, cells also need to remove and take in larger molecules and particles. Some cells are even capable of engulfing entire unicellular microorganisms. You might have correctly hypothesized that the uptake and release of large particles by the cell requires energy. A large particle, however, cannot pass through the membrane, even with energy supplied by the cell.

[8] This content is available online at <http://cnx.org/content/m57973/1.1/>.

3.6.1 Primary Active Transport

There are several types of active transport. The principle one that will be discussed is primary active transport, which uses a combination of ATP energy and a transport protein to move substances across the membrane against the concentration gradient. ATP is hydrolyzed, via an enzyme-catalyzed reaction, to ADP and the lost phosphate group attaches to the protein. This joining causes a conformational change in the shape of the transport protein and the particular substance is moved across the membrane against the concentration gradient. An example of primary active transport is the sodium-potassium pump, which is involved in nerve impulses and is discussed in a later chapter.

3.6.2 Endocytosis

Endocytosis is a type of active transport that moves particles, such as large molecules, parts of cells, and even whole cells, into a cell. There are different variations of endocytosis, but all share a common characteristic: The plasma membrane of the cell invaginates, forming a pocket around the target particle. The pocket pinches off, resulting in the particle being contained in a newly created vacuole that is formed from the plasma membrane.

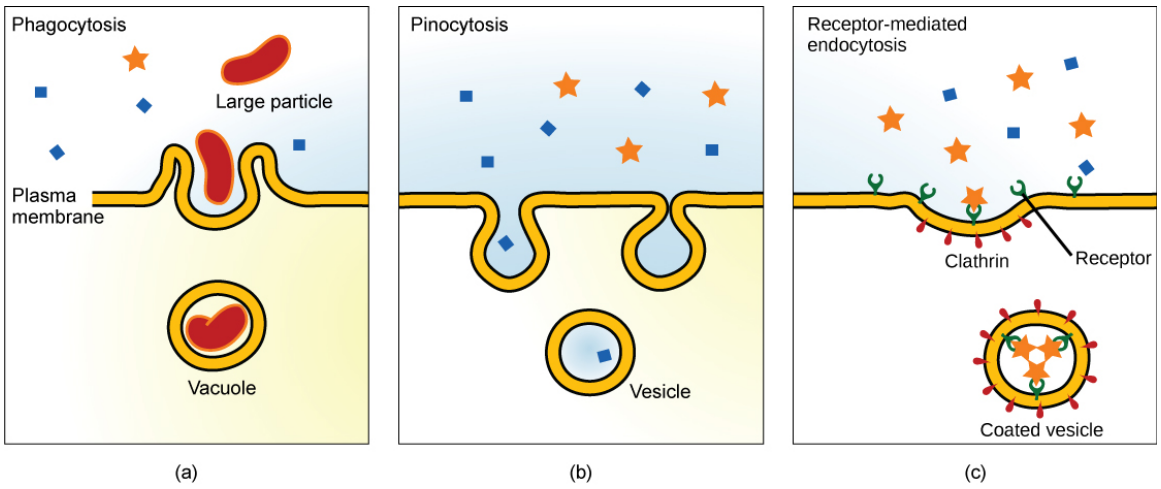

Figure 3.16: Three variations of endocytosis are shown. (a) In one form of endocytosis, phagocytosis, the cell membrane surrounds the particle and pinches off to form an intracellular vacuole. (b) In another type of endocytosis, pinocytosis, the cell membrane surrounds a small volume of fluid and pinches off, forming a vesicle. (c) In receptor-mediated endocytosis, uptake of substances by the cell is targeted to a single type of substance that binds at the receptor on the external cell membrane. (credit: modification of work by Mariana Ruiz Villarreal)

Phagocytosis is the process by which large particles, such as cells, are taken in by a cell. For example, when microorganisms invade the human body, a type of white blood cell called a neutrophil removes the invader through this process, surrounding and engulfing the microorganism, which is then destroyed by the neutrophil (Figure 3.16).

3.6.3 Exocytosis

In contrast to these methods of moving material into a cell is the process of exocytosis. **Exocytosis** is the opposite of the processes discussed above in that its purpose is to expel material from the cell into the extracellular fluid. A particle enveloped in membrane fuses with the interior of the plasma membrane. This fusion opens the membranous envelope to the exterior of the cell, and the particle is expelled into the extracellular space (Figure 3.17).

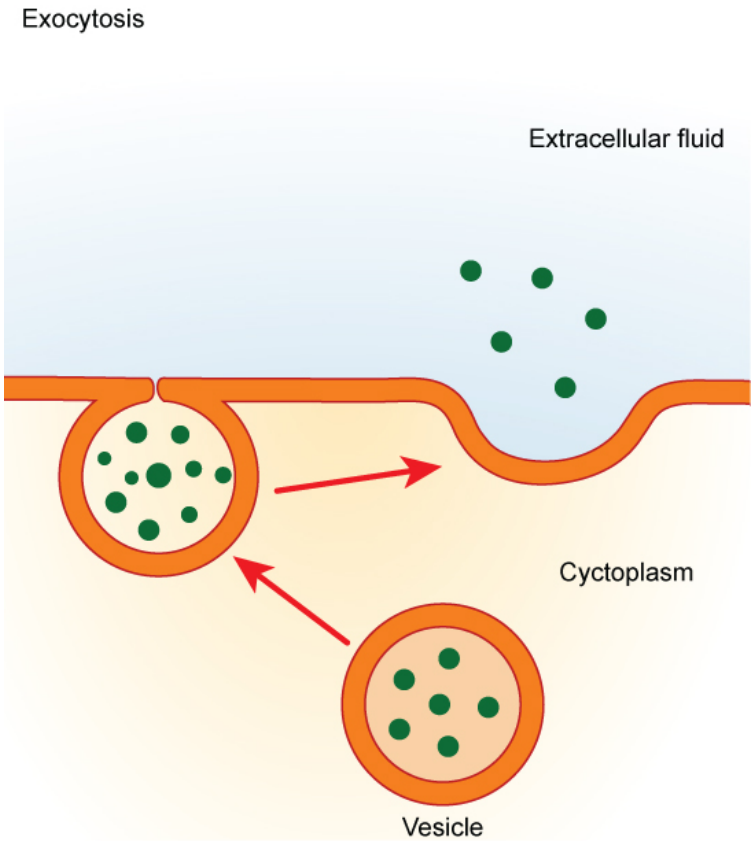

Figure 3.17: In exocytosis, a vesicle migrates to the plasma membrane, binds, and releases its contents to the outside of the cell. (credit: modification of work by Mariana Ruiz Villarreal)

3.6.4 Section Summary

Primary active transport uses energy stored in ATP to fuel the transport. Active transport of small molecular-size material uses integral proteins in the cell membrane to move the material—these proteins are analogous to pumps. Some pumps, which carry out primary active transport, couple directly with ATP to drive their action.

Endocytosis methods require the direct use of ATP to fuel the transport of large particles such as macromolecules; parts of cells or whole cells can be engulfed by other cells in a process called phagocytosis.

In phagocytosis, a portion of the membrane invaginates and flows around the particle, eventually pinching off and leaving the particle wholly enclosed by an envelope of plasma membrane. The cell expels waste and other particles through the reverse process, exocytosis. Wastes are moved outside the cell, pushing a membranous vesicle to the plasma membrane, allowing the vesicle to fuse with the membrane and incorporating itself into the membrane structure, releasing its contents to the exterior of the cell.

3.6.5 Multiple Choice

Exercise 3.6.1 ***(Solution on p. 88.)***

Active transport must function continuously because _____.

a. plasma membranes wear out
b. cells must be in constant motion
c. facilitated transport opposes active transport
d. diffusion is constantly moving the solutes in the other direction

3.6.6 Free Response

Exercise 3.6.2 ***(Solution on p. 88.)***

Where does the cell get energy for active transport processes?

Solutions to Exercises in Chapter 3

to Exercise 3.2.1 (p. 64)
D
to Exercise 3.2.2 (p. 65)
A
to Exercise 3.2.3 (p. 65)
Organelles are membrane-bound compartments or sacs that have specialized functions in eukaryotic cells.
to Exercise 3.3.1 (p. 73)
Figure 3.9 Because that face receives chemicals from the ER, which is toward the center of the cell.
to Exercise 3.3.2 (p. 73)
D
to Exercise 3.3.3 (p. 74)
A
to Exercise 3.3.4 (p. 74)
"Form follows function" refers to the idea that the function of a body part dictates the form of that body part. As an example, organisms like birds or fish that fly or swim quickly through the air or water have streamlined bodies that reduce drag. At the level of the cell, in tissues involved in secretory functions, such as the salivary glands, the cells have abundant Golgi.
to Exercise 3.4.1 (p. 78)
A
to Exercise 3.4.2 (p. 78)
D
to Exercise 3.4.3 (p. 78)
The fluidity of the cell membrane is necessary for the operation of some enzymes and transport mechanisms within the membrane.
to Exercise 3.5.1 (p. 84)
Figure 3.15 No, it must have been hypotonic, as a hypotonic solution would cause water to enter the cells, thereby making them burst.
to Exercise 3.5.2 (p. 84)
C
to Exercise 3.5.4 (p. 84)
Water moves through a semipermeable membrane in osmosis because there is a concentration gradient across the membrane of solute and solvent. The solute cannot effectively move to balance the concentration on both sides of the membrane, so water moves to achieve this balance.
to Exercise 3.6.1 (p. 87)
D
to Exercise 3.6.2 (p. 87)
The cell harvests energy from ATP produced by its own metabolism to power active transport processes, such as pumps.

Chapter 4

DNA and Gene Expression

4.1 Introduction to the Central Dogma of Molecular Biology[1]

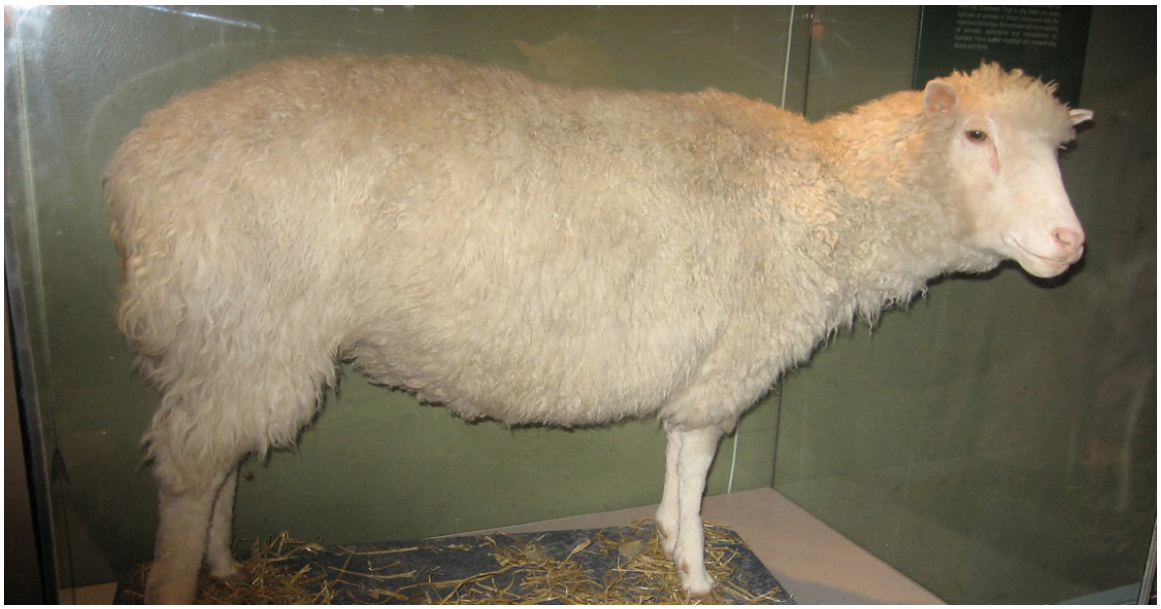

Figure 4.1: This is Dolly, the first sheep produced using a novel type of molecular genetic technology that involved transfer of the nucleus from an adult udder cell to an unfertilized egg whose nucleus had been removed. This egg was then transplanted into another female sheep to undergo development during pregnancy.

Sheep, as well as humans, normally begin life as a single cell called a fertilized egg or zygote. From this one cell, trillions of cells will ultimately be derived through the process of cell division. Prior to each cell division event, the DNA must replicate. Also, cells must produce proteins needed to accomplish specific functions.

[1] This content is available online at <http://cnx.org/content/m57974/1.1/>.

These events are described by the central dogma of molecular biology, which states that DNA contains information to replicate itself and that specific regions of the DNA (called genes) contains the information needed to make RNA, which is in turn used to produce needed proteins. In this chapter, we will learn more about the steps of these processes.

4.2 DNA and RNA[2]

In the 1950s, Francis Crick and James Watson worked together at the University of Cambridge, England, to determine the structure of DNA. Other scientists, such as Linus Pauling and Maurice Wilkins, were also actively exploring this field. Pauling had discovered the secondary structure of proteins using X-ray crystallography. X-ray crystallography is a method for investigating molecular structure by observing the patterns formed by X-rays shot through a crystal of the substance. The patterns give important information about the structure of the molecule of interest. In Wilkins' lab, researcher Rosalind Franklin was using X-ray crystallography to understand the structure of DNA. Watson and Crick were able to piece together the puzzle of the DNA molecule using Franklin's data (Figure 4.2). Watson and Crick also had key pieces of information available from other researchers such as Chargaff's rules. Chargaff had shown that of the four kinds of monomers (nucleotides) present in a DNA molecule, two types were always present in equal amounts and the remaining two types were also always present in equal amounts. This meant they were always paired in some way. In 1962, James Watson, Francis Crick, and Maurice Wilkins were awarded the Nobel Prize in Medicine for their work in determining the structure of DNA.

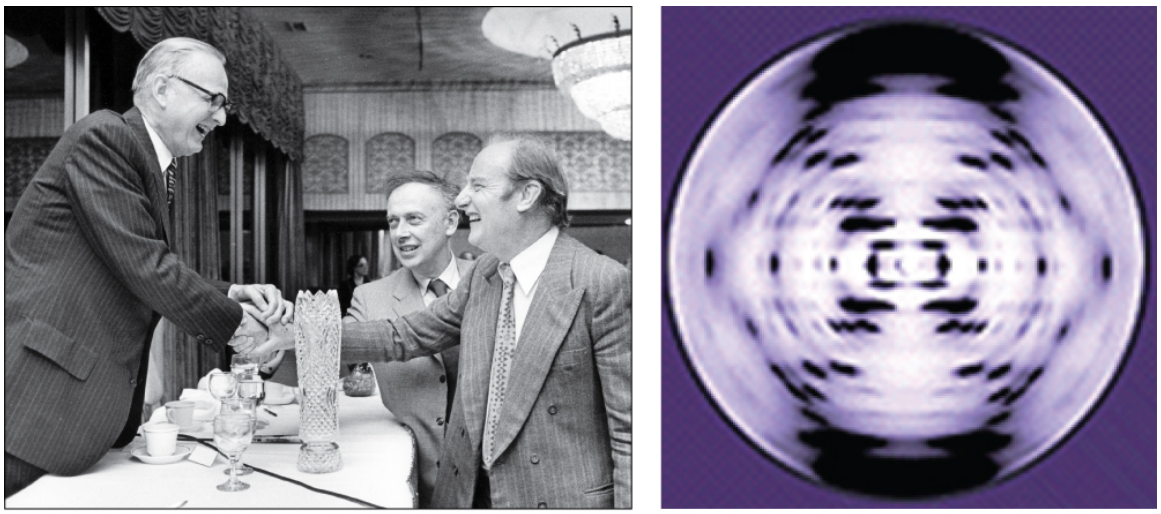

Figure 4.2: Pioneering scientists (a) James Watson and Francis Crick are pictured here with American geneticist Maclyn McCarty. Scientist Rosalind Franklin discovered (b) the X-ray diffraction pattern of DNA, which helped to elucidate its double helix structure. (credit a: modification of work by Marjorie McCarty; b: modification of work by NIH)

[2]This content is available online at <http://cnx.org/content/m57975/1.1/>.

Now let's consider the structure of the two types of nucleic acids, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). The building blocks of DNA are nucleotides, which are made up of three parts: a **deoxyribose** (a 5-carbon sugar with the carbons designated as 1', 2', 3', 4' and 5'), a **phosphate group** attached to the 5'carbon, and a **nitrogenous base** attached to the 1'carbon(Figure 4.3). There are four types of nitrogenous bases in DNA. Adenine (A) and guanine (G) are double-ringed purines, and cytosine (C) and thymine (T) are smaller, single-ringed pyrimidines. The nucleotide is named according to the nitrogenous base it contains.

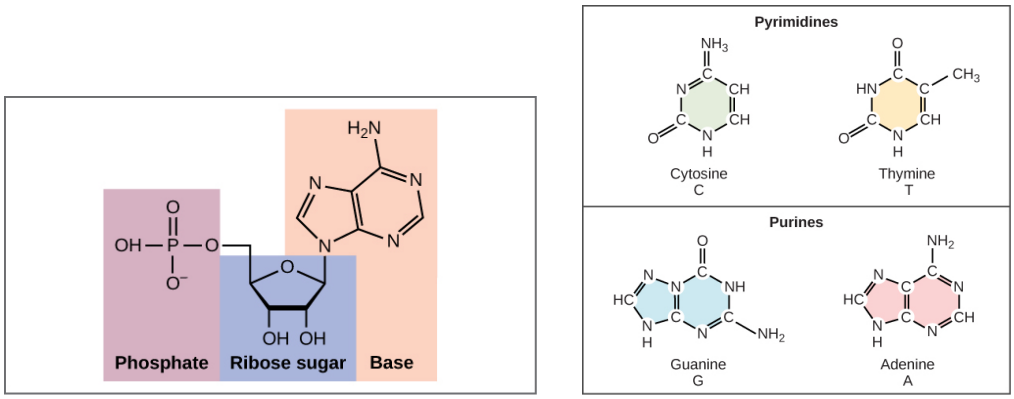

Figure 4.3: (a) Each DNA nucleotide is made up of a sugar, a phosphate group, and a base. Four of the five carbon atoms in the sugar are not shown to simplify the diagram; each point on the ring is where a carbon (1' to 4') would be would be located; the position of the 5' carbon is above the ring at the point adjacent to an oxygen of the phosphate group. (b) Cytosine and thymine are pyrimidines. Guanine and adenine are purines. Note: As the 2' carbon is attached to an -OH group, the sugar shown is actually ribose, not deoxyribose as intended.

The phosphate group of one nucleotide bonds covalently with the sugar molecule of the next nucleotide, and so on, forming a long polymer of nucleotide monomers. The sugar–phosphate groups line up in a "backbone" for each single strand of DNA, and the nucleotide bases stick out from this backbone. The carbon atoms of the five-carbon sugar are numbered clockwise from the oxygen as 1', 2', 3', 4', and 5' (1' is read as "one prime"). The phosphate group is attached to the 5' carbon of one nucleotide and the 3' carbon of the next nucleotide. In its natural state, each DNA molecule is actually composed of two single strands held together along their length with hydrogen bonds between the bases.

Watson and Crick proposed that the DNA is made up of two strands that are twisted around each other to form a right-handed helix, called a **double helix**. Base-pairing takes place between a purine and pyrimidine: namely, A pairs with T, and G pairs with C. In other words, adenine and thymine are complementary base pairs, and cytosine and guanine are also complementary base pairs. This is the basis for Chargaff's rule; because of their complementarity, there is as much adenine as thymine in a DNA molecule and as much guanine as cytosine. Adenine and thymine are connected by two hydrogen bonds, and cytosine and guanine are connected by three hydrogen bonds. The two strands are anti-parallel in nature; that is, one strand will have the 3' carbon of the sugar in the "upward" position, whereas the other strand will have the 5' carbon in the upward position. The diameter of the DNA double helix is uniform throughout because a purine (two rings) always pairs with a pyrimidine (one ring) and their combined lengths are always equal. (Figure 4.4).

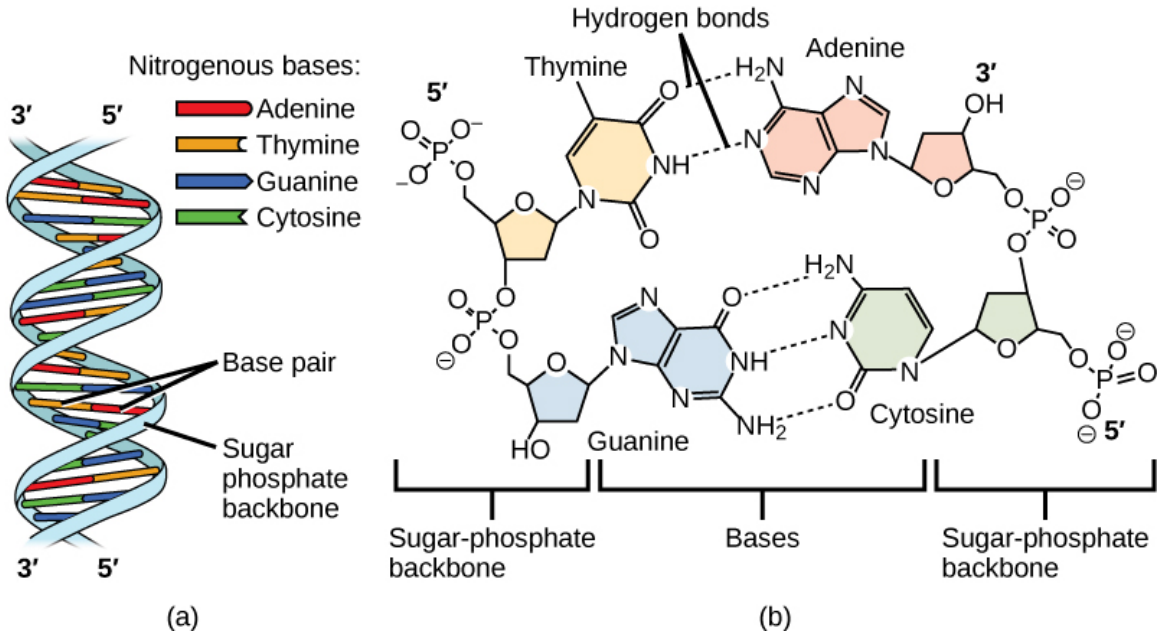

Figure 4.4: DNA (a) forms a double stranded helix, and (b) adenine pairs with thymine and cytosine pairs with guanine. (credit a: modification of work by Jerome Walker, Dennis Myts)

4.2.1 The Structure of RNA

There is a second nucleic acid in all cells called ribonucleic acid, or RNA. Like DNA, RNA is a polymer of nucleotides. Each of the nucleotides in RNA is made up of a nitrogenous base, a five-carbon sugar, and a phosphate group. In the case of RNA, the five-carbon sugar is ribose, not deoxyribose. Ribose has a hydroxyl group at the 2' carbon, unlike deoxyribose, which has only a hydrogen atom (Figure 4.5).

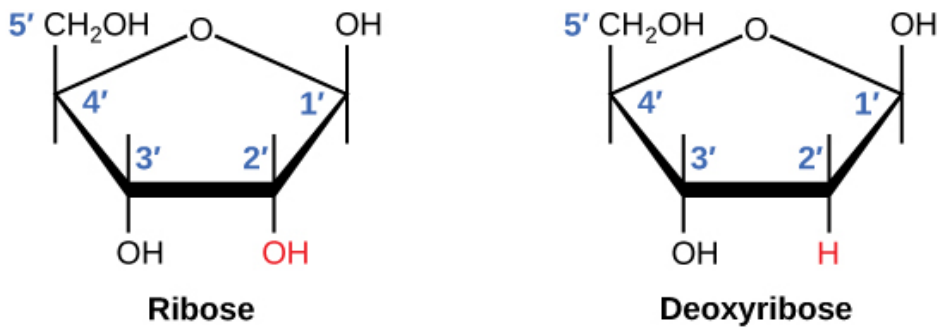

Figure 4.5: The difference between the ribose found in RNA and the deoxyribose found in DNA is that ribose has a hydroxyl group at the 2' carbon.

RNA nucleotides contain the nitrogenous bases adenine, cytosine, and guanine. However, they do not contain thymine, which is instead replaced by uracil, symbolized by a "U." RNA exists as a single-stranded molecule rather than a double-stranded helix. Molecular biologists have named several kinds of RNA on the basis of their function. These include messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA)—molecules that are involved in the production of proteins from the DNA code.

4.2.2 How DNA Is Arranged in the Cell

DNA is a working molecule; it must be replicated when a cell is ready to divide, and it must be "read" to produce the molecules, such as proteins, to carry out the functions of the cell. For this reason, the DNA is protected and packaged in very specific ways. In addition, DNA molecules can be very long. Stretched end-to-end, the DNA molecules in a single human cell would come to a length of about 2 meters,or 6.5 feet. Thus, the DNA for a cell must be packaged in a very ordered way to fit and function within a structure (the cell) that is not visible to the naked eye. The chromosomes of prokaryotes are much simpler than those of eukaryotes in many of their features (Figure 4.6). Most prokaryotes contain a single, circular chromosome that is found in an area in the cytoplasm called the nucleoid.

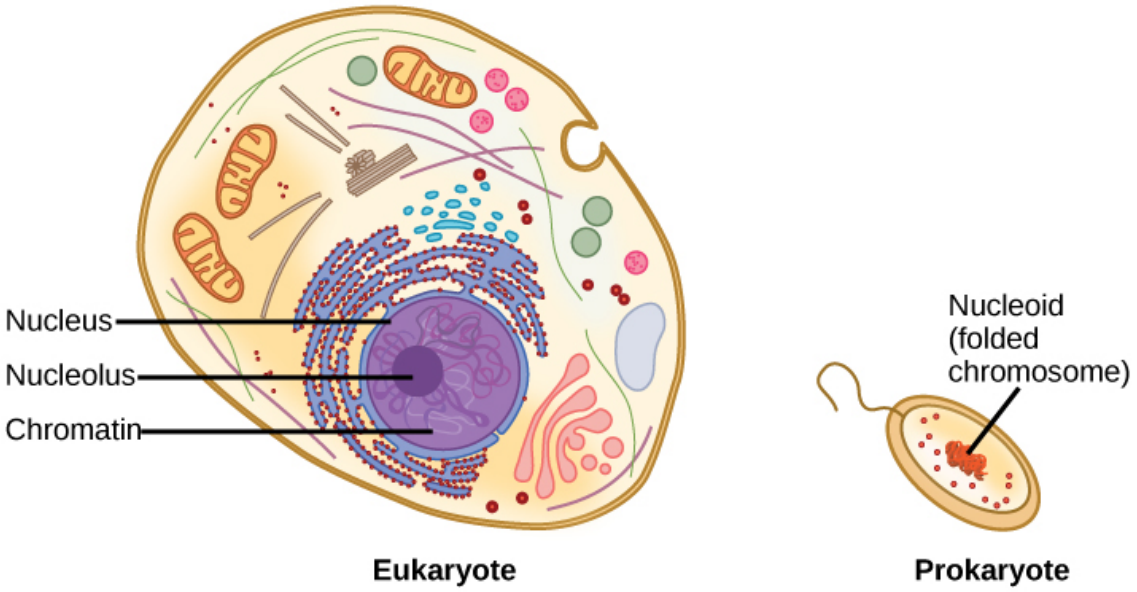

Figure 4.6: A eukaryote contains a well-defined nucleus, whereas in prokaryotes, the chromosome lies in the cytoplasm in an area called the nucleoid.

The size of the genome in one of the most well-studied prokaryotes, *Escherichia coli,* is 4.6 million base pairs, which would extend a distance of about 1.6 millimeters (0.06 inches) if stretched out. So how does this fit inside a small bacterial cell? The DNA is twisted beyond the double helix in what is known as supercoiling. Some proteins are known to be involved in the supercoiling; other proteins and enzymes help in maintaining the supercoiled structure.

Eukaryotes, whose chromosomes each consist of a linear DNA molecule, employ a different type of packing strategy to fit their DNA inside the nucleus (Figure 4.7). At the most basic level, DNA is wrapped around proteins known as histones to form structures called nucleosomes. The DNA is wrapped tightly around the histone core. This nucleosome is linked to the next one by a short strand of DNA that is free of histones. This is also known as the "beads on a string" structure; the nucleosomes are the "beads" and the short lengths of DNA between them are the "string." The nucleosomes, with their DNA coiled around them, stack compactly onto each other to form a 30-nanometers–wide fiber. This fiber is further coiled into a thicker and more compact structure. At the metaphase stage of mitosis, when the chromosomes are lined up in the center of the cell, the chromosomes are at their most compacted. They are approximately 700 nanometers in width, and are found in association with scaffold proteins.

In interphase, the phase of the cell cycle between mitoses at which the chromosomes are decondensed, eukaryotic chromosomes have two distinct regions that can be distinguished by staining. There is a tightly packaged region that stains darkly, and a less dense region. The darkly staining regions usually contain genes that are not active, and are found in the regions of the centromere and telomeres. The lightly staining regions usually contain genes that are active, with DNA packaged around nucleosomes but not further compacted.

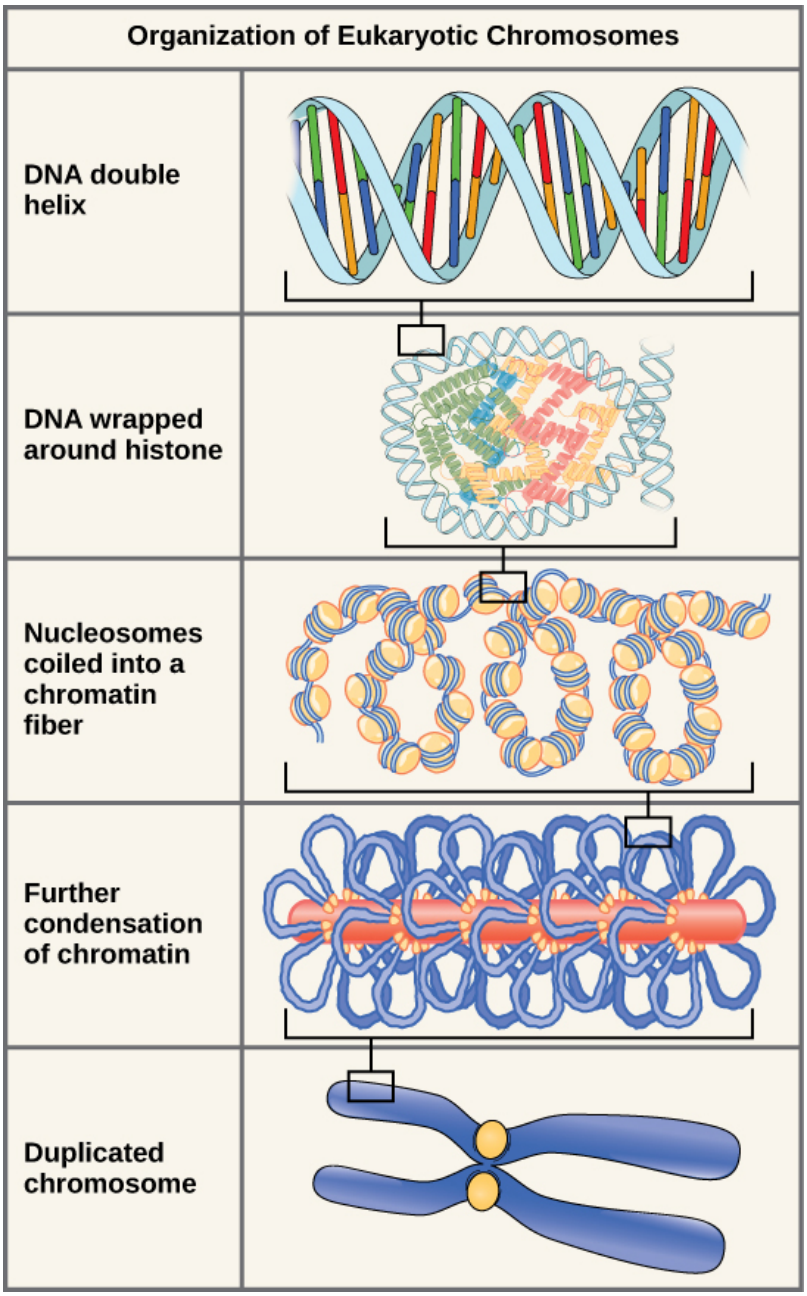

Figure 4.7: These figures illustrate the compaction of the eukaryotic chromosome.

: Watch this animation[3] of DNA packaging.

4.2.3 Section Summary

The model of the double-helix structure of DNA was proposed by Watson and Crick. The DNA molecule is a polymer of nucleotides. Each nucleotide is composed of a nitrogenous base, a five-carbon sugar (deoxyribose), and a phosphate group. There are four nitrogenous bases in DNA, two purines (adenine and guanine) and two pyrimidines (cytosine and thymine). A DNA molecule is composed of two strands. Each strand is composed of nucleotides bonded together covalently between the phosphate group of one and the deoxyribose sugar of the next. From this backbone extend the bases. The bases of one strand bond to the bases of the second strand with hydrogen bonds. Adenine always bonds with thymine, and cytosine always bonds with guanine. The bonding causes the two strands to spiral around each other in a shape called a double helix. Ribonucleic acid (RNA) is a second nucleic acid found in cells. RNA is a single-stranded polymer of nucleotides. It also differs from DNA in that it contains the sugar ribose, rather than deoxyribose, and the nucleotide uracil rather than thymine. Various RNA molecules function in the process of forming proteins from the genetic code in DNA.

Eukaryotes contain double-stranded linear DNA molecules packaged into chromosomes. The DNA helix is wrapped around proteins to form nucleosomes. The protein coils are further coiled, and during mitosis and meiosis, the chromosomes become even more greatly coiled to facilitate their movement.

4.2.4 Multiple Choice

Exercise 4.2.1 *(Solution on p. 112.)*

Which of the following does cytosine pair with?

a. guanine
b. thymine
c. adenine
d. a pyrimidine

Exercise 4.2.2 *(Solution on p. 112.)*

Prokaryotes contain a _____chromosome, and eukaryotes contain _____ chromosomes.

a. single-stranded circular; single-stranded linear
b. single-stranded linear; single-stranded circular
c. double-stranded circular; double-stranded linear
d. double-stranded linear; double-stranded circular

[3] http://openstaxcollege.org/l/DNA_packaging

4.2.5 Free Response

Exercise 4.2.3 *(Solution on p. 112.)*
Describe the organization of the eukaryotic chromosome.

Exercise 4.2.4 *(Solution on p. 112.)*
Describe the structure and complementary base pairing of DNA.

4.3 The Basics of DNA Replication[4]

When a cell divides, it is important that each daughter cell receives an identical copy of the DNA. This is accomplished by the process of DNA replication. The replication of DNA occurs during the synthesis phase, or S phase, of the cell cycle, before the cell enters mitosis or meiosis.

The elucidation of the structure of the double helix provided a hint as to how DNA is copied. Recall that adenine nucleotides pair with thymine nucleotides, and cytosine with guanine. This means that the two strands are complementary to each other. For example, a strand of DNA with a nucleotide sequence of AGTCATGA will have a complementary strand with the sequence TCAGTACT (Figure 4.8).

[4]This content is available online at <http://cnx.org/content/m57976/1.1/>.

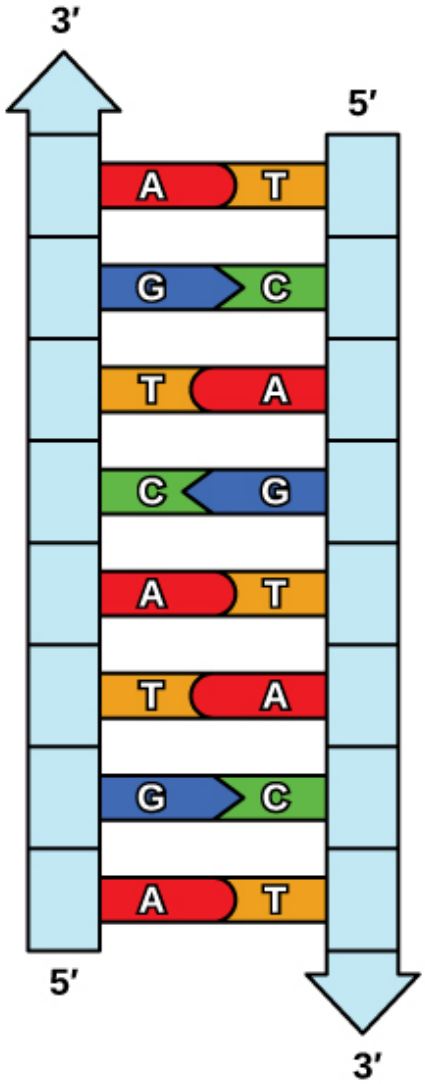

Figure 4.8: The two strands of DNA are complementary, meaning the sequence of bases in one strand can be used to create the correct sequence of bases in the other strand.

Because of the complementarity of the two strands, having one strand means that it is possible to recreate the other strand. This model for replication suggests that the two strands of the double helix separate during replication, and each strand serves as a template from which the new complementary strand is copied (Figure 4.9).

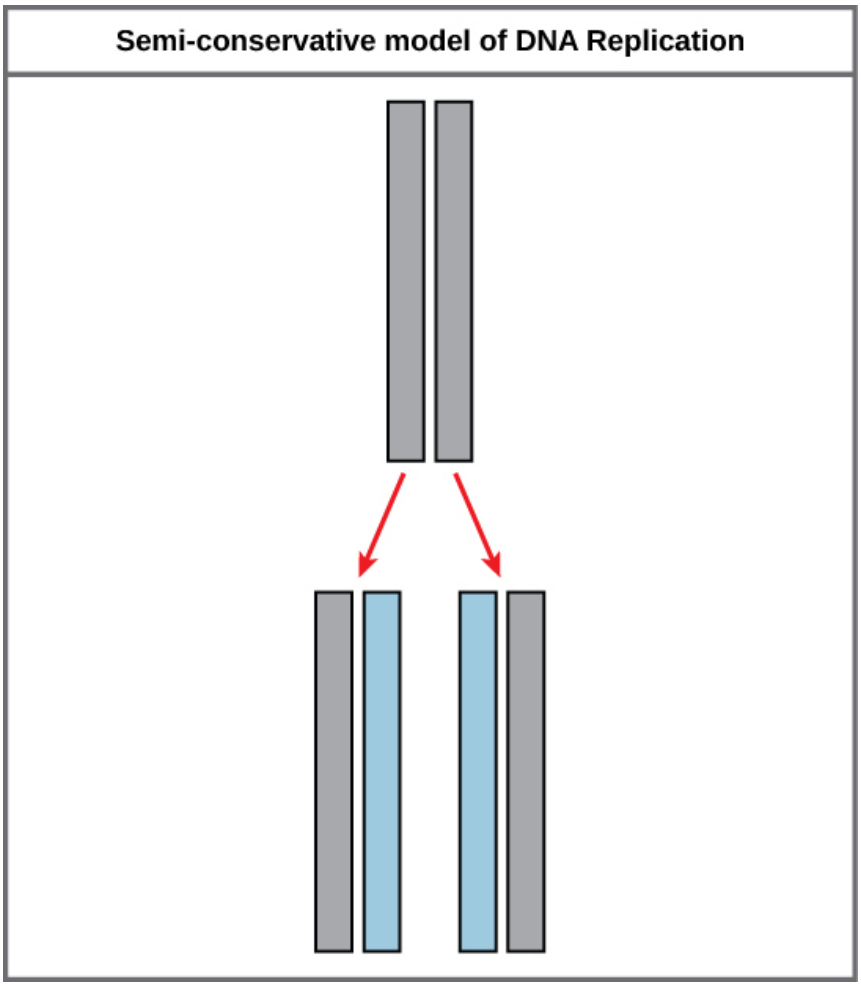

Figure 4.9: The semiconservative model of DNA replication is shown. Gray indicates the original DNA strands, and blue indicates newly synthesized DNA.

During DNA replication, each of the two strands that make up the double helix serves as a template from which new strands are copied. The name of the enzyme that copies the DNA is called DNA polymerase. It joins the complementary nucleotides together to make up the new strand, which is complementary to the parental or "old" strand. Each new double helix consists of one parental strand and one new daughter strand. This is known as **semiconservative replication**. When two DNA copies are formed, they have an identical sequence of nucleotide bases and are divided equally into two daughter cells during cell division. Therefore, each of the two daughter cells has a complete copy of each chromosome.

4.3.1 DNA Repair

DNA polymerase can sometimes make an error by inserting a noncomplementary base during DNA replication. Most mistakes are quickly corrected; if they are not, they may result in a **mutation**—defined as a permanent change in the DNA sequence. Mutations in genes may lead to serious consequences because

incorrect proteins are produced.

4.3.2 Section Summary

DNA replicates by a semi-conservative method in which each of the two parental DNA strands act as a template for new DNA to be synthesized. After replication, each DNA has one parental or "old" strand, and one daughter or "new" strand.

4.3.3 Multiple Choice

Exercise 4.3.1 *(Solution on p. 112.)*

DNA replicates by which of the following models?

a. conservative
b. semiconservative
c. dispersive
d. none of the above

4.3.4 Free Response

Exercise 4.3.2 *(Solution on p. 112.)*

The sequence one strand of a DNA double helix is: *ATGGCTACAA Beginning at the * end, what is the complimentary sequence?

4.4 Transcription[5]

The second function of DNA (the first was replication) is to provide the information needed to construct the proteins necessary so that the cell can perform all of its functions. To do this, the DNA is "read" or transcribed into an **mRNA** molecule. The mRNA then provides the code to form a protein by a process called translation. Through the processes of transcription and translation, a protein is built with a specific sequence of amino acids that was originally encoded in the DNA. This module discusses the details of transcription.

4.4.1 The Central Dogma of Molecular Biology: DNA Encodes RNA; RNA Encodes Protein

The flow of genetic information in cells from DNA to mRNA to protein is described by the central dogma (Figure 4.10), which states that genes specify the sequences of mRNAs, which in turn specify the sequences of proteins.

[5]This content is available online at <http://cnx.org/content/m57978/1.1/>.

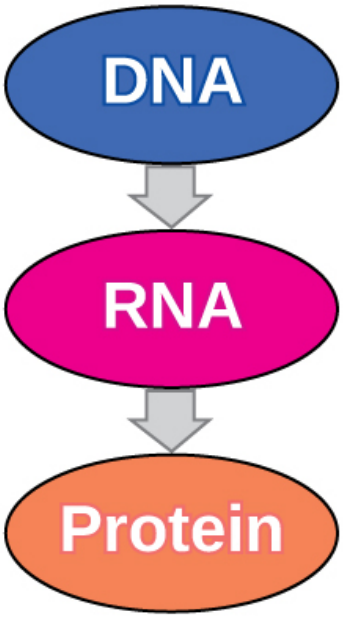

Figure 4.10: The central dogma of molecular biology states that DNA encodes RNA, which in turn encodes protein.

The copying of DNA to mRNA (i.e. transcription) is relatively straightforward, with one nucleotide being added to the mRNA strand for every complementary nucleotide read in the DNA strand. The translation to protein is more complex because groups of three mRNA nucleotides correspond to one amino acid of the protein sequence. However, as we shall see in the next module, the translation to protein is still systematic, such that nucleotides 1 to 3 correspond to amino acid 1, nucleotides 4 to 6 correspond to amino acid 2, and so on. The groups of three nucleotides that specify an amino acid are called codons.

4.4.2 Transcription: from DNA to mRNA

With the genes bound in the nucleus, transcription occurs in the nucleus of the cell and the mRNA transcript must be transported to the cytoplasm. Transcription occurs in three main stages: initiation, elongation, and termination.

4.4.2.1 Initiation

Transcription requires the DNA double helix to partially unwind in the region of mRNA synthesis. The region of unwinding is called a **transcription bubble**. The DNA sequence onto which the proteins and enzymes involved in transcription bind to initiate the process is called a **promoter**. In most cases, promoters exist upstream of the genes they regulate. The specific sequence of a promoter is very important because it determines whether the corresponding gene is transcribed all of the time, some of the time, or hardly at all (Figure 4.11).

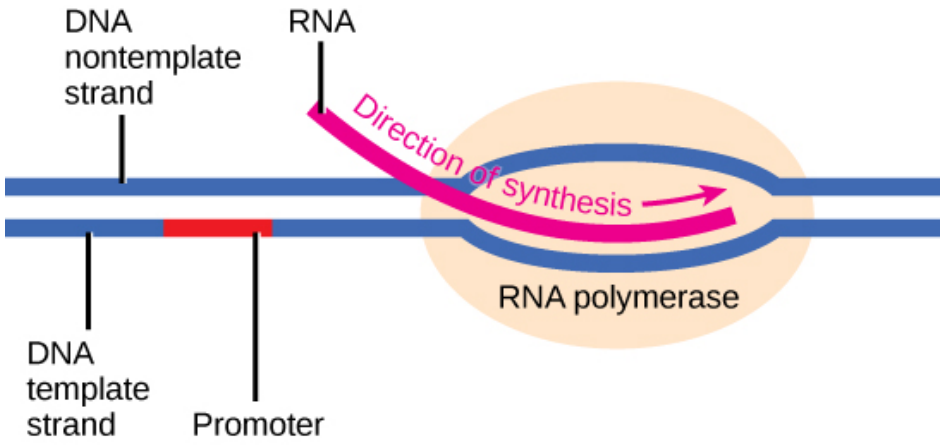

Figure 4.11: The initiation of transcription begins when DNA is unwound, forming a transcription bubble. Enzymes and other proteins involved in transcription bind at the promoter.

4.4.2.2 Elongation

Transcription always proceeds from one of the two DNA strands, which is called the **template strand**. The mRNA product is complementary to the template strand and is almost identical to the other DNA strand, called the **nontemplate strand**, with the exception that RNA contains a uracil (U) in place of the thymine (T) found in DNA. During elongation, an enzyme called **RNA polymerase** proceeds along the DNA template adding nucleotides by base pairing with the DNA template in a manner similar to DNA replication, with the difference that an RNA strand is being synthesized that does not remain bound to the DNA template. As elongation proceeds, the DNA is continuously unwound ahead of the enzyme and rewound behind it (Figure 4.12).

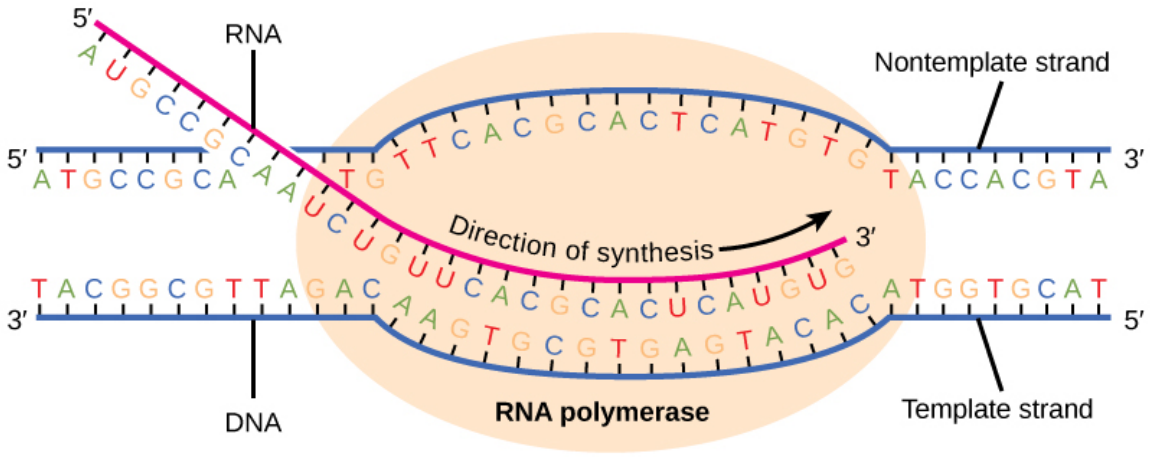

Figure 4.12: During elongation, RNA polymerase tracks along the DNA template, synthesizes mRNA in the 5' to 3' direction, and unwinds then rewinds the DNA as it is read.

4.4.2.3 Termination

Once a gene is transcribed, the RNA polymerase needs to be instructed to dissociate from the DNA template and liberate the newly made mRNA. Depending on the gene being transcribed, there are two kinds of termination signals, but both involve repeated nucleotide sequences in the DNA template that result in RNA polymerase stalling, leaving the DNA template, and freeing the mRNA transcript.

4.4.3 Eukaryotic RNA Processing

The newly transcribed eukaryotic mRNAs must undergo several processing steps before they can be transferred from the nucleus to the cytoplasm and translated into a protein.

The mRNA transcript is first coated in RNA-stabilizing proteins to prevent it from degrading while it is processed and exported out of the nucleus. This occurs while the pre-mRNA still is being synthesized by adding a special nucleotide "cap" to the 5' end of the growing transcript. In addition to preventing degradation, factors involved in protein synthesis recognize the cap to help initiate translation by ribosomes.

Once elongation is complete, an enzyme then adds a string of approximately 200 adenine residues to the 3' end, called the poly-A tail. This modification further protects the pre-mRNA from degradation and signals to cellular factors that the transcript needs to be exported to the cytoplasm.

Eukaryotic genes are composed of protein-coding sequences called **exons** (*ex*-on signifies that they are expressed) and *int*ervening sequences called **introns** (*int*-ron denotes their *int*ervening role). Introns are removed from the pre-mRNA during processing. Intron sequences in mRNA do not encode functional proteins. It is essential that all of a pre-mRNA's introns be completely and precisely removed before protein synthesis so that the exons join together to code for the correct amino acids. If the process errs by even a single nucleotide, the sequence of the rejoined exons would be shifted, and the resulting protein would be nonfunctional. The process of removing introns and reconnecting exons is called **splicing** (Figure 4.13). Introns are removed and degraded while the pre-mRNA is still in the nucleus.

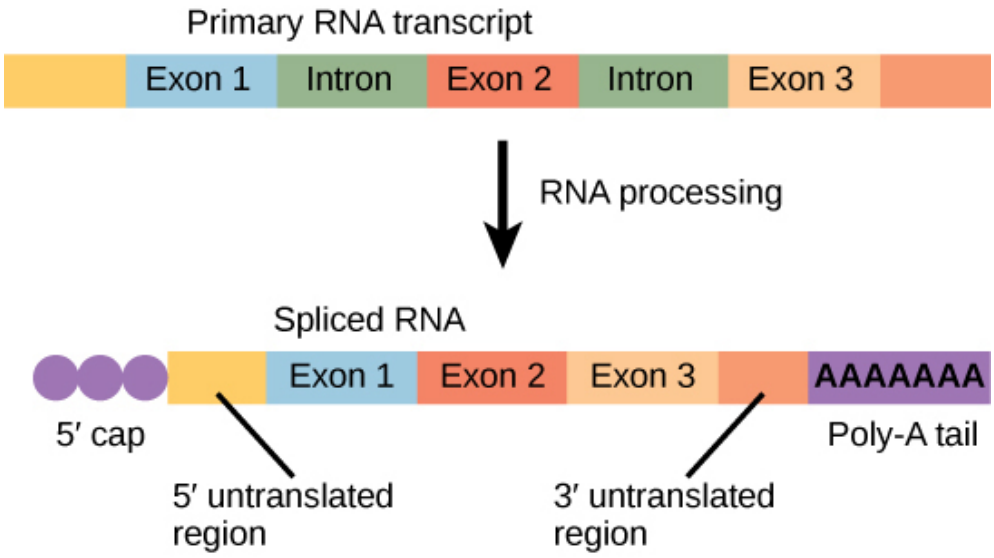

Figure 4.13: Eukaryotic mRNA contains introns that must be spliced out. A 5' cap and 3' tail are also added.

4.4.4 Section Summary

mRNA synthesis is initiated at a promoter sequence on the DNA template. Elongation synthesizes new mRNA (called a pre-mRNA). Termination liberates the mRNA and occurs by mechanisms that stall the RNA polymerase and cause it to fall off the DNA template. Newly transcribed mRNAs are modified with a cap and a poly-A tail. These structures protect the mature mRNA from degradation and help export it from the nucleus. mRNAs also undergo splicing, in which introns are removed and exons are reconnected with single-nucleotide accuracy. Only finished mRNAs are exported from the nucleus to the cytoplasm.

4.4.5 Multiple Choice

Exercise 4.4.1 *(Solution on p. 112.)*

A promoter is _____.

a. a specific sequence of DNA nucleotides
b. a specific sequence of RNA nucleotides
c. a protein that binds to DNA
d. an enzyme that synthesizes RNA

Exercise 4.4.2 *(Solution on p. 112.)*

Portions of eukaryotic mRNA sequence that are removed during RNA processing are _____.

a. exons
b. caps
c. poly-A tails
d. introns

4.5 Translation[6]

The synthesis of proteins is one of a cell's most energy-consuming metabolic processes. In turn, proteins account for more mass than any other component of living organisms (with the exception of water), and proteins perform a wide variety of the functions of a cell. The process of translation, or protein synthesis, involves decoding an mRNA message into a polypeptide product. Amino acids are covalently strung together in lengths ranging from approximately 50 amino acids to more than 1,000.

4.5.1 The Protein Synthesis Machinery

In addition to the mRNA template, many other molecules contribute to the process of translation. The composition of each component may vary across species; for instance, ribosomes may consist of different numbers of ribosomal RNAs (**rRNA**) and polypeptides depending on the organism. However, the general structures and functions of the protein synthesis machinery are comparable from bacteria to human cells. Translation requires the input of an mRNA template, ribosomes, tRNAs, and various enzymatic factors (Figure 4.14).

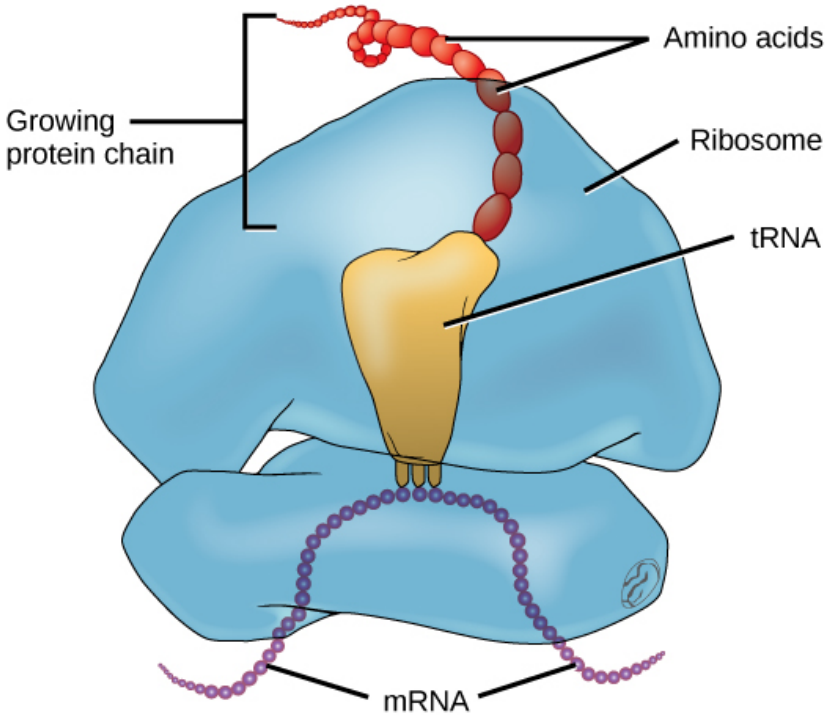

Figure 4.14: The protein synthesis machinery includes the large and small subunits of the ribosome, mRNA, and tRNA. (credit: modification of work by NIGMS, NIH)

[6]This content is available online at <http://cnx.org/content/m57979/1.2/>.

Ribosomes are located in the cytoplasm and endoplasmic reticulum of eukaryotes. Ribosomes are made up of a large and a small subunit that come together for translation. The small subunit is responsible for binding the mRNA template, whereas the large subunit sequentially binds **tRNAs**, a type of RNA molecule that brings amino acids to the growing chain of the polypeptide. Each mRNA molecule is simultaneously translated by many ribosomes, all synthesizing protein in the same direction.

Depending on the species, 40 to 60 types of tRNA exist in the cytoplasm. Serving as adaptors, specific tRNAs bind to sequences on the mRNA template and add the corresponding amino acid to the polypeptide chain. Therefore, tRNAs are the molecules that actually "translate" the language of RNA into the language of proteins. For each tRNA to function, it must have its specific amino acid bonded to it. In the process of tRNA "charging," each tRNA molecule is bonded to its correct amino acid.

4.5.2 The Genetic Code

To summarize what we know to this point, the cellular process of transcription generates messenger RNA (mRNA), a mobile molecular copy of one or more genes with an alphabet of A, C, G, and uracil (U). Translation of the mRNA template converts nucleotide-based genetic information into a protein product. Protein sequences consist of 20 commonly occurring amino acids; therefore, it can be said that the protein alphabet consists of 20 letters. Each amino acid is defined by a three-nucleotide sequence called the triplet **codon**. The relationship between a nucleotide codon and its corresponding amino acid is called the **genetic code**.

Given the different numbers of "letters" in the mRNA and protein "alphabets," combinations of nucleotides corresponded to single amino acids. Using a three-nucleotide code means that there are a total of 64 ($4 \times 4 \times 4$) possible combinations; therefore, a given amino acid is encoded by more than one nucleotide triplet (Figure 4.15).

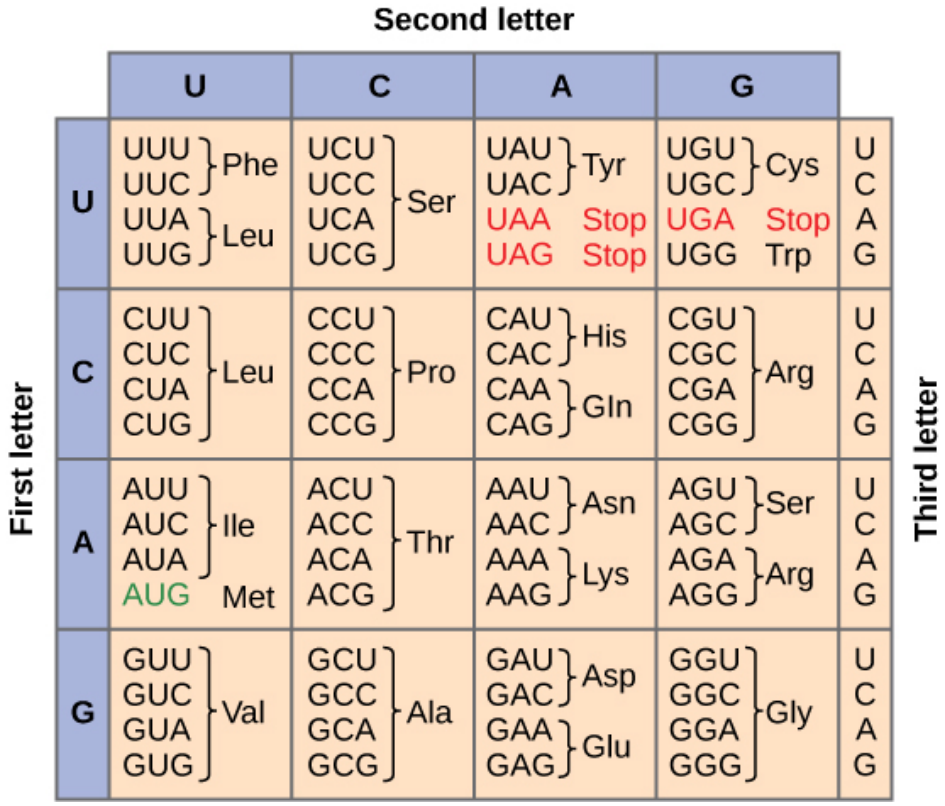

Figure 4.15: This figure shows the genetic code for translating each nucleotide triplet, or codon, in mRNA into an amino acid or a termination signal in a nascent protein. (credit: modification of work by NIH)

Three of the 64 codons terminate protein synthesis and release the polypeptide from the translation machinery. These triplets are called **stop codons**. Another codon, AUG, also has a special function. In addition to specifying the amino acid methionine, it also serves as the **start codon** to initiate translation. The reading frame for translation is set by the AUG start codon near the 5' end of the mRNA. The genetic code is universal. With a few exceptions, virtually all species use the same genetic code for protein synthesis, which is powerful evidence that all life on Earth shares a common origin.

4.5.3 The Mechanism of Protein Synthesis

Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination.

Protein synthesis begins with the formation of an initiation complex. This complex involves the small ribosome subunit, the mRNA template,and a tRNA that interacts with the AUG start codon, and is linked to the amino acid methionine.

In polypeptide elongation the large ribosomal subunit consists of three compartments: P, A, and E sites. The A site binds incoming charged tRNAs (tRNAs with their attached specific amino acids). The P site binds charged tRNAs carrying amino acids that have formed bonds with the growing polypeptide chain but have not yet dissociated from their corresponding tRNA. The E site releases dissociated tRNAs so they can

be recharged with free amino acids. The ribosome shifts one codon at a time, catalyzing each process that occurs in the three sites. With each step, a charged tRNA enters the complex, the polypeptide becomes one amino acid longer, and an uncharged tRNA departs.

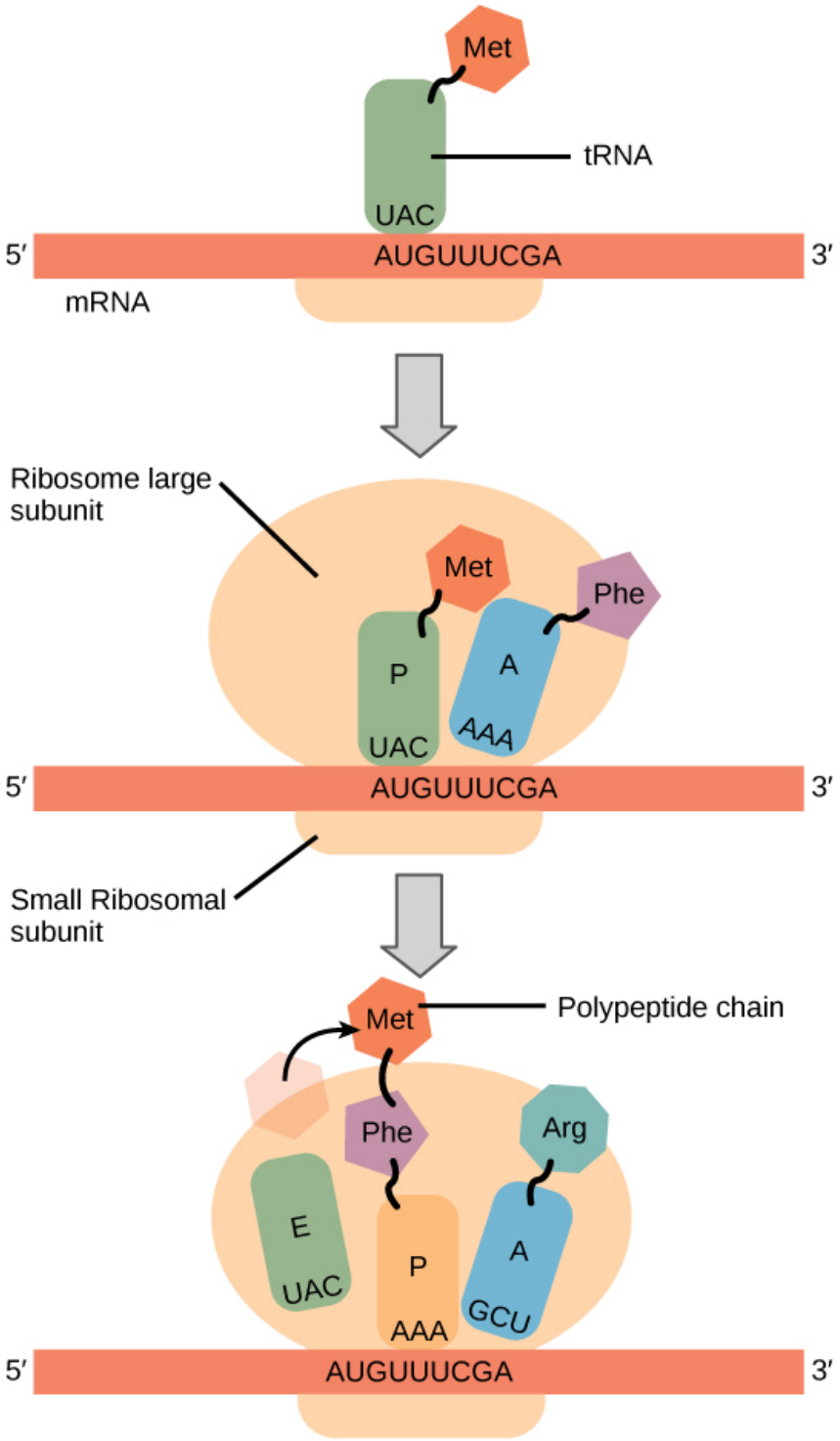

Figure 4.16: Translation begins when a tRNA anticodon recognizes a codon on the mRNA. The large ribosomal subunit joins the small subunit, and a second tRNA is recruited. As the mRNA moves relative to the ribosome, the polypeptide chain is formed. Entry of a release factor into the A site terminates translation and the components dissociate.

Termination of translation occurs when a stop codon (UAA, UAG, or UGA) is encountered. When the ribosome encounters the stop codon, the growing polypeptide is released and the ribosome subunits dissociate and leave the mRNA. After many ribosomes have completed translation, the mRNA is degraded so the nucleotides can be reused in another transcription reaction.

: Transcribe a gene and translate it to protein using complementary pairing and the genetic code at this site[7] .

4.5.4 Section Summary

The central dogma describes the flow of genetic information in the cell from genes to mRNA to proteins. Genes are used to make mRNA by the process of transcription; mRNA is used to synthesize proteins by the process of translation. The genetic code is the correspondence between the three-nucleotide mRNA codon and an amino acid. The genetic code is "translated" by the tRNA molecules, which associate a specific codon with a specific amino acid. The genetic code is degenerate because 64 triplet codons in mRNA specify only 20 amino acids and three stop codons. This means that more than one codon corresponds to an amino acid. Almost every species on the planet uses the same genetic code.

The players in translation include the mRNA template, ribosomes, tRNAs, and various enzymatic factors. The small ribosomal subunit binds to the mRNA template. Translation begins at the initiating AUG on the mRNA. The formation of bonds occurs between sequential amino acids specified by the mRNA template according to the genetic code. The ribosome accepts charged tRNAs, and as it steps along the mRNA, it catalyzes bonding between the new amino acid and the end of the growing polypeptide. The entire mRNA is translated in three-nucleotide "steps" of the ribosome. When a stop codon is encountered, a release factor binds and dissociates the components and frees the new protein.

4.5.5 Multiple Choice

Exercise 4.5.1 *(Solution on p. 112.)*

The RNA components of ribosomes are synthesized in the _ _ _ _ _ _ _ _.

a. cytoplasm
b. nucleus
c. nucleolus
d. endoplasmic reticulum

Exercise 4.5.2 *(Solution on p. 112.)*

How long would the peptide be that is translated from this MRNA sequence: 5'-AUGGGCUACCGA-3'?

a. 0
b. 2

[7] http://openstaxcollege.org/l/create_protein2

c. 3
d. 4

4.5.6 Free Response

Exercise 4.5.3 ***(Solution on p. 112.)***

Transcribe and translate the following DNA sequence (nontemplate strand): 5'-ATGGCCGGTTATTAAGCA-3'

Solutions to Exercises in Chapter 4

to Exercise 4.2.1 (p. 96)
A
to Exercise 4.2.2 (p. 96)
C
to Exercise 4.2.3 (p. 97)
The DNA is wound around proteins called histones. The histones then stack together in a compact form that creates a fiber that is 30-nm thick. The fiber is further coiled for greater compactness.
to Exercise 4.2.4 (p. 97)
A single strand of DNA is a polymer of nucleotides joined covalently between the phosphate group of one and the deoxyribose sugar of the next to form a phosphodiester "backbone" from which the nitrogenous bases stick out. In its natural state, DNA has two strands wound around each other in a double helix. The bases on each strand are bonded to each other with hydrogen bonds. Only specific bases bond with each other; adenine bonds with thymine, and cytosine bonds with guanine.
to Exercise 4.3.1 (p. 100)
B
to Exercise 4.3.2 (p. 100)
TACCGATGTT
to Exercise 4.4.1 (p. 104)
A
to Exercise 4.4.2 (p. 104)
D
to Exercise 4.5.1 (p. 110)
C
to Exercise 4.5.2 (p. 110)
D
to Exercise 4.5.3 (p. 111)
The mRNA would be: 5'-AUGGCCGGUUAUUAAGCA-3'. The protein would be: Met Ala Gly Tyr. Even though there are six codons, the fifth codon corresponds to a stop (UAA) so the sixth codon would not be translated.

Chapter 5

Digestive System

5.1 Homeostasis[1]

Before moving on to discussing organ systems, it is important to review the concept of internal balance. Homeostasis refers to the relatively stable state inside the body. Human organs and organ systems constantly adjust to internal and external changes in order to maintain this steady state. Examples of internal conditions maintained homeostatically are the level of blood glucose, body temperature, and blood calcium level. These conditions remain stable because of physiologic processes that result in negative feedback relationships. If the blood glucose or calcium rises, this sends a signal to organs responsible for lowering blood glucose or calcium. The signals that restore the normal levels are examples of negative feedback. When homeostatic mechanisms fail, the results can be unfavorable. Homeostatic mechanisms keep the body in dynamic equilibrium by constantly adjusting to the changes that the body's systems encounter. Even when a person is inactive, he/she is maintaining this homeostatic equilibrium. An examples of a factor that is regulated homeostatically is body temperature in a process called thermoregulation.

5.1.1 Homeostasis

The goal of homeostasis is the maintenance of equilibrium around a specific value of some aspect of the body or its cells called a **set point**. While there are normal fluctuations from the set point, the body's systems will usually attempt to go back to this point. A change in the internal or external environment is called a stimulus and is detected by a receptor; the response of the system is to adjust the activities of the system so the value moves back toward the set point. For instance, if the body becomes too warm, adjustments are made to cool it. If glucose levels in the blood rise after a meal, adjustments are made to lower them and to get the nutrient into tissues that need it or to store it for later use.

When a change occurs in an animal's environment, an adjustment must be made so that the internal environment of the body and cells remains stable. The receptor that senses the change in the environment is part of a feedback mechanism. The stimulus—temperature, glucose, or calcium levels—is detected by the receptor. The receptor sends information to a control center, often the brain, which relays appropriate signals to an effector organ that is able to cause an appropriate change, either up or down, depending on the information the sensor was sending.

5.1.2 Thermoregulation

Animals, such as humans, that maintain a constant body temperature in the face of differing environmental temperatures, are called **endotherms**. We are able to maintain this temperature by generating internal

[1] This content is available online at <http://cnx.org/content/m57980/1.2/>.

heat (a waste product of the cellular chemical reactions of metabolism) that keeps the cellular processes operating optimally even when the environment is cold.

Endotherms use their circulatory systems to help maintain body temperature. Vasodilation, the opening up of arteries to the skin by relaxation of their smooth muscles, brings more blood and heat to the body surface, facilitating radiation and evaporative heat loss, cooling the body. Vasoconstriction, the narrowing of blood vessels to the skin by contraction of their smooth muscles, reduces blood flow in peripheral blood vessels, forcing blood toward the core and vital organs, conserving heat.

Thermoregulation is coordinated by the nervous system (Figure 5.1). The processes of temperature control are centered in a region of the brain called the hypothalamus. The hypothalamus maintains the set point for body temperature through reflexes that cause vasodilation or vasoconstriction and shivering or sweating. The hypothalamus directs the responses that effect the changes in temperature loss or gain that return the body to the set point. The set point may be adjusted in some instances. During an infection, compounds called pyrogens are produced and circulate to the hypothalamus resetting the thermostat to a higher value. This allows the body's temperature to increase to a new homeostatic equilibrium point in what is commonly called a fever. The increase in body heat makes the body less optimal for bacterial growth and increases the activities of cells so they are better able to fight the infection.

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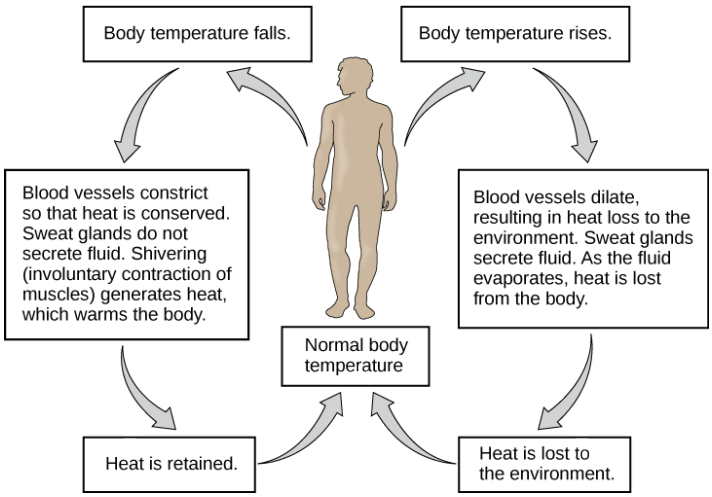

Figure 5.1: The body is able to regulate temperature in response to signals from the nervous system.

5.1.3 Section Summary

Homeostasis is a dynamic equilibrium that is maintained in body tissues and organs. It is dynamic because it is constantly adjusting to the changes that the systems encounter. It is an equilibrium because body functions are kept within a normal range, with some fluctuations around a set point.

5.1.4 Art Connections

Exercise 5.1.1 ***(Solution on p. 125.)***

Figure 5.1 When bacteria are destroyed by leukocytes, pyrogens are released into the blood. Pyrogens reset the body's thermostat to a higher temperature, resulting in fever. How might pyrogens cause the body temperature to rise?

5.1.5 Review Questions

Exercise 5.1.2 *(Solution on p. 125.)*

When faced with a sudden drop in environmental temperature, an endothermic animal will _____.

a. experience a drop in its body temperature
b. wait to see if it goes lower
c. increase muscle activity to generate heat
d. add fur or fat to increase insulation

Exercise 5.1.3 *(Solution on p. 125.)*

What is the cause of a fever of 38.3 °C (101 °F)?

a. too much heat produced by the body
b. upward adjustment of the body temperature set point
c. inadequate cooling mechanisms in the body
d. the heat caused by a viral or bacterial infection

5.1.6 Free Response

Exercise 5.1.4 *(Solution on p. 125.)*

Describe how the body's mechanisms maintain homeostasis?

5.2 The Digestive System[2]

All living organisms need nutrients to survive. While plants can obtain nutrients from their roots and the energy molecules required for cellular function through the process of photosynthesis, animals obtain their nutrients by the consumption of other organisms. At the cellular level, the biological molecules necessary for animal function are amino acids, lipid molecules, nucleotides, and simple sugars. However, the food consumed consists of protein, fat, and complex carbohydrates. Animals must convert these macromolecules into the simple molecules required for maintaining cellular function. The conversion of the food consumed to the nutrients required is a multistep process involving digestion and absorption. During digestion, food particles are broken down to smaller components, which are later absorbed by the body. This happens by both physical means, such as chewing, and by chemical means, via enzyme-catalyzed reactions.

One of the challenges in human nutrition is maintaining a balance between food intake, storage, and energy expenditure. Taking in more food energy than is used in activity leads to storage of the excess in the form of fat deposits. The rise in obesity and the resulting diseases like type 2 diabetes makes understanding the role of diet and nutrition in maintaining good health all the more important.

[2]This content is available online at <http://cnx.org/content/m57981/1.2/>.

5.2.1 The Human Digestive System

The process of digestion begins in the mouth (oral cavity) with the intake of food (Figure 5.2). The teeth play an important role in masticating (chewing) or physically breaking food into smaller particles. This action not only decreases the size of the food particles to facilitate swallowing, but also increases surface area for chemical digestion. The enzymes present in saliva (amylase and lipase) also begin to chemically break down food (starch and fats, respectively). The food is then swallowed and enters the **esophagus**—a long tube that connects the mouth to the stomach. Using **peristalsis**, or wave-like smooth-muscle contractions, the muscles of the esophagus push the food toward the stomach. The stomach contents are extremely acidic, with a pH between 1.5 and 2.5. This acidity kills microorganisms, breaks down food tissues, and activates digestive enzymes. Further breakdown of food takes place in the small intestine where bile produced by the liver, and enzymes produced by the small intestine and the pancreas, continue the process of digestion. The smaller molecules are absorbed into the blood stream through the epithelial cells lining the walls of the small intestine. The waste material travels on to the large intestine where water is absorbed and the drier waste material is compacted into feces; it is stored in the rectum until it is excreted through the anus.

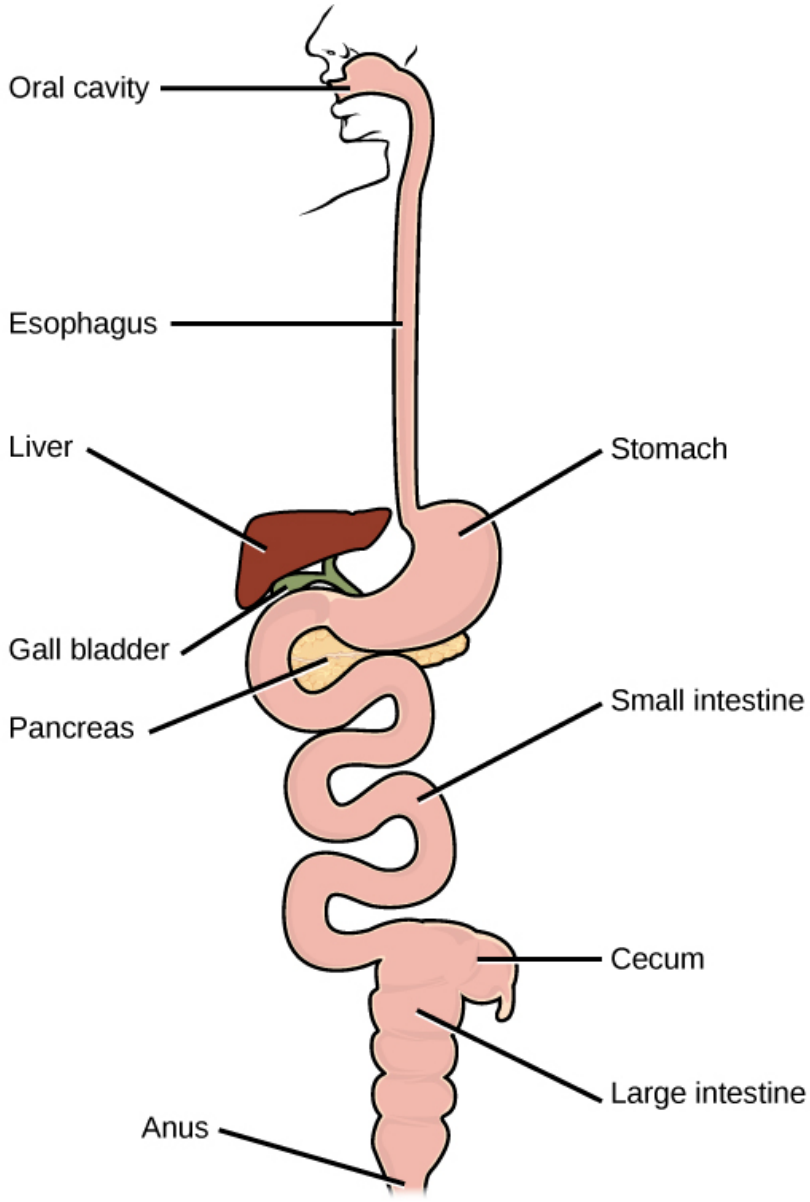

Figure 5.2: The components of the human digestive system are shown. The GI tract is the tube that includes the oral cavity, esophagus, stomach, small intestine, large intestine, and rectum. The accessory organs are those that indirectly join to this tube via ducts and include the salivary glands, liver, gall bladder, and pancreas.

5.2.1.1 Oral Cavity

Both physical and chemical digestion begin in the mouth or **oral cavity**, which is the point of entry of food into the digestive system. The food is broken into smaller particles by mastication, the chewing action of the teeth. All mammals have teeth and can chew their food to begin the process of physically breaking it down into smaller particles.

The chemical process of digestion begins during chewing as food mixes with saliva, produced by the **salivary glands** (Figure 5.3). Saliva contains mucus that moistens food and buffers the pH of the food. Saliva also contains lysozyme, which has antibacterial action. It also contains an enzyme called salivary **amylase** that begins the process of converting starches in the food into a disaccharide called maltose. Another enzyme called **lipase** is produced by cells in the tongue to break down fats. The chewing and wetting action provided by the teeth and saliva prepare the food into a mass called the **bolus** for swallowing. The tongue helps in swallowing—moving the bolus from the mouth into the pharynx. The pharynx opens to two passageways: the esophagus and the trachea. The esophagus leads to the stomach and the trachea leads to the lungs. The epiglottis is a flap of tissue that covers the tracheal opening during swallowing to prevent food from entering the lungs.

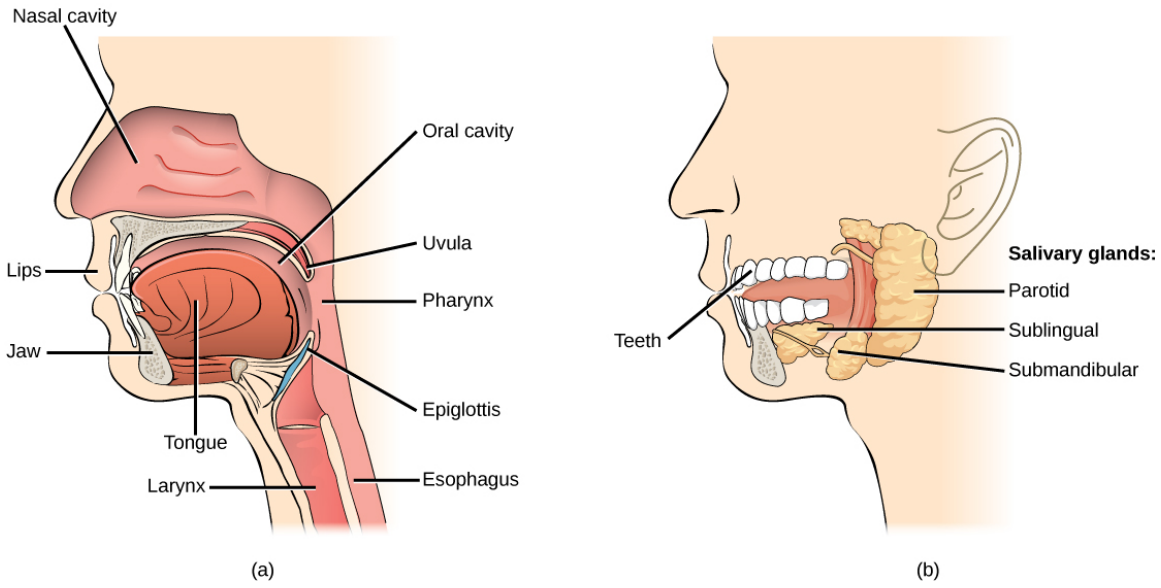

Figure 5.3: (a) Digestion of food begins in the mouth. (b) Food is masticated by teeth and moistened by saliva secreted from the salivary glands. Enzymes in the saliva begin to digest starches and fats. With the help of the tongue, the resulting bolus is moved into the esophagus by swallowing. (credit: modification of work by Mariana Ruiz Villareal)

5.2.1.2 Esophagus

The esophagus is a tubular organ that connects the mouth to the stomach. The chewed and softened food (i.e. the bolus) passes through the esophagus after being swallowed. The smooth muscles of the esophagus undergo peristalsis (contractions) that pushes the food toward the stomach. The peristaltic wave is unidirectional—it moves food from the mouth the stomach, and reverse movement is not possible, except

in the case of the vomit reflex. The peristaltic movement of the esophagus is an involuntary reflex; it takes place in response to the act of swallowing and you don't exert conscious control over it.

Ring-like muscles called sphincters form valves in the digestive system. The gastro-esophageal sphincter (a.k.a. lower esophageal or cardiac sphincter) is located at the stomach end of the esophagus. In response to swallowing and the pressure exerted by the bolus of food, this sphincter opens, and the bolus enters the stomach. When there is no swallowing action, this sphincter is shut and prevents the contents of the stomach from traveling up the esophagus. Acid reflux or "heartburn" occurs when the acidic digestive juices escape back into the esophagus and the low pH irritates the unprotected surface. Prolonged and repeated exposure of the esophagus to this acidity can cause physical damage.

5.2.1.3 Stomach

A large part of protein digestion occurs in the stomach (Figure 5.5). The **stomach** is a saclike organ that secretes gastric digestive juices.

Protein digestion is carried out by an enzyme called **pepsin** in the stomach chamber. The highly acidic environment kills many microorganisms in the food and, combined with the action of the enzyme pepsin, results in the catabolism of protein in the food. Chemical digestion is facilitated by the churning action of the stomach caused by contraction and relaxation of smooth muscles. The partially digested food and gastric juice mixture is called **chyme**. Gastric emptying occurs within two to six hours after a meal. Only a small amount of chyme is released into the small intestine at a time. The movement of chyme from the stomach into the small intestine is regulated by hormones, stomach distension and muscular reflexes that influence the pyloric sphincter. The low pH of the stomach will denature the amylase and lipase that were secreted in the mouth. Therefore, over time, chemical digestion of starches and fats will decrease in the stomach.

The stomach lining is unaffected by pepsin and the acidity because pepsin is released in an inactive form (pepsinogen) that is activated by the low pH. The stomach also has a thick mucus lining that protects the underlying tissue.

5.2.1.4 Small Intestine

Chyme moves from the stomach to the small intestine. The **small intestine** is the organ where the digestion of protein, fats, and carbohydrates is completed. The small intestine is a long tube-like organ with a highly folded surface containing finger-like projections called the villi. The top surface of each villus has many microscopic projections called microvilli. The epithelial cells at the surface of these structures absorb nutrients from the digested food and release them to the bloodstream on the other side. Methods of transport previously discussed (e.g.active transport)are used during this movement. The villi and microvilli, with their many folds, increase the surface area of the small intestine and increase absorption efficiency of the nutrients.

The human small intestine is over 6 m (19.6 ft) long and is divided into three parts: the duodenum, the jejunum and the ileum. The duodenum is separated from the stomach by the pyloric sphincter. The chyme is mixed with pancreatic juices, an alkaline/basic solution rich in bicarbonate that neutralizes the acidity of chyme from the stomach. This result raises the pH and creates an environment that is appropriate for enzymes. Pancreatic juices contain several digestive enzymes (amylase, trypsin, and lipase) that break down starches, proteins, and fats, respectively. **Bile** is produced in the liver and stored and concentrated in the gallbladder; it enters the duodenum through the bile duct. Bile contains bile salts, which make lipids accessible to the water-soluble enzymes. This is accomplished via a process called emulsification, a type of physical digestion. Bile keeps fat droplets from coming back together again, thus increasing the surface area available to lipase. The wall of the small intestines secrete disaccharidases, which faciltate digestion of disaccharides (e.g. maltose, sucrose, and lactose) into their respective monosaccharides. The monosaccharides, amino acids, bile salts, vitamins, and other nutrients are absorbed by the cells of the intestinal lining.

The undigested food is sent to the colon from the ileum via peristaltic movements. The ileum ends and the large intestine begins at the ileocecal valve. The vermiform, "worm-like," appendix is located at the ileocecal valve. The appendix of humans has a minor role in immunity.

5.2.1.5 Large Intestine

The **large intestine** reabsorbs the water from indigestible food material and processes the waste material (Figure 5.4). The human large intestine is much smaller in length compared to the small intestine but larger in diameter. It has three parts: the cecum, the colon, and the rectum. The cecum joins the ileum to the colon and is the receiving pouch for the waste matter. The colon is home to many bacteria or "intestinal flora" that aid in the digestive processes. The **colon** has four regions, the ascending colon, the transverse colon, the descending colon and the sigmoid colon. The main functions of the colon are to extract the water and mineral salts from undigested food, and to store waste material.

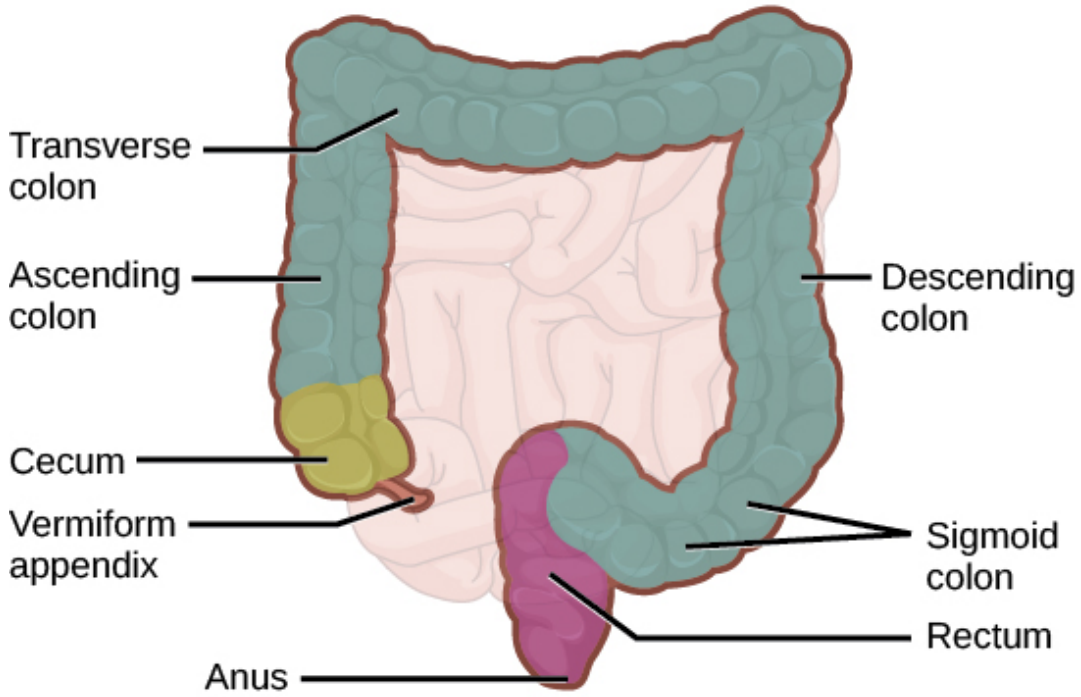

Figure 5.4: The large intestine reabsorbs water from undigested food and stores waste until it is eliminated. (credit: modification of work by Mariana Ruiz Villareal)

The **rectum** (Figure 5.4) stores feces until defecation. The feces are propelled using peristaltic movements during elimination. The **anus** is an opening at the far-end of the digestive tract and is the exit point for the waste material. Two sphincters regulate the exit of feces, the inner sphincter is involuntary and the outer sphincter is voluntary.

5.2.1.6 Accessory Organs

The organs discussed above are the organs of the digestive tract through which food passes. Accessory organs add secretions and enzymes that break down food into nutrients. Accessory organs include the salivary glands, the liver, the pancreas, and the gall bladder. The secretions of the liver, pancreas, and gallbladder are regulated by hormones in response to food consumption.

The **liver** is the largest internal organ in humans and it plays an important role in digestion of fats and detoxifying blood. The liver produces bile, a digestive juice that is required for the breakdown of fats in the duodenum. The liver also processes the absorbed vitamins and fatty acids and synthesizes many plasma proteins. The **gallbladder** is a small organ that aids the liver by storing bile and concentrating bile salts.

The **pancreas** secretes bicarbonate that neutralizes the acidic chyme and a variety of enzymes (trypsin, amylase, and lipase) for the digestion of proteins, carbohydrates, and fats, respectively.

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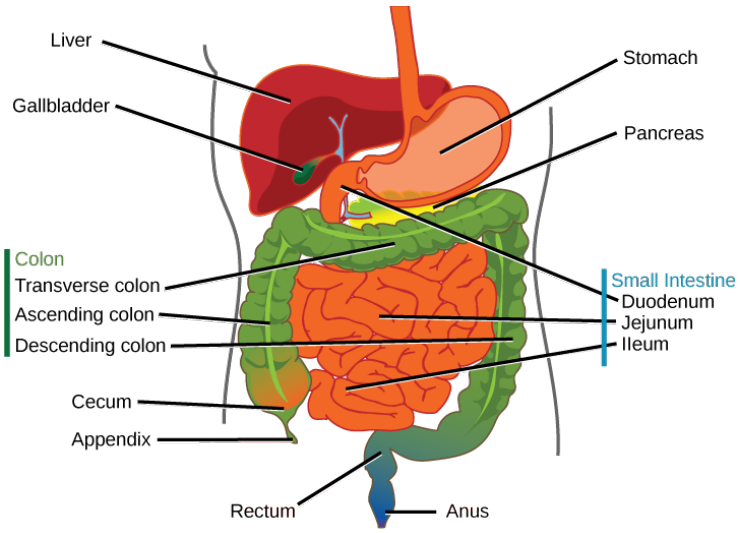

Figure 5.5: The stomach has an extremely acidic environment where most of the protein gets digested. (credit: modification of work by Mariana Ruiz Villareal)

5.2.2 Nutrition

The human diet should be well balanced to provide nutrients required for bodily function and the minerals and vitamins required for maintaining structure and regulation necessary for good health and reproductive capability (Figure 5.6).

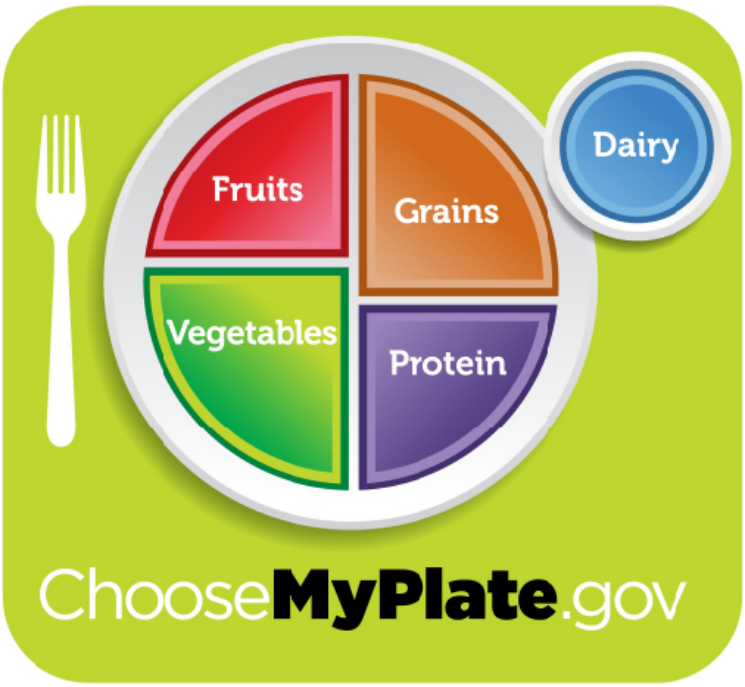

Figure 5.6: For humans, a balanced diet includes fruits, vegetables, grains, protein, and dairy. (credit: USDA)

: Explore this interactive United States Department of Agriculture website[3] to learn more about each food group and the recommended daily amounts.

The organic molecules required for building cellular material and tissues must come from food. During digestion, digestible carbohydrates are ultimately broken down into glucose and used to provide energy within the cells of the body. Complex carbohydrates, including polysaccharides, can be broken down into glucose through biochemical modification; however, humans do not produce the enzyme necessary to digest cellulose (fiber). The intestinal flora in the human gut are able to extract some nutrition from these plant fibers. These plant fibers are known as dietary fiber and are an important component of the diet. The excess sugars in the body are converted into glycogen and stored for later use in the liver and muscle tissue.

[3] http://openstaxcollege.org/l/food_groups2

Glycogen stores are used to fuel prolonged exertions, such as long-distance running, and to provide energy during food shortage. Fats are stored under the skin of mammals for insulation and energy reserves.

Proteins in food are broken down during digestion and the resulting amino acids are absorbed. All of the proteins in the body must be formed from these amino-acid constituents; no proteins are obtained directly from food.

Fats add flavor to food and promote a sense of satiety or fullness. Fatty foods are also significant sources of energy, and fatty acids are required for the construction of lipid membranes. Fats are also required in the diet to aid the absorption of fat-soluble vitamins and the production of fat-soluble hormones.

While the animal body can synthesize many of the molecules required for function from precursors, there are some nutrients that must be obtained from food. These nutrients are termed **essential nutrients**, meaning they must be eaten, because the body cannot produce them. Essential nutrients include some fatty acids, some amino acids, vitamins, and minerals.

5.2.3 Section Summary

There are many organs that work together to digest food and absorb nutrients. The mouth is the point of ingestion and the location where both mechanical and chemical breakdown of food begins. Saliva contains an enzyme called amylase that breaks down carbohydrates and an enxyme lipase that breaks down triglycerides. The food bolus travels through the esophagus by peristaltic movements to the stomach. The stomach has an extremely acidic environment. The enzyme pepsin digests protein in the stomach. Further digestion and absorption take place in the small intestine. The large intestine reabsorbs water from the undigested food and stores waste until elimination.

Carbohydrates, proteins, and fats are the primary components of food. Some essential nutrients are required for cellular function but cannot be produced by the animal body. These include vitamins (both fat and water soluble) , minerals, some fatty acids, and some amino acids. Food intake in more than necessary amounts is stored as glycogen in the liver and muscle cells, and in adipose tissue. Excess adipose storage can lead to obesity and serious health problems.

5.2.4 Art Connections

Exercise 5.2.1 ***(Solution on p. 125.)***

Figure 5.5 Which of the following statements about the digestive system is false?

a. Chyme is a mixture of food and digestive juices that is produced in the stomach.
b. Food enters the large intestine before the small intestine.
c. In the small intestine, chyme mixes with bile, which emulsifies fats.
d. The stomach is separated from the small intestine by the pyloric sphincter.

5.2.5 Review Questions

Exercise 5.2.2 ***(Solution on p. 125.)***

Where does the majority of fat digestion take place?

a. mouth
b. stomach
c. small intestine
d. large intestine

Exercise 5.2.3 ***(Solution on p. 125.)***

The bile from the liver is delivered to the _ _ _ _ _ _ _ _.

a. stomach
b. liver
c. small intestine
d. colon

Exercise 5.2.4 *(Solution on p. 125.)*
Which of the following statements is not true?

a. Essential nutrients can be synthesized by the body.
b. Vitamins are required in small quantities for bodily function.
c. Some amino acids can be synthesized by the body, while others need to be obtained from diet.
d. Vitamins come in two categories: fat-soluble and water-soluble.

5.2.6 Free Response

Exercise 5.2.5 *(Solution on p. 125.)*
What is the role of the accessory organs in digestion?

Solutions to Exercises in Chapter 5

to Exercise 5.1.1 (p. 114)
Figure 5.1 Pyrogens increase body temperature by causing the blood vessels to constrict, inducing shivering, and stopping sweat glands from secreting fluid.
to Exercise 5.1.2 (p. 115)
C
to Exercise 5.1.3 (p. 115)
B
to Exercise 5.1.4 (p. 115)
The body has a sensor that detects a deviation of the state of the cells or the body from the set point. The information is relayed to a control center, usually the brain, where signals go to effectors. Those effectors cause a negative feedback response that moves the state of the body in a direction back toward the set point.
to Exercise 5.2.1 (p. 123)
Figure 5.5 B
to Exercise 5.2.2 (p. 123)
C
to Exercise 5.2.3 (p. 123)
C
to Exercise 5.2.4 (p. 124)
A
to Exercise 5.2.5 (p. 124)
Accessory organs play an important role in producing and delivering digestive juices to the intestine during digestion and absorption. Specifically, the salivary glands, liver, pancreas, and gallbladder play important roles. Malfunction of any of these organs can lead to disease states.

Chapter 6

Energy Considerations

6.1 Introduction to Metabolism[1]

Figure 6.1: A hummingbird needs energy to maintain prolonged flight. The bird obtains its energy from taking in food and transforming the energy contained in food molecules into forms of energy to power its flight through a series of biochemical reactions. (credit: modification of work by Cory Zanker)

Virtually every task performed by living organisms requires energy. Energy is needed to perform heavy labor and exercise, but humans also use energy while thinking, and even during sleep. In fact, the living cells of every organism constantly use energy. Nutrients and other molecules are imported into the cell,

[1] This content is available online at <http://cnx.org/content/m57982/1.1/>.

metabolized (broken down) and possibly synthesized into new molecules, modified if needed, transported around the cell, and possibly distributed to the entire organism. For example, the large proteins that make up muscles are built from smaller molecules imported from dietary amino acids. Complex carbohydrates are broken down into simple sugars that the cell uses for energy. Just as energy is required to both build and demolish a building, energy is required for the synthesis and breakdown of molecules as well as the transport of molecules into and out of cells. In addition, processes such as ingesting and breaking down pathogenic bacteria and viruses, exporting wastes and toxins, and movement of the cell require energy. From where, and in what form, does this energy come? How do living cells obtain energy, and how do they use it? This chapter will discuss different forms of energy and the physical laws that govern energy transfer. This chapter will also describe how cells use energy and replenish it, and how chemical reactions in the cell are performed with great efficiency.

6.2 Energy and Metabolism[2]

6.2.1 Metabolic Pathways

Cellular processes such as the building and breaking down of complex molecules occur through stepwise chemical reactions. Some of these chemical reactions are spontaneous and release energy, whereas others require energy to proceed. Just as living things must continually consume food to replenish their energy supplies, cells must continually produce more energy to replenish that used by the many energy-requiring chemical reactions that constantly take place. Together, all of the chemical reactions that take place inside cells, including those that consume or generate energy, are referred to as the cell's **metabolism**. Consider the metabolism of sugar. This is a classic example of one of the many cellular processes that use and produce energy. Living things consume sugars as a major energy source, because sugar molecules have a great deal of energy stored within their bonds. For the most part, photosynthesizing organisms like plants produce these sugars. During photosynthesis, plants use energy (originally from sunlight) to convert carbon dioxide gas (CO_2) into sugar molecules (like glucose: $C_6H_{12}O_6$). They consume carbon dioxide and produce oxygen as a waste product. This reaction is summarized as:

$$6CO_2 + 6H_2O - - > C_6H_{12}O_6 + 6O_2 \tag{6.1}$$

Because this process involves synthesizing an energy-storing molecule, it requires energy input to proceed. During the light reactions of photosynthesis, energy is provided by a molecule called adenosine triphosphate (ATP), which is the primary energy currency of all cells. Just as the dollar is used as currency to buy goods, cells use molecules of ATP as energy currency to perform immediate work. In contrast, energy-storage molecules such as glucose are consumed only to be broken down to use their energy. The reaction that harvests the energy of a sugar molecule in cells requiring oxygen to survive can be summarized by the reverse reaction to photosynthesis. In this reaction, oxygen is consumed and carbon dioxide is released as a waste product. The reaction is summarized as:

$$C_6H_{12}O_6 + 6O_2 - - > 6H_2O + 6CO_2 \tag{6.2}$$

Both of these reactions involve many steps.

The processes of making and breaking down sugar molecules illustrate two examples of metabolic pathways. A metabolic pathway is a series of chemical reactions that takes a starting molecule and modifies it, step-by-step, through a series of metabolic intermediates, eventually yielding a final product. In the example of sugar metabolism, the first metabolic pathway synthesized sugar from smaller molecules, and the other pathway broke sugar down into smaller molecules. These two opposite processes—the first requiring energy and the second producing energy—are referred to as **anabolic** pathways (building polymers) and **catabolic** pathways (breaking down polymers into their monomers), respectively. Consequently, metabolism is composed of synthesis (anabolism) and degradation (catabolism) (Figure 6.2).

[2]This content is available online at <http://cnx.org/content/m57983/1.2/>.

It is important to know that the chemical reactions of metabolic pathways do not take place on their own. Each reaction step is facilitated, or catalyzed, by a protein called an enzyme. Enzymes are important for catalyzing all types of biological reactions—those that require energy as well as those that release energy.

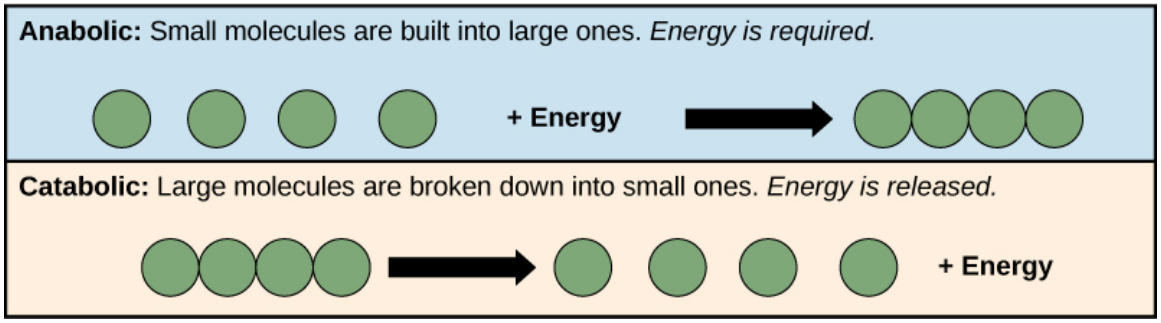

Figure 6.2: Catabolic pathways are those that generate energy by breaking down larger molecules. Anabolic pathways are those that require energy to synthesize larger molecules. Both types of pathways are required for maintaining the cell's energy balance.

6.2.2 Energy

Thermodynamics refers to the study of energy and energy transfer involving physical matter. The matter relevant to a particular case of energy transfer is called a system, and everything outside of that matter is called the surroundings. For instance, when heating a pot of water on the stove, the system includes the stove, the pot, and the water. Energy is transferred within the system (between the stove, pot, and water). There are two types of systems: open and closed. In an open system, energy can be exchanged with its surroundings. The stovetop system is open because heat can be lost to the air. A closed system cannot exchange energy with its surroundings.

Biological organisms are open systems. Energy is exchanged between them and their surroundings as they use energy from the sun to perform photosynthesis or consume energy-storing molecules and release energy to the environment by doing work and releasing heat. Like all things in the physical world, energy is subject to physical laws. The laws of thermodynamics govern the transfer of energy in and among all systems in the universe.

In general, energy is defined as the ability to do work, or to create some kind of change. Energy exists in different forms. For example, electrical energy, light energy, and heat energy are all different types of energy. To appreciate the way energy flows into and out of biological systems, it is important to understand two of the physical laws that govern energy.

6.2.3 Thermodynamics

The first law of thermodynamics states that the total amount of energy in the universe is constant and conserved. In other words, there has always been, and always will be, exactly the same amount of energy in the universe. Energy exists in many different forms. According to the first law of thermodynamics, energy may be transferred from place to place or transformed into different forms, but it cannot be created or destroyed. The transfers and transformations of energy take place around us all the time. Light bulbs

transform electrical energy into light and heat energy. Gas stoves transform chemical energy from natural gas into heat energy. Plants perform one of the most biologically useful energy transformations on earth: that of converting the energy of sunlight to chemical energy stored within organic molecules. Some examples of energy transformations are shown in Figure 6.3.

The challenge for all living organisms is to obtain energy from their surroundings in forms that they can transfer or transform into usable energy to do work. Living cells have evolved to meet this challenge. Chemical energy stored within organic molecules such as sugars and fats is transferred and transformed through a series of cellular chemical reactions into energy within molecules of ATP. Energy in ATP molecules is easily accessible to do work. Examples of the types of work that cells need to do include building complex molecules, transporting materials, powering the motion of cilia or flagella, and contracting muscle fibers to create movement.

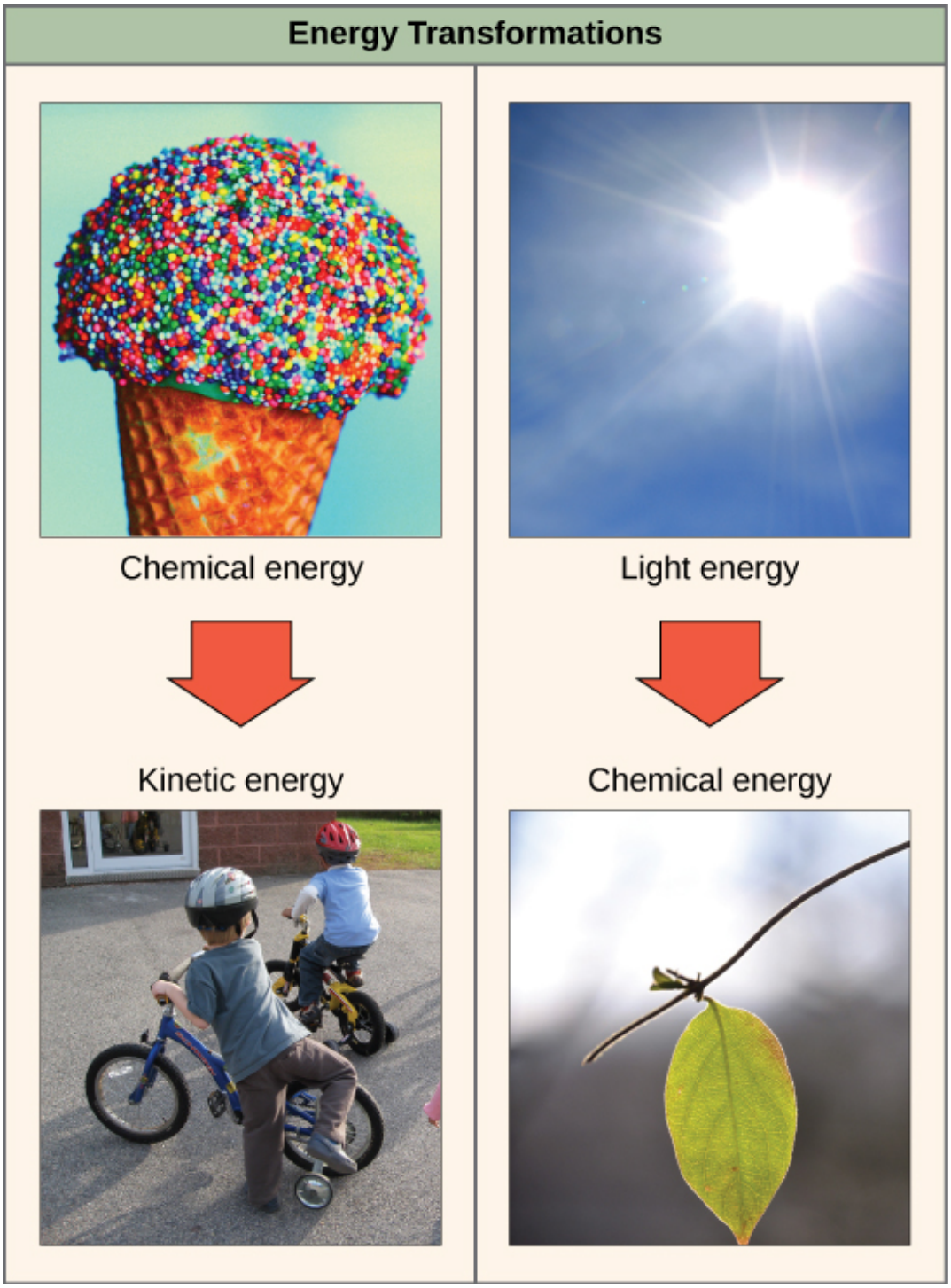

Figure 6.3: Shown are some examples of energy transferred and transformed from one system to another and from one form to another. The food we consume provides our cells with the energy required to carry out bodily functions, just as light energy provides plants with the means to create the chemical energy they need. (credit "ice cream": modification of work by D. Sharon Pruitt; credit "kids": modification of work by Max from Providence; credit "leaf": modification of work by Cory Zanker)

A living cell's primary tasks of obtaining, transforming, and using energy to do work may seem simple. However, the second law of thermodynamics explains why these tasks are harder than they appear. The second law of thermodynamics says that energy will always be lost as heat in energy transfers or transformations. All energy transfers and transformations are never completely efficient. In every energy transfer, some amount of energy is lost in a form that is unusable. In most cases, this form is heat energy. Thermodynamically, **heat energy** is defined as the energy transferred from one system to another that is not work. For example, when a light bulb is turned on, some of the energy being converted from electrical energy into light energy is lost as heat energy. Likewise, some energy is lost as heat energy during cellular metabolic reactions.

6.2.4 Potential and Kinetic Energy

When an object is in motion, there is energy associated with that object. Think of a wrecking ball. Even a slow-moving wrecking ball can do a great deal of damage to other objects. Energy associated with objects in motion is called **kinetic energy** (Figure 6.4). A speeding bullet, a walking person, and the rapid movement of molecules in the air (which produces heat) all have kinetic energy.

Now what if that same motionless wrecking ball is lifted two stories above ground with a crane? If the suspended wrecking ball is unmoving, is there energy associated with it? The answer is yes. The energy that was required to lift the wrecking ball did not disappear, but is now stored in the wrecking ball by virtue of its position and the force of gravity acting on it. This type of energy is called **potential energy** (Figure 6.4). If the ball were to fall, the potential energy would be transformed into kinetic energy until all of the potential energy was exhausted when the ball rested on the ground. Wrecking balls also swing like a pendulum; through the swing, there is a constant change of potential energy (highest at the top of the swing) to kinetic energy (highest at the bottom of the swing). Other examples of potential energy include the energy of water held behind a dam or a person about to skydive out of an airplane.

Figure 6.4: Still water has potential energy; moving water, such as in a waterfall or a rapidly flowing river, has kinetic energy. (credit "dam": modification of work by "Pascal"/Flickr; credit "waterfall": modification of work by Frank Gualtieri)

Potential energy is not only associated with the location of matter, but also with the structure of matter. Even a spring on the ground has potential energy if it is compressed; so does a rubber band that is pulled taut. On a molecular level, the bonds that hold the atoms of molecules together exist in a particular structure that has potential energy. Remember that anabolic cellular pathways require energy to synthesize complex molecules from simpler ones and catabolic pathways release energy when complex molecules are broken down. The fact that energy can be released by the breakdown of certain chemical bonds implies that those bonds have potential energy. In fact, there is potential energy stored within the bonds of all the food molecules we eat, which is eventually harnessed for use. This is because these bonds can release energy when broken. The type of potential energy that exists within chemical bonds, and is released when those bonds are broken, is called chemical energy. Chemical energy is responsible for providing living cells with energy from food. The release of energy occurs when the molecular bonds within food molecules are broken.

6.2.5 Free and Activation Energy

After learning that chemical reactions release energy when energy-storing bonds are broken, an important next question is the following: How is the energy associated with these chemical reactions quantified and expressed? How can the energy released from one reaction be compared to that of another reaction? A measurement of free energy is used to quantify these energy transfers. Recall that according to the second law of thermodynamics, all energy transfers involve the loss of some amount of energy in an unusable form such as heat. Free energy specifically refers to the energy associated with a chemical reaction that is available after the losses are accounted for. In other words, free energy is usable energy, or energy that is available to do work.

If energy is released during a chemical reaction, then the change in free energy, signified as ΔG (delta G) will be a negative number. A negative change in free energy also means that the products of the reaction have less free energy than the reactants, because they release some free energy during the reaction. Reactions that have a negative change in free energy and consequently release free energy are called **exergonic reactions**. Think: exergonic means energy is exiting the system. These reactions are also referred to as spontaneous reactions, and their products have less stored energy than the reactants. An important distinction must be drawn between the term spontaneous and the idea of a chemical reaction occurring immediately. Contrary to the everyday use of the term, a spontaneous reaction is not one that suddenly or quickly occurs. The rusting of iron is an example of a spontaneous reaction that occurs slowly, little by little, over time.

If a chemical reaction absorbs energy rather than releases energy on balance, then the ΔG for that reaction will be a positive value. In this case, the products have more free energy than the reactants. Thus, the products of these reactions can be thought of as energy-storing molecules. These chemical reactions are called **endergonic reactions** and they are non-spontaneous. An endergonic reaction will not take place on its own without the addition of free energy.

There is another important concept that must be considered regarding endergonic and exergonic reactions. Exergonic reactions require a small amount of energy input to get going, before they can proceed with their energy-releasing steps. These reactions have a net release of energy, but still require some energy input in the beginning. This small amount of energy input necessary for all chemical reactions to occur is called the **activation energy**.

6.2.6 Enzymes

A substance that helps a chemical reaction to occur is called a catalyst, and the molecules that catalyze biochemical reactions are called **enzymes**. Most enzymes are proteins and perform the critical task of lowering the activation energies of chemical reactions inside the cell. Most of the reactions critical to a living cell happen too slowly at normal temperatures to be of any use to the cell. Without enzymes to speed up these reactions, life could not persist. Enzymes do this by binding to the reactant molecules and holding them in such a way as to make the chemical bond-breaking and -forming processes take place more easily. It is important to remember that enzymes do not change whether a reaction is exergonic (spontaneous) or endergonic. This is because they do not change the free energy of the reactants or products. They only

reduce the activation energy required for the reaction to go forward (Figure 6.5). In addition, an enzyme itself is unchanged by the reaction it catalyzes. Once one reaction has been catalyzed, the enzyme is able to participate in other reactions.

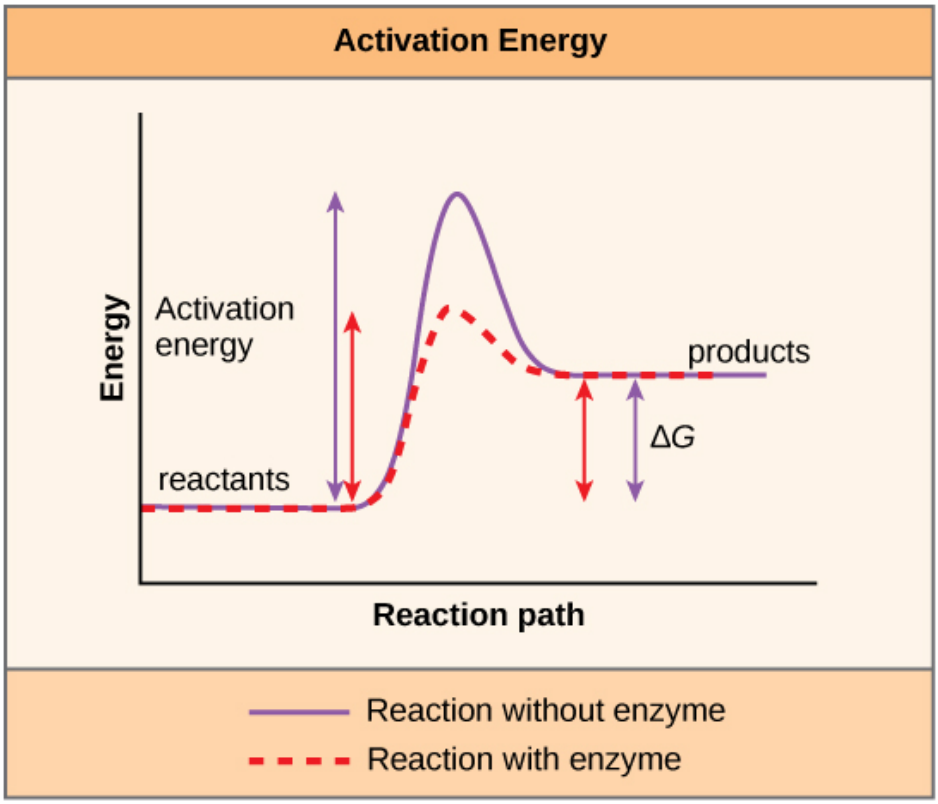

Figure 6.5: Enzymes lower the activation energy of the reaction but do not change the free energy of the reaction.

The chemical reactants to which an enzyme binds are called the enzyme's **substrates**. There may be one or more substrates, depending on the particular chemical reaction. In some reactions, a single reactant substrate is broken down into multiple products. In others, two substrates may come together to create one larger molecule. Two reactants might also enter a reaction and both become modified, but they leave the reaction as two products. The location within the enzyme where the substrate binds is called the enzyme's **active site**. The active site is where the "action" happens. Since enzymes are proteins, there is a unique combination of amino acid side chains within the active site. Each side chain is characterized by different properties. They can be large or small, weakly acidic or basic, hydrophilic or hydrophobic, positively or negatively charged, or neutral. The unique combination of side chains creates a very specific chemical environment within the active site. This specific environment is suited to bind to one specific chemical substrate (or substrates).

Active sites are subject to influences of the local environment. Increasing the environmental temperature generally increases reaction rates, enzyme-catalyzed or otherwise. However, temperatures outside of an optimal range reduce the rate at which an enzyme catalyzes a reaction. Hot temperatures will eventually

cause enzymes to denature, an irreversible change in the three-dimensional shape and therefore the function of the enzyme. Enzymes are also suited to function best within a certain pH and salt concentration range, and, as with temperature, extreme pH, and salt concentrations can cause enzymes to denature.

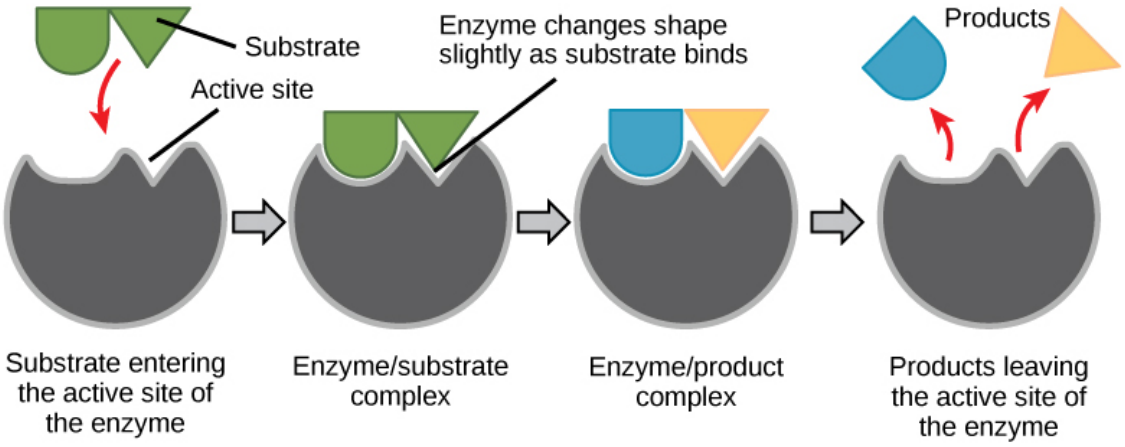

Figure 6.6: In this diagram, a substrate binds the active site of an enzyme and, in the process, both the shape of the enzyme and the shape of the substrate change. The substrate is converted to product, which leaves the active site.

Enzymes can also be regulated in ways that either promote or reduce enzyme activity. There are many kinds of molecules that inhibit or promote enzyme function, and various mechanisms by which they do so. In some cases of enzyme inhibition, an inhibitor molecule is similar enough to a substrate that it can bind to the active site and simply block the substrate from binding. When this happens, the enzyme is inhibited through **competitive inhibition**, because an inhibitor molecule competes with the substrate for binding to the active site.

6.2.7 Section Summary

Cells perform the functions of life through various chemical reactions. A cell's metabolism refers to the combination of chemical reactions that take place within it. Catabolic reactions break down complex chemicals into simpler ones and are associated with energy release. Anabolic processes build complex molecules out of simpler ones and require energy.

In studying energy, the term system refers to the matter and environment involved in energy transfers. Entropy is a measure of the disorder of a system. The physical laws that describe the transfer of energy are the laws of thermodynamics. The first law states that the total amount of energy in the universe is constant. The second law of thermodynamics states that every energy transfer involves some loss of energy in an unusable form, such as heat energy. Energy comes in different forms: kinetic, potential, and free. The change in free energy of a reaction can be negative (releases energy, exergonic) or positive (consumes energy, endergonic). All reactions require an initial input of energy to proceed, called the activation energy.

Enzymes are chemical catalysts that speed up chemical reactions by lowering their activation energy. Enzymes have an active site with a unique chemical environment that fits particular chemical reactants for that enzyme, called substrates. Enzyme action is regulated to conserve resources and respond optimally to the environment.

6.2.8 Review Questions

Exercise 6.2.1 *(Solution on p. 149.)*

Which of the following is not an example of an energy transformation?

a. Heating up dinner in a microwave
b. Solar panels at work
c. Formation of static electricity
d. None of the above

Exercise 6.2.2 *(Solution on p. 149.)*

Which of the following is not true about enzymes?

a. They are consumed by the reactions they catalyze.
b. They are usually made of amino acids.
c. They lower the activation energy of chemical reactions.
d. Each one is specific to the particular substrate(s) to which it binds.

6.2.9 Free Response

Exercise 6.2.3 *(Solution on p. 149.)*

Does physical exercise to increase muscle mass involve anabolic and/or catabolic processes? Give evidence for your answer.

6.3 Glycolysis[3]

Even exergonic, energy-releasing reactions require a small amount of activation energy to proceed. However, consider endergonic reactions, which require much more energy input because their products have more free energy than their reactants. Within the cell, where does energy to power such reactions come from? The answer lies with an energy-supplying molecule called adenosine triphosphate, or **ATP**. ATP is a small, relatively simple molecule, but within its bonds contains the potential for a quick burst of energy that can be harnessed to perform cellular work. This molecule can be thought of as the primary energy currency of cells in the same way that money is the currency that people exchange for things they need. ATP is used to power the majority of energy-requiring cellular reactions.

6.3.1 ATP in Living Systems

A living cell cannot store significant amounts of free energy. Excess free energy would result in an increase of heat in the cell, which would denature enzymes and other proteins, and thus destroy the cell. Rather, a cell must be able to store energy safely and release it for use only as needed. Living cells accomplish this using ATP, which can be used to fill any energy need of the cell. How? It functions as a rechargeable battery.

When ATP is broken down, usually by the removal of its terminal phosphate group, energy is released. This energy is used to do work by the cell, usually by the binding of the released phosphate to another molecule, thus activating it. For example, in the mechanical work of muscle contraction, ATP supplies energy to move the contractile muscle proteins.

[3] This content is available online at <http://cnx.org/content/m57984/1.1/>.

6.3.1.1 ATP Structure and Function

At the heart of ATP is a molecule of adenosine monophosphate (AMP), which is composed of an adenine molecule bonded to both a ribose molecule and a single phosphate group (Figure 6.7). Ribose is a five-carbon sugar found in RNA and AMP is one of the nucleotides in RNA. The addition of a second phosphate group to this core molecule results in adenosine diphosphate (ADP); the addition of a third phosphate group forms adenosine triphosphate (ATP).

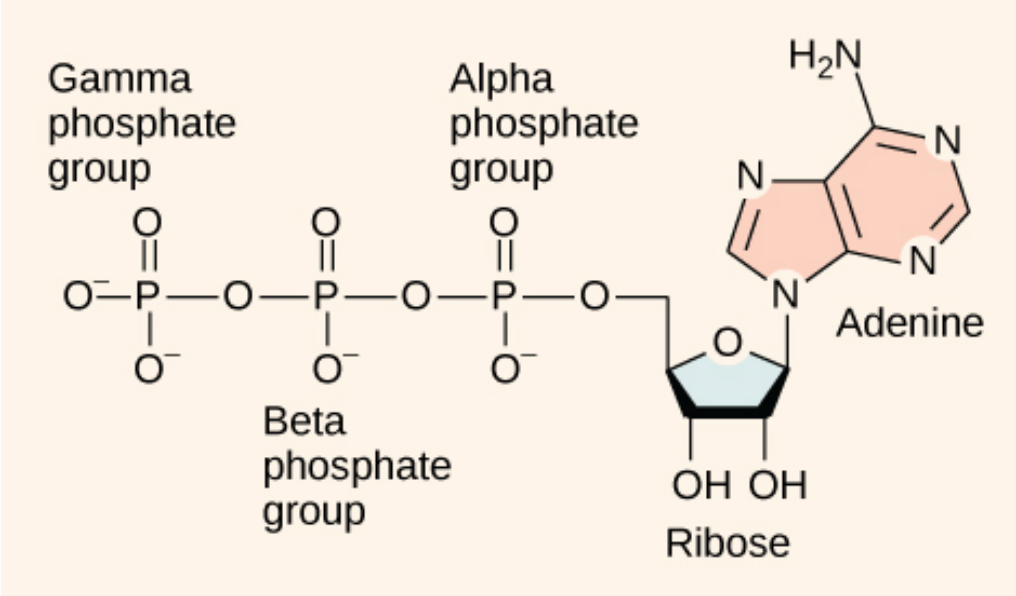

Figure 6.7: The structure of ATP shows the basic components of a two-ring adenine, five-carbon ribose, and three phosphate groups.

The addition of a phosphate group to a molecule requires a high amount of energy and results in a high-energy bond. Phosphate groups are negatively charged and thus repel one another when they are arranged in series, as they are in ADP and ATP. This repulsion makes the ADP and ATP molecules inherently unstable. The release of one or two phosphate groups from ATP, a process called hydrolysis, releases energy. Hydrolysis occurs when water is added to break the chemical bond and is the opposite of dehydration synthesis reactions discussed previously.

6.3.2 Glycolysis

You have read that nearly all of the energy used by living things comes to them in the bonds of the sugar, glucose. **Glycolysis** is the first step in the breakdown of glucose to extract energy for cell metabolism. Many living organisms carry out glycolysis as part of their metabolism. Glycolysis takes place in the cytoplasm of eukaryotic cells.

Glycolysis begins with the six-carbon, ring-shaped structure of a single glucose molecule and ends with two molecules of a three-carbon sugar called pyruvate. Glycolysis consists of two distinct phases. In the first part of the glycolysis pathway, energy is used to make adjustments so that the six-carbon sugar molecule can be split evenly into two three-carbon pyruvate molecules. In the second part of glycolysis, ATP and

nicotinamide-adenine dinucleotide (NADH) are produced (Figure 6.8). NAD+ is the form of the coenzyme that is able to accept electrons and hydrogen from the glucose. NADH carries the electrons to a later stage in metabolism to be used to provide energy (indirectly) to catalyze the endergonic reaction of adding a phosphate group to ADP to make ATP.

If the cell cannot catabolize the pyruvate molecules further, it will harvest only two ATP molecules from one molecule of glucose. For example, mature mammalian red blood cells are only capable of glycolysis, which is their sole source of ATP. If glycolysis is interrupted, these cells would eventually die.

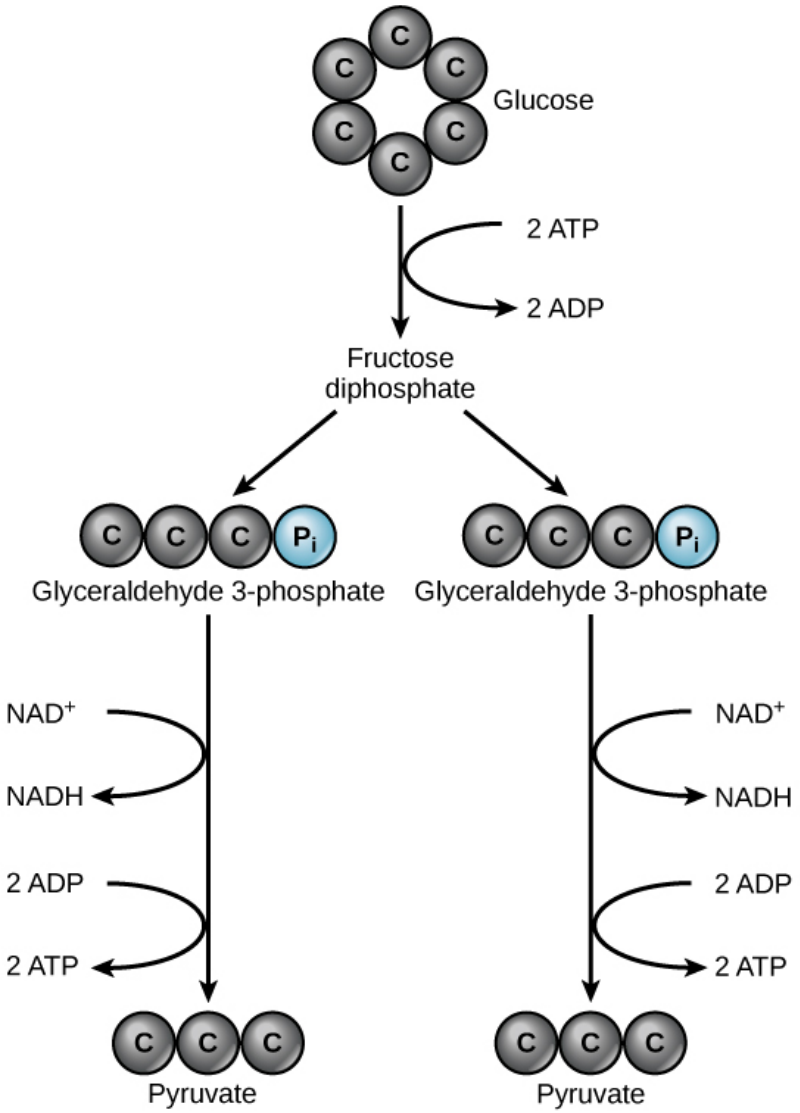

Figure 6.8: In glycolysis, a glucose molecule is converted into two pyruvate molecules. Notice that each of the two molecules has three carbon atoms, representing the six carbons that were present in the glucose that started the process. This means that no carbon dioxide is released in glycolysis, as the carbon to make it comes from the glucose molecule.

6.3.3 Section Summary

ATP functions as the energy currency for cells. It allows cells to store energy briefly and transport it within itself to support endergonic chemical reactions. The structure of ATP is that of an RNA nucleotide with three phosphate groups attached. As ATP is used for energy, a phosphate group is detached, and ADP is

produced. Energy derived from glucose catabolism is used to recharge ADP into ATP.

Glycolysis is the first pathway used in the breakdown of glucose to extract energy. Because it is used by nearly all organisms on earth, it must have evolved early in the history of life. Glycolysis consists of two parts: The first part prepares the six-carbon ring of glucose for separation into two three-carbon sugars. Energy from ATP is invested into the molecule during this step to energize the separation. The second half of glycolysis extracts ATP and high-energy electrons from hydrogen atoms and attaches them to NAD^+. Two ATP molecules are invested in the first half and four ATP molecules are formed during the second half. This produces a net gain of two ATP molecules per molecule of glucose for the cell.

6.3.4 Multiple Choice

Exercise 6.3.1 *(Solution on p. 149.)*

Energy is stored long-term in the bonds of _____ and used short-term to perform work from a(n) _____ molecule.

a. ATP : glucose
b. an anabolic molecule : catabolic molecule
c. glucose : ATP
d. a catabolic molecule : anabolic molecule

Exercise 6.3.2 *(Solution on p. 149.)*

The energy currency used by cells is _____.

a. ATP
b. ADP
c. AMP
d. adenosine

Exercise 6.3.3 *(Solution on p. 149.)*

The glucose that enters the glycolysis pathway is split into two molecules of _____.

a. ATP
b. phosphate
c. NADH
d. pyruvate

6.4 The Transition Reaction, Citric Acid/Kreb's Cycle and Electron Transport Chain/Oxidative Phosphorylation[4]

6.4.1 The Transition Reaction and Citric Acid/Kreb's Cycle

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. The resulting compound is called **acetyl CoA**. (Figure 6.9). This set of reactions is referred to as the transition reaction, as it happens during pyruvate transport into the mitochondria. The major function of acetyl CoA is to deliver the acetyl group (2 carbon fragment) derived from pyruvate to the next pathway

[4]This content is available online at <http://cnx.org/content/m57985/1.2/>.

in glucose catabolism, which is the citric acid/Kreb's cycle. Note that during the transition reaction, each pyruvate/pyruvic acid molecule loses one carbon as carbon dioxide and one molecule of NADH is produced. Therefore, a total of two molecules of carbon dioxide and two molecules of NADH are produced per glucose that started glycolysis.

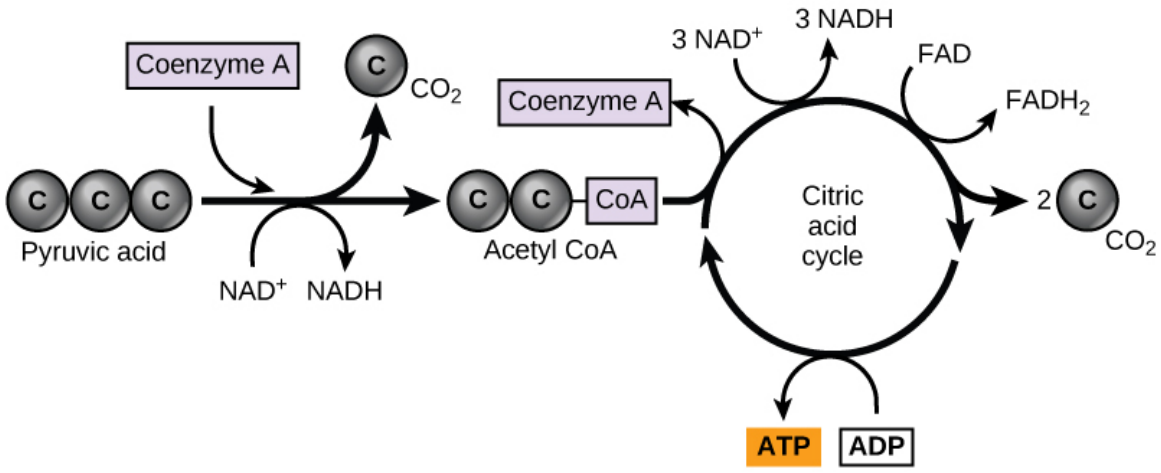

Figure 6.9: During the transition reaction, pyruvate is converted into acetyl-CoA before entering the citric acid/Kreb's cycle.

Like the conversion of pyruvate to acetyl CoA, the **citric acid cycle** (also called the Kreb's cycle) in eukaryotic cells takes place in the matrix of the mitochondria. Unlike glycolysis, the citric acid cycle is a closed loop: The last part of the pathway regenerates the compound used in the first step. The eight steps of the cycle are a series of chemical reactions that produces two carbon dioxide molecules, one ATP molecule (or an equivalent), and reduced forms (NADH and $FADH_2$) of NAD^+ and FAD^+, important coenzymes in the cell. Part of this is considered an aerobic pathway (oxygen-requiring) because the NADH and $FADH_2$ produced must transfer their electrons to the next pathway in the system, which will use oxygen. If oxygen is not present, this transfer does not occur. Note that per glucose that started glycolysis, processing of the two pyruvate/pyruvic acid molecules in the citric acid cycle will result in the production of a total of six NADH, two $FADH_2$, and two ATP. Also note that at this point, a total of six molecules of carbon dioxide have been released, which accounts for the six carbons in the starting glucose molecule. The high-energy NADH and $FADH_2$ will be used in the last stage of aerobic respiration to produce additional ATP molecules.

6.4.2 Electron Transport Chain/Oxidative Phosphorylation

You have just read about two pathways in glucose catabolism—glycolysis and the citric acid cycle—that generate ATP. Most of the ATP generated during the aerobic catabolism of glucose, however, is not generated directly from these pathways. Rather, it derives from a process that begins with passing electrons through a series of chemical reactions to a final electron acceptor, oxygen. These reactions take place in specialized protein complexes located in the inner membrane of the mitochondria. The energy of the electrons is harvested and used to generate a electrochemical gradient of hydrogen ions across the inner mitochondrial membrane. The potential energy of this gradient is used to generate ATP by providing the energy to add phosphate groups to ADP molecules. The entirety of this process is called **oxidative phosphorylation**, as oxygen is required as the terminal electron acceptor and phosphate groups are added to ADP molecules.

The electron transport chain (Figure 6.10**a**) is the last component of aerobic respiration and is the only part of metabolism that uses atmospheric oxygen. Oxygen continuously diffuses into plants for this purpose. In animals, oxygen enters the body through the respiratory system. Electron transport is a series of chemical reactions that resembles a bucket brigade in that electrons are passed rapidly from one component to the next, to the endpoint of the chain where oxygen is the final electron acceptor and water is produced. There are four complexes composed of proteins, labeled I through IV in Figure 6.10**c**, and the aggregation of these four complexes, together with associated mobile, accessory electron carriers, is called the **electron transport chain**. The electron transport chain is present in multiple copies in the inner mitochondrial membrane of eukaryotes and in the plasma membrane of prokaryotes. In each transfer of an electron through the electron transport chain, the electron loses energy, but with some transfers, the energy is stored as potential energy by using it to pump hydrogen ions across the inner mitochondrial membrane into the intermembrane space, creating an electrochemical gradient.

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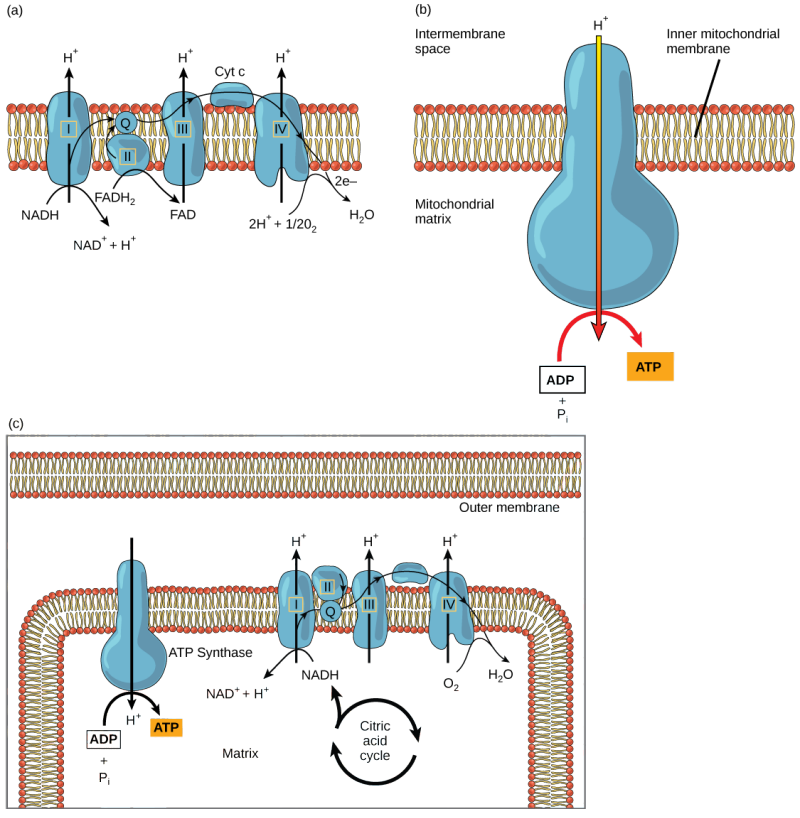

Figure 6.10: (a) The electron transport chain is a set of molecules that supports a series of oxidation-reduction reactions. (b) ATP synthase is a complex, molecular machine that uses an H^+ gradient to regenerate ATP from ADP. (c) An overview of the entire process.

Electrons from NADH and $FADH_2$ are passed to protein complexes in the electron transport chain. As they are passed from one complex to another (there are a total of four), the electrons lose energy, and some of that energy is used to pump hydrogen ions from the mitochondrial matrix into the intermembrane space. In the fourth protein complex, the electrons are accepted by oxygen, the terminal acceptor. The oxygen with

its extra electrons then combines with two hydrogen ions, further enhancing the electrochemical gradient, to form water. If there were no oxygen present in the mitochondrion, the electrons could not be removed from the system, and the entire electron transport chain would back up and stop. The mitochondria would be unable to generate new ATP in this way, and the cell would ultimately die from lack of energy. This is the reason we must breathe to draw in new oxygen.

In the electron transport chain, the free energy from the series of reactions just described is used to pump hydrogen ions (via active transport) across the membrane. The uneven distribution of H^+ ions across the membrane establishes an electrochemical gradient, owing to the H^+ ions' positive charge and their higher concentration on one side of the membrane.

Hydrogen ions diffuse through the inner membrane through a membrane protein called **ATP synthase** (Figure 6.10**b**). This complex protein acts as a tiny generator, turned by the force of the hydrogen ions diffusing through it, down their electrochemical gradient from the intermembrane space, where there are many mutually repelling hydrogen ions to the matrix, where there are few. The turning of the parts of this molecular machine regenerate ATP from ADP and phosphate.

Chemiosmosis (Figure 6.10**c**) is used to generate 90 percent of the ATP made during aerobic glucose catabolism. The result of the reactions is the production of ATP from the energy of the electrons removed from hydrogen atoms. These atoms were originally part of a glucose molecule. At the end of the electron transport system, the electrons are used to reduce an oxygen molecule to oxygen ions. The extra electrons on the oxygen ions attract hydrogen ions (protons) from the surrounding medium, and water is formed.

6.4.3 ATP Yield

The number of ATP molecules generated from the catabolism of glucose varies. In general, processing of each NADH yields approximately 3 ATP and each $FADH_2$ yields approximately 2 ATP. Overall, a total of 10 NADH and 2 $FADH_2$ were produced in glycolysis, transition reaction, and the citric acid cycle per glucose molecule. This results in the production of approximately 34 ATP. Remember, that two additional ATP were produced directly in both glycolysis and the citric acid cycle, resulting in a total yield of 38 ATP per glucose. This represents an efficiency of approximately 35%, with the remaining energy potential lost as heat or other products.

: **Mitochondrial Disease Physician**

What happens when the critical reactions of cellular respiration do not proceed correctly? Mitochondrial diseases are genetic disorders of metabolism. Mitochondrial disorders can arise from mutations in nuclear or mitochondrial DNA, and they result in the production of less energy than is normal in body cells. Symptoms of mitochondrial diseases can include muscle weakness, lack of coordination, stroke-like episodes, and loss of vision and hearing. Most affected people are diagnosed in childhood, although there are some adult-onset diseases. Identifying and treating mitochondrial disorders is a specialized medical field. The educational preparation for this profession requires a college education, followed by medical school with a specialization in medical genetics. Medical geneticists can be board certified by the American Board of Medical Genetics and go on to become associated with professional organizations devoted to the study of mitochondrial disease, such as the Mitochondrial Medicine Society and the Society for Inherited Metabolic Disease.

6.4.4 Section Summary

The citric acid cycle is a series of chemical reactions that removes high-energy electrons and uses them in the electron transport chain to generate ATP. One molecule of ATP (or an equivalent) is produced per each turn of the cycle.

The electron transport chain is the portion of aerobic respiration that uses free oxygen as the final electron acceptor for electrons removed from the intermediate compounds in glucose catabolism. The electrons are passed through a series of chemical reactions, with a small amount of free energy used at three points to

transport hydrogen ions across the membrane. This contributes to the gradient used in chemiosmosis. As the electrons are passed from NADH or $FADH_2$ down the electron transport chain, they lose energy. The products of the electron transport chain are water and ATP. A number of intermediate compounds can be diverted into the anabolism of other biochemical molecules, such as nucleic acids, non-essential amino acids, sugars, and lipids. These same molecules, except nucleic acids, can serve as energy sources for the glucose pathway.

6.4.5 Multiple Choice

Exercise 6.4.1 *(Solution on p. 149.)*

What do the electrons added to NAD^+ do?

a. They become part of a fermentation pathway.
b. They go to another pathway for ATP production.
c. They energize the entry of the acetyl group into the citric acid cycle.
d. They are converted into NADP.

Exercise 6.4.2 *(Solution on p. 149.)*

What provides the energy for ATP synthase?

a. the movement of electrons
b. the movement of hydrogen atoms
c. the movement of hydrogen ions
d. the movement of glucose
e. the movement of carbon dioxide

6.4.6 Free Response

Exercise 6.4.3 *(Solution on p. 149.)*

We inhale oxygen when we breathe and exhale carbon dioxide. What is the oxygen used for and where does the carbon dioxide come from?

6.5 Fermentation[5]

In aerobic respiration, the final electron acceptor is an oxygen molecule, O_2. If aerobic respiration occurs, then ATP will be produced using the energy of the high-energy electrons carried by NADH or $FADH_2$ to the electron transport chain. If aerobic respiration does not occur, NADH must be reoxidized to NAD^+ for reuse as an electron carrier for glycolysis to continue. How is this done? Humans use an organic molecule (pyruvate/pyruvic acid)as the final electron acceptor. Processes that use an organic molecule to regenerate NAD^+ from NADH are collectively referred to as **fermentation**.

6.5.1 Lactic Acid Fermentation

The fermentation method used by animals and some bacteria like those in yogurt is lactic acid fermentation (Figure 6.11). This occurs routinely in mammalian red blood cells and in skeletal muscle that has insufficient oxygen supply to allow aerobic respiration to continue (that is, in muscles used to the point of fatigue). In

[5]This content is available online at <http://cnx.org/content/m57986/1.2/>.

muscles, lactic acid produced by fermentation must be removed by the blood circulation and brought to the liver for further metabolism. The chemical reaction of lactic acid fermentation is the following:

$$\text{Pyruvic acid} + \text{NADH} \leftrightarrow \text{lactic acid} + \text{NAD}^{+} \tag{6.3}$$

:

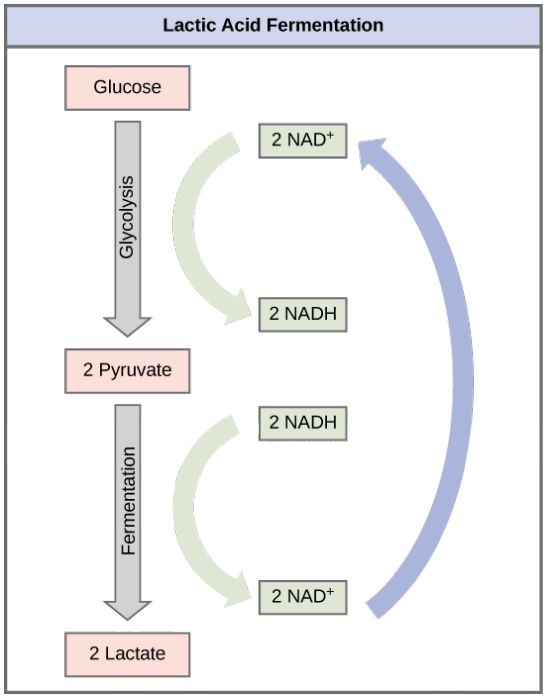

Figure 6.11: Lactic acid fermentation is common in muscles that have become exhausted by use.

6.5.2 Alcohol Fermentation

Another familiar fermentation process is alcohol fermentation (Figure 6.12), which produces ethanol, an alcohol. The alcohol fermentation reaction is the following:

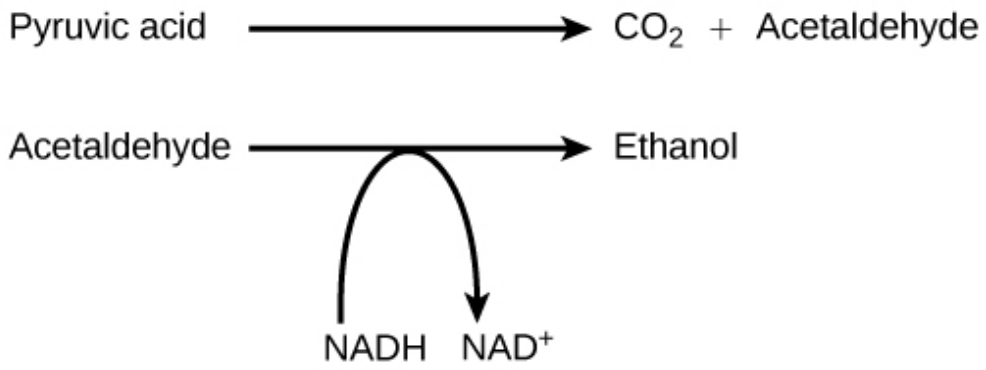

Figure 6.12: The reaction resulting in alcohol fermentation is shown.

In the first reaction, a carboxyl group is removed from pyruvic acid, releasing carbon dioxide as a gas. The loss of carbon dioxide reduces the molecule by one carbon atom, making acetaldehyde. The second reaction removes an electron from NADH, forming NAD^+ and producing ethanol from the acetaldehyde, which accepts the electron. The fermentation of pyruvic acid by yeast produces the ethanol found in alcoholic beverages (Figure 6.13). If the carbon dioxide produced by the reaction is not vented from the fermentation chamber, for example in beer and sparkling wines, it remains dissolved in the medium until the pressure is released. Ethanol above 12 percent is toxic to yeast, so natural levels of alcohol in wine occur at a maximum of 12 percent.

Figure 6.13: Fermentation of grape juice to make wine produces CO_2 as a byproduct. Fermentation tanks have valves so that pressure inside the tanks can be released.

6.5.3 Section Summary

If NADH cannot be metabolized through aerobic respiration, another electron acceptor is used. Most organisms will use some form of fermentation to accomplish the regeneration of NAD^+, ensuring the continuation of glycolysis. The regeneration of NAD^+ in fermentation is not accompanied by ATP production; therefore, the potential for NADH to produce ATP using an electron transport chain is not utilized.

6.5.4 Review Questions

Exercise 6.5.1 *(Solution on p. 149.)*

Which of the following fermentation methods can occur in animal skeletal muscles deprived of oxygen?

a. lactic acid fermentation
b. alcohol fermentation
c. mixed acid fermentation
d. propionic fermentation

6.5.5 Free Response

Exercise 6.5.2 *(Solution on p. 149.)*

When muscle cells run out of oxygen, what happens to the potential for energy extraction from sugars and what pathways do the cell use?

Solutions to Exercises in Chapter 6

to Exercise 6.2.1 (p. 136)
D
to Exercise 6.2.2 (p. 136)
A
to Exercise 6.2.3 (p. 136)
Physical exercise involves both anabolic and catabolic processes. Body cells break down sugars to provide ATP to do the work necessary for exercise, such as muscle contractions. This is catabolism. Muscle cells also must repair muscle tissue damaged by exercise by building new muscle. This is anabolism.
to Exercise 6.3.1 (p. 140)
C
to Exercise 6.3.2 (p. 140)
A
to Exercise 6.3.3 (p. 140)
D
to Exercise 6.4.1 (p. 144)
B
to Exercise 6.4.2 (p. 144)
C
to Exercise 6.4.3 (p. 144)
The oxygen we inhale is the final electron acceptor in the electron transport chain and allows aerobic respiration to proceed, which is the most efficient pathway for harvesting energy in the form of ATP from food molecules. The carbon dioxide we breathe out is formed during the transition reaction and the citric acid cycle when the bonds in carbon compounds are broken.
to Exercise 6.5.1 (p. 147)
A
to Exercise 6.5.2 (p. 148)
Without oxygen, the transition, the citric acid cycle, and the electron transport chain stop, so ATP is no longer generated through this mechanism, which extracts the greatest amount of energy from a sugar molecule. In addition, NADH accumulates, preventing glycolysis from going forward because of an absence of NAD^+. Lactic acid fermentation uses the electrons in NADH to generate lactic acid from pyruvate, which allows glycolysis to continue and thus a smaller amount of ATP can be generated by the cell (2 versus 38 ATP per glucose).

Available for free at Connexions <http://cnx.org/content/col11903/1.3>

Chapter 7

Blood

7.1 Introduction to the Cardiovascular System - Blood[1]

Blood Cells

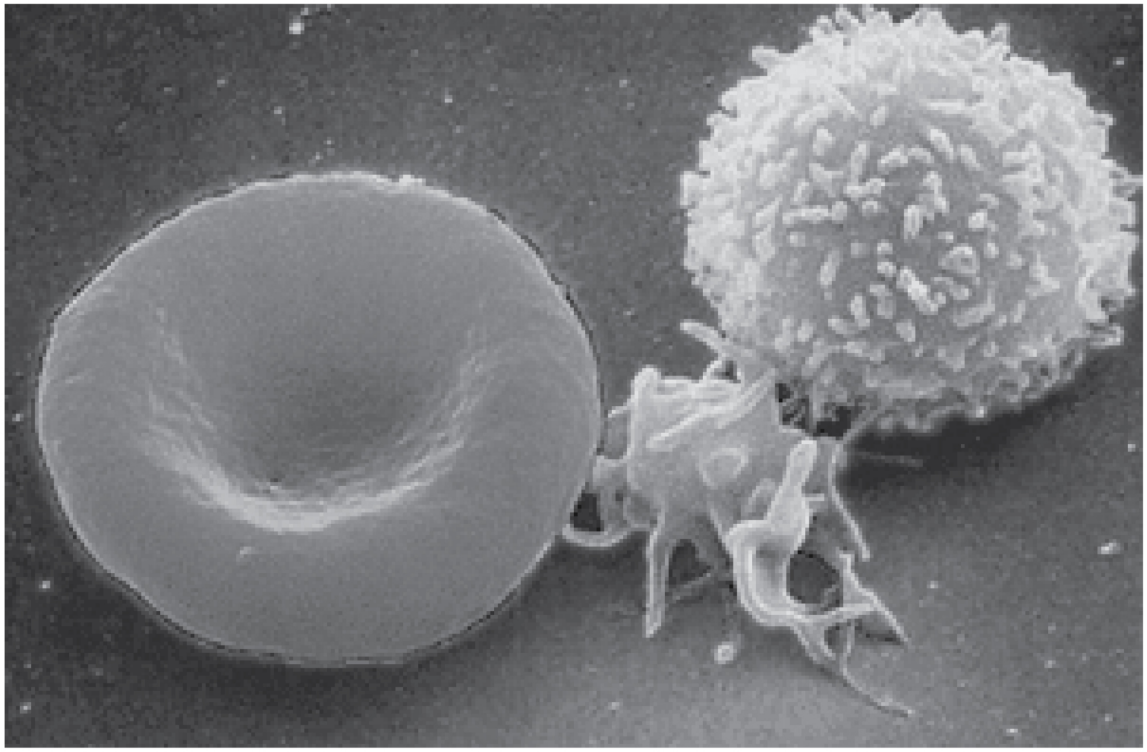

Figure 7.1: A single drop of blood contains millions of red blood cells, white blood cells, and platelets. One of each type is shown here (from left to right) isolated from a scanning electron micrograph.

[1] This content is available online at <http://cnx.org/content/m57987/1.3/>.

NOTE: After studying this chapter, you will be able to:

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

The human body needs blood to deliver nutrients to and remove wastes from our trillions of cells. The heart pumps blood throughout the body in a network of blood vessels. Together, these three components—blood, heart, and vessels—makes up the cardiovascular system. This chapter focuses on the medium of transport: blood.

7.2 An Overview of Blood[2]

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

7.2.1 Functions of Blood

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

7.2.1.1 Transportation

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

7.2.1.2 Defense

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

When damage to the vessels results in bleeding, blood platelets and certain proteins dissolved in the plasma, the fluid portion of the blood, interact to block the ruptured areas of the blood vessels involved. This protects the body from further blood loss.

[2]This content is available online at <http://cnx.org/content/m57989/1.2/>.

7.2.1.3 Maintenance of Homeostasis

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

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

7.2.2 Composition of Blood

You have probably had blood drawn from a superficial vein in your arm, which was then sent to a lab for analysis. Some of the most common blood tests—for instance, those measuring lipid or glucose levels in plasma—determine which substances are present within blood and in what quantities. Other blood tests check for the composition of the blood itself, including the quantities and types of formed elements.

One such test, called a **hematocrit**, measures the percentage of RBCs, clinically known as erythrocytes, in a blood sample. It is performed by spinning the blood sample in a specialized centrifuge, a process that causes the heavier elements suspended within the blood sample to separate from the lightweight, liquid plasma (Figure 7.2 (Composition of Blood)). Because the heaviest elements in blood are the erythrocytes, these settle at the very bottom of the hematocrit tube. Located above the erythrocytes is a pale, thin layer composed of the remaining formed elements of blood. These are the WBCs, clinically known as leukocytes, and the platelets, cell fragments also called thrombocytes. This layer is referred to as the **buffy coat** because of its color; it normally constitutes less than 1 percent of a blood sample. Above the buffy coat is the blood plasma, normally a pale, straw-colored fluid, which constitutes the remainder of the sample.

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

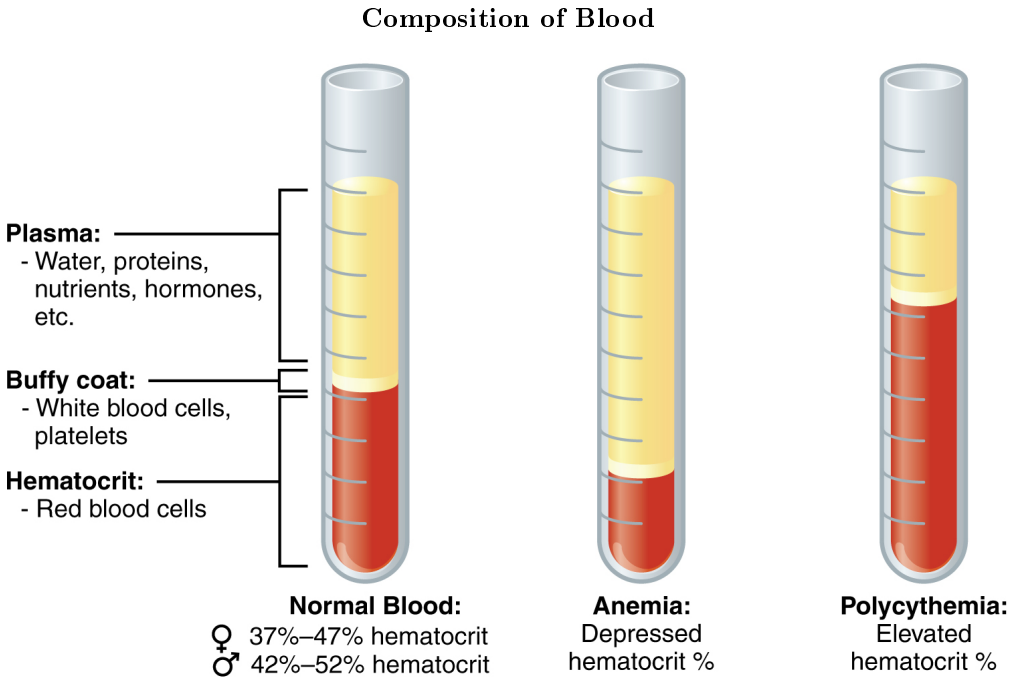

Figure 7.2: The cellular elements of blood include a vast number of erythrocytes and comparatively fewer leukocytes and platelets. Plasma is the fluid in which the formed elements are suspended. A sample of blood spun in a centrifuge reveals that plasma is the lightest component. It floats at the top of the tube separated from the heaviest elements, the erythrocytes, by a buffy coat of leukocytes and platelets. Hematocrit is the percentage of the total sample that is comprised of erythrocytes. Depressed and elevated hematocrit levels are shown for comparison.

7.2.3 Characteristics of Blood

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

The normal temperature of blood is slightly higher than normal body temperature—about 38 °C (or 100.4 °F), compared to 37 °C (or 98.6 °F) for an internal body temperature reading, although daily variations of 0.5 °C are normal. Although the surface of blood vessels is relatively smooth, as blood flows through them, it experiences some friction and resistance, especially as vessels age and lose their elasticity, thereby producing heat. This accounts for its slightly higher temperature.

The pH of blood averages about 7.4; however, it can range from 7.35 to 7.45 in a healthy person. Blood is therefore somewhat more basic (alkaline) on a chemical scale than pure water, which has a pH of 7.0. Blood contains numerous buffers that actually help to regulate pH.

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

7.2.4 Blood Plasma

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

7.2.4.1 Plasma Proteins

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

The three major groups of plasma proteins are as follows:

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

7.2.4.2 Other Plasma Solutes

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

: **Phlebotomy and Medical Lab Technology**

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

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

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

7.2.5 Chapter Review

Blood is a fluid connective tissue critical to the transportation of nutrients, gases, and wastes throughout the body; to defend the body against infection and other threats; and to the homeostatic regulation of pH, temperature, and other internal conditions. Blood is composed of formed elements—erythrocytes, leukocytes, and cell fragments called platelets—and a fluid extracellular matrix called plasma. More than 90 percent of plasma is water. The remainder is mostly plasma proteins—mainly albumin, globulins, and fibrinogen—and other dissolved solutes such as glucose, lipids, electrolytes, and dissolved gases. Blood is also slightly alkaline, and its temperature is slightly higher than normal body temperature.

7.2.6 Critical Thinking Questions

Exercise 7.2.1 ***(Solution on p. 171.)***

Why would it be incorrect to refer to the formed elements as cells?

7.3 Erythrocytes[3]

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

7.3.1 Shape and Structure of Erythrocytes

As an erythrocyte matures in the red bone marrow, it extrudes its nucleus and most of its other organelles. Lacking mitochondria, for example, they rely on fermentation. This means that they do not utilize any of the oxygen they are transporting, so they can deliver it all to the tissues. They also lack endoplasmic reticula and do not synthesize proteins, so they are unable to repair themselves. This is why the lifespan of a red blood cell is approximately 115 days. However, during this time, the red blood cell has traveled approximately 300 miles and made approximately 170,000 circuits through the heart (http://www.uptodate.com/contents/red-blood-cell-survival-normal-values-and-measurement).

[3]This content is available online at <http://cnx.org/content/m58119/1.2/>.

Erythrocytes are biconcave disks; that is, they are plump at their periphery and very thin in the center (Figure 7.3 (Shape of Red Blood Cells)). Since they lack most organelles, there is more interior space for the presence of the hemoglobin molecules that, as you will see shortly, transport gases. The biconcave shape also provides a greater surface area across which gas exchange can occur, relative to its volume; a sphere of a similar diameter would have a lower surface area-to-volume ratio. In the capillaries, the oxygen carried by the erythrocytes can diffuse into the plasma and then through the capillary walls to reach the cells, whereas some of the carbon dioxide produced by the cells as a waste product diffuses into the capillaries to be picked up by the erythrocytes. Capillary beds are extremely narrow, slowing the passage of the erythrocytes and providing an extended opportunity for gas exchange to occur. However, the space within capillaries can be so minute that, despite their own small size, erythrocytes may have to fold in on themselves if they are to make their way through. Fortunately, their structural proteins are flexible, allowing them to bend over themselves to a surprising degree, then spring back again when they enter a wider vessel.

Shape of Red Blood Cells

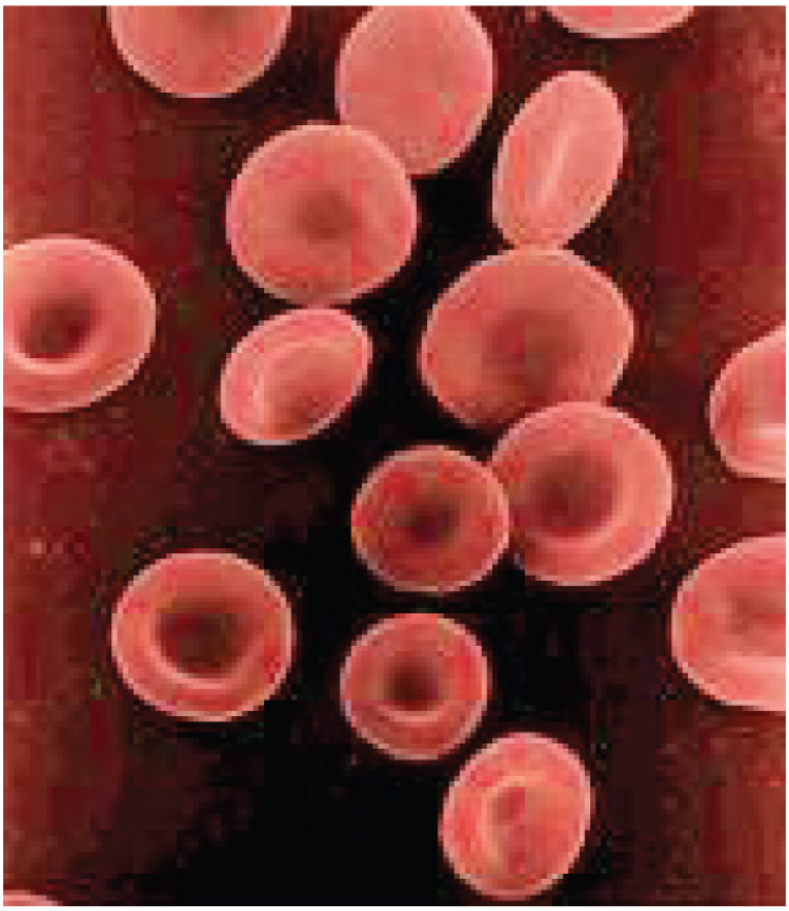

Figure 7.3: Erythrocytes are biconcave discs with very shallow centers. This shape optimizes the ratio of surface area to volume, facilitating gas exchange. It also enables them to fold up as they move through narrow blood vessels.

7.3.2 Hemoglobin

Hemoglobin is a large molecule made up of proteins and iron. It consists of four folded chains of a protein called **globin**, designated alpha 1 and 2, and beta 1 and 2 (Figure 7.4 (Hemoglobin)**a**). Each of these globin molecules is bound to a red pigment molecule called **heme**, which contains an ion of iron (Fe^{2+}) (Figure 7.4 (Hemoglobin)**b**).

Hemoglobin

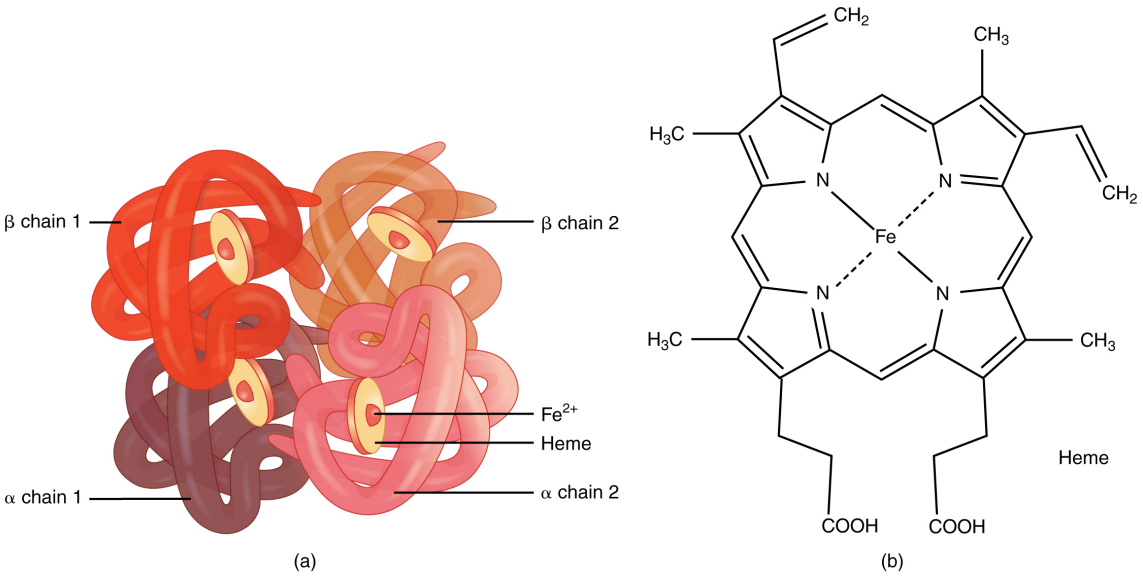

Figure 7.4: (a) A molecule of hemoglobin contains four globin proteins, each of which is bound to one molecule of the iron-containing pigment heme. (b) A single erythrocyte can contain 300 million hemoglobin molecules, and thus more than 1 billion oxygen molecules.

Each iron ion in the heme can bind to one oxygen molecule; therefore, each hemoglobin molecule can transport four oxygen molecules. An individual erythrocyte may contain about 300 million hemoglobin molecules, and therefore can bind to and transport up to 1.2 billion oxygen molecules (see Figure 7.4 (Hemoglobin)**b**).

In the lungs, hemoglobin picks up oxygen, which binds to the iron ions, forming **oxyhemoglobin**. The bright red, oxygenated hemoglobin travels to the body tissues, where it releases some of the oxygen molecules, becoming darker red **deoxyhemoglobin**. Oxygen release depends on the need for oxygen in the surrounding tissues, so hemoglobin rarely if ever leaves all of its oxygen behind. In the capillaries, carbon dioxide enters the bloodstream. About 76 percent dissolves in the plasma, some of it remaining as dissolved CO_2, and the remainder forming bicarbonate ion. About 23–24 percent of it binds to the amino acids in hemoglobin, forming a molecule known as **carbaminohemoglobin**. From the capillaries, the hemoglobin carries carbon dioxide back to the lungs, where it releases it for exchange of oxygen.

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

Percent saturation is normally monitored using a device known as a pulse oximeter, which is applied to a thin part of the body, typically the tip of the patient's finger. The device works by sending two different wavelengths of light (one red, the other infrared) through the finger and measuring the light with a photodetector as it exits. Hemoglobin absorbs light differentially depending upon its saturation with oxygen. The machine calibrates the amount of light received by the photodetector against the amount absorbed by the partially oxygenated hemoglobin and presents the data as percent saturation. Normal pulse oximeter readings range from 95–100 percent. Lower percentages reflect **hypoxemia**, or low blood oxygen. The term hypoxia is more generic and simply refers to low oxygen levels. Oxygen levels are also directly monitored from free oxygen in the plasma typically following an arterial stick. When this method is applied, the amount of oxygen present is expressed in terms of partial pressure of oxygen or simply pO_2 and is typically recorded in units of millimeters of mercury, mm Hg.

7.3.3 Lifecycle of Erythrocytes

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

Erythrocytes live up to 120 days in the circulation, after which the worn-out cells are removed by a type of phagocytic cell called a **macrophage**, located primarily within the bone marrow, liver, and spleen. The components of the degraded erythrocytes' hemoglobin are further processed, with some being retained by the body and others being released in the urine and feces.

The breakdown pigments formed from the destruction of hemoglobin can be seen in a variety of situations. At the site of an injury, biliverdin from damaged RBCs produces some of the dramatic colors associated with bruising. With a failing liver, bilirubin cannot be removed effectively from circulation and causes the body to assume a yellowish tinge associated with jaundice. Stercobilins within the feces produce the typical brown color associated with this waste. And the yellow of urine is associated with the urobilins.

7.3.4 Disorders of Erythrocytes

The size, shape, and number of erythrocytes, and the number of hemoglobin molecules can have a major impact on a person's health. When the number of RBCs or hemoglobin is deficient, the general condition is called **anemia**. There are more than 400 types of anemia and more than 3.5 million Americans suffer from this condition. Anemia can be broken down into three major groups: those caused by blood loss, those caused by faulty or decreased RBC production, and those caused by excessive destruction of RBCs. The effects of the various anemias are widespread, because reduced numbers of RBCs or hemoglobin will result in lower levels of oxygen being delivered to body tissues. Since oxygen is required for tissue functioning, anemia produces fatigue, lethargy, and an increased risk for infection. An oxygen deficit in the brain impairs the ability to think clearly, and may prompt headaches and irritability. Lack of oxygen leaves the patient short of breath, even as the heart and lungs work harder in response to the deficit.

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

- A characteristic change in the shape of erythrocytes is seen in **sickle cell disease** (also referred to as sickle cell anemia). A genetic disorder, it is caused by production of an abnormal type of hemoglobin, called hemoglobin S, which delivers less oxygen to tissues and causes erythrocytes to assume a sickle (or crescent) shape, especially at low oxygen concentrations (Figure 7.5 (Sickle Cells)). These abnormally shaped cells can then become lodged in narrow capillaries because they are unable to fold in on themselves to squeeze through, blocking blood flow to tissues and causing a variety of serious problems from painful joints to delayed growth and even blindness and cerebrovascular accidents (strokes). Sickle cell anemia is a genetic condition particularly found in individuals of African descent.

Sickle Cells

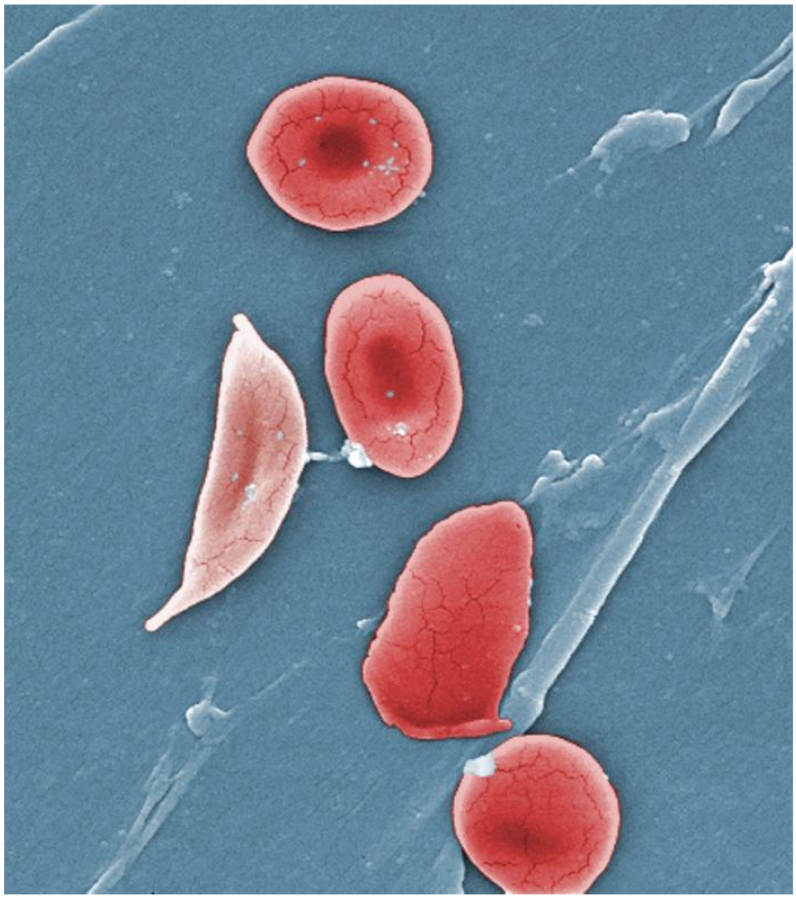

Figure 7.5: Sickle cell anemia is caused by a mutation in one of the hemoglobin genes. Erythrocytes produce an abnormal type of hemoglobin, which causes the cell to take on a sickle or crescent shape. (credit: Janice Haney Carr)

- Iron deficiency anemia is the most common type and results when the amount of available iron is insufficient to allow production of sufficient heme. This condition can occur in individuals with a deficiency of iron in the diet and is especially common in teens and children as well as in vegans and vegetarians. Additionally, iron deficiency anemia may be caused by either an inability to absorb and transport iron or slow, chronic bleeding.
- Vitamin-deficient anemias generally involve insufficient vitamin B12 and folate.
  - Pernicious anemia is caused by poor absorption of vitamin B12 and is often seen in patients with Crohn's disease (a severe intestinal disorder often treated by surgery), surgical removal of the intestines or stomach (common in some weight loss surgeries), intestinal parasites, and AIDS.
  - Pregnancies, some medications, excessive alcohol consumption, and some diseases such as celiac disease are also associated with vitamin deficiencies. It is essential to provide sufficient folic acid

during the early stages of pregnancy to reduce the risk of neurological defects, including spina bifida, a failure of the neural tube to close.

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

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

7.3.5 Chapter Review

The most abundant formed elements in blood, erythrocytes are red, biconcave disks packed with an oxygen-carrying compound called hemoglobin. The hemoglobin molecule contains four globin proteins bound to a pigment molecule called heme, which contains an ion of iron. In the bloodstream, iron picks up oxygen in the lungs and drops it off in the tissues; the amino acids in hemoglobin then transport carbon dioxide from the tissues back to the lungs. Erythrocytes live approximately 115 days on average, and thus must be continually replaced. Worn-out erythrocytes are phagocytized by macrophages and their hemoglobin is broken down. The breakdown products are recycled or removed as wastes. Anemia is a deficiency of RBCs or hemoglobin, whereas polycythemia is an excess of RBCs.

7.3.6 Review Questions

Exercise 7.3.1 *(Solution on p. 171.)*

Which of the following statements about mature, circulating erythrocytes is true?

a. They have no nucleus.
b. They are packed with mitochondria.
c. They survive for an average of 4 days.
d. All of the above

Exercise 7.3.2 *(Solution on p. 171.)*

A molecule of hemoglobin _____.

a. is shaped like a biconcave disk packed almost entirely with iron
b. contains four glycoprotein units studded with oxygen
c. consists of four globin proteins, each bound to a molecule of heme
d. can carry up to 120 molecules of oxygen

Exercise 7.3.3 *(Solution on p. 171.)*
The production of healthy erythrocytes depends upon the availability of _ _ _ _ _ _ _ _.

a. copper
b. zinc
c. vitamin B_{12}
d. copper, zinc, and vitamin B_{12}

Exercise 7.3.4 *(Solution on p. 171.)*
Aging and damaged erythrocytes are removed from the circulation by _ _ _ _ _ _ _ _.

a. myeoblasts
b. monocytes
c. macrophages
d. mast cells

7.3.7 Critical Thinking Questions

Exercise 7.3.5 *(Solution on p. 171.)*
A young woman has been experiencing unusually heavy menstrual bleeding for several years. She follows a strict vegan diet (no animal foods). She is at risk for what disorder, and why?

7.4 Blood Typing and Transfusions[4]

Blood transfusions in humans were risky procedures until the discovery of the major human blood groups by Karl Landsteiner, an Austrian biologist and physician, in 1900. Until that point, physicians did not understand that death sometimes followed blood transfusions, when the type of donor blood infused into the patient was incompatible with the patient's own blood. Blood groups are determined by the presence or absence of specific marker molecules, called antigens, on the plasma membranes of erythrocytes. With their discovery, it became possible for the first time to match patient-donor blood types and prevent transfusion reactions and deaths.

7.4.1 Antigens, Antibodies, and Transfusion Reactions

Antigens are substances that the body does not recognize as belonging to the "self" and that therefore trigger a defensive response from the leukocytes (WBC) of the immune system. Here, we will focus on the role of immunity, antigens, and antibodies in blood transfusion reactions.

Antigens are generally large proteins, but may include other classes of organic molecules, including carbohydrates, lipids, and nucleic acids. Following an infusion of incompatible blood, erythrocytes with foreign antigens appear in the bloodstream and trigger an immune response. Proteins called antibodies (immunoglobulins), which are produced by certain B lymphocytes called plasma cells, attach to the antigens on the plasma membranes of the infused erythrocytes and cause them to stick to one another (i.e. agglutinate). The clumps of erythrocytes block small blood vessels throughout the body, depriving tissues of oxygen and nutrients. As the erythrocyte clumps are degraded, in a process called **hemolysis**, their hemoglobin is released into the bloodstream. This hemoglobin travels to the kidneys, which are responsible for filtration of the blood. However, the load of hemoglobin released can easily overwhelm the kidney's capacity to clear it, and the patient can quickly develop kidney failure.

[4]This content is available online at <http://cnx.org/content/m57991/1.1/>.

More than 50 antigens have been identified on erythrocyte membranes, but the most significant in terms of their potential harm to patients are classified in two groups: the ABO blood group and the Rh blood group.

7.4.2 The ABO Blood Group

Although the **ABO blood group** name consists of three letters, ABO blood typing designates the presence or absence of just two antigens, A and B. Both are glycoproteins. People whose erythrocytes have A antigens on their erythrocyte membrane surfaces are designated blood type A, and those whose erythrocytes have B antigens are blood type B. People can also have both A and B antigens on their erythrocytes, in which case they are blood type AB. People with neither A nor B antigens are designated blood type O. ABO blood types are genetically determined.

Normally the body must be exposed to a foreign antigen before an antibody can be produced. This is not the case for the ABO blood group. Individuals with type A blood—without any prior exposure to incompatible blood—have preformed antibodies to the B antigen circulating in their blood plasma. These antibodies, referred to as anti-B antibodies, will cause agglutination and hemolysis if they ever encounter erythrocytes with B antigens. Similarly, an individual with type B blood has pre-formed anti-A antibodies. Individuals with type AB blood, which has both antigens, do not have preformed antibodies to either of these. People with type O blood lack antigens A and B on their erythrocytes, but both anti-A and anti-B antibodies circulate in their blood plasma.

7.4.3 Rh Blood Groups

The **Rh blood group** is classified according to the presence or absence of a second erythrocyte antigen identified as Rh. (It was first discovered in a type of primate known as a rhesus macaque, which is often used in research, because its blood is similar to that of humans.) Although dozens of Rh antigens have been identified, only one, designated D, is clinically important. Those who have the Rh D antigen present on their erythrocytes—about 85 percent of Americans—are described as Rh positive (Rh^+) and those who lack it are Rh negative (Rh^-). Note that the Rh group is distinct from the ABO group, so any individual, no matter their ABO blood type, may have or lack this Rh antigen. When identifying a patient's blood type, the Rh group is designated by adding the word positive or negative to the ABO type. For example, A positive (A^+) means ABO group A blood with the Rh antigen present, and AB negative (AB^-) means ABO group AB blood without the Rh antigen.

Table 7.1 summarizes the distribution of the ABO and Rh blood types within the United States.

Summary of ABO and Rh Blood Types within the United States					
Blood Type	**African-Americans**	**Asian-Americans**	**Caucasian-Americans**	**Latino/Latina-Americans**	
A^+	24	27	33	29	
A^-	2	0.5	7	2	
B^+	18	25	9	9	

continued on next page

B^-	1	0.4	2	1	
AB^+	4	7	3	2	
AB^-	0.3	0.1	1	0.2	
O^+	47	39	37	53	
O^-	4	1	8	4	

Table 7.1

In contrast to the ABO group antibodies, which are preformed, antibodies to the Rh antigen are produced only in Rh^- individuals after exposure to the antigen. This process, called sensitization, occurs following a transfusion with Rh-incompatible blood or, more commonly, with the birth of an Rh^+ baby to an Rh^- mother. Problems are rare in a first pregnancy, since the baby's Rh^+ cells rarely cross the placenta (the organ of gas and nutrient exchange between the baby and the mother). However, during or immediately after birth, the Rh^- mother can be exposed to the baby's Rh^+ cells (Figure 7.6 (Erythroblastosis Fetalis)). Research has shown that this occurs in about 13–14 percent of such pregnancies. After exposure, the mother's immune system begins to generate anti-Rh antibodies. If the mother should then conceive another Rh^+ baby, the Rh antibodies she has produced can cross the placenta into the fetal bloodstream and destroy the fetal RBCs. This condition, known as **hemolytic disease of the newborn (HDN)** or erythroblastosis fetalis, may cause anemia in mild cases, but the agglutination and hemolysis can be so severe that without treatment the fetus may die in the womb or shortly after birth.

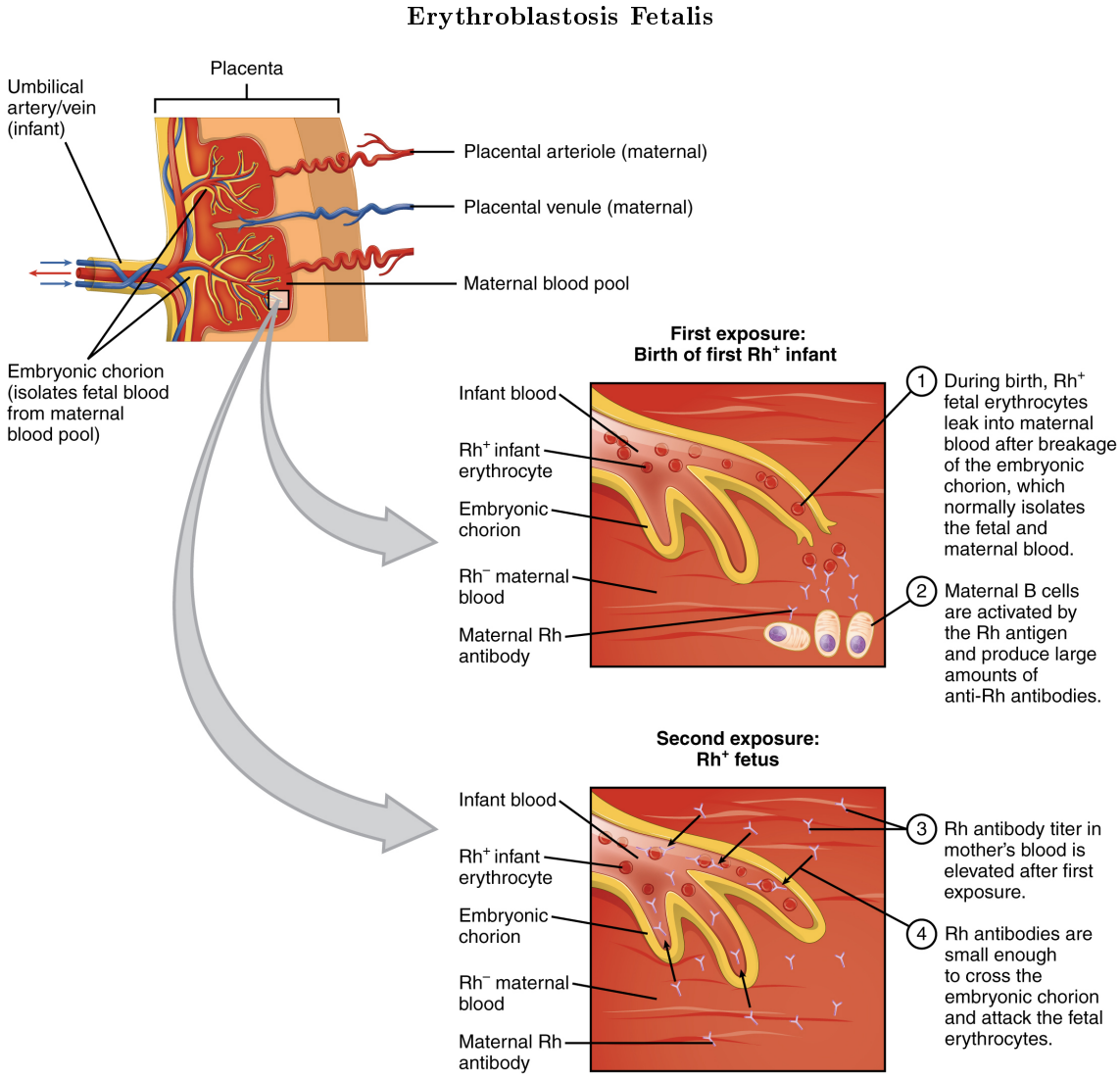

Figure 7.6: The first exposure of an Rh^- mother to Rh^+ erythrocytes during pregnancy induces sensitization. Anti-Rh antibodies begin to circulate in the mother's bloodstream. A second exposure occurs with a subsequent pregnancy with an Rh^+ fetus in the uterus. Maternal anti-Rh antibodies may cross the placenta and enter the fetal bloodstream, causing agglutination and hemolysis of fetal erythrocytes.

A drug known as RhoGAM, short for Rh immune globulin, can temporarily prevent the development of Rh antibodies in the Rh^- mother, thereby averting this potentially serious disease for the fetus. RhoGAM antibodies destroy any fetal Rh^+ erythrocytes that may cross the placental barrier. RhoGAM is normally administered to Rh^- mothers during weeks 26–28 of pregnancy and within 72 hours following birth. It has proven remarkably effective in decreasing the incidence of HDN. Earlier we noted that the incidence of HDN in an Rh^+ subsequent pregnancy to an Rh^- mother is about 13–14 percent without preventive treatment.

Since the introduction of RhoGAM in 1968, the incidence has dropped to about 0.1 percent in the United States.

7.4.4 Determining ABO Blood Types

Clinicians are able to determine a patient's blood type quickly and easily using commercially prepared antibodies. An unknown blood sample is allocated into separate wells. Into one well a small amount of anti-A antibody is added, and to another a small amount of anti-B antibody. If the antigen is present, the antibodies will cause visible agglutination of the cells (Figure 7.7 (Cross Matching Blood Types)). The blood should also be tested for Rh antibodies.

Cross Matching Blood Types

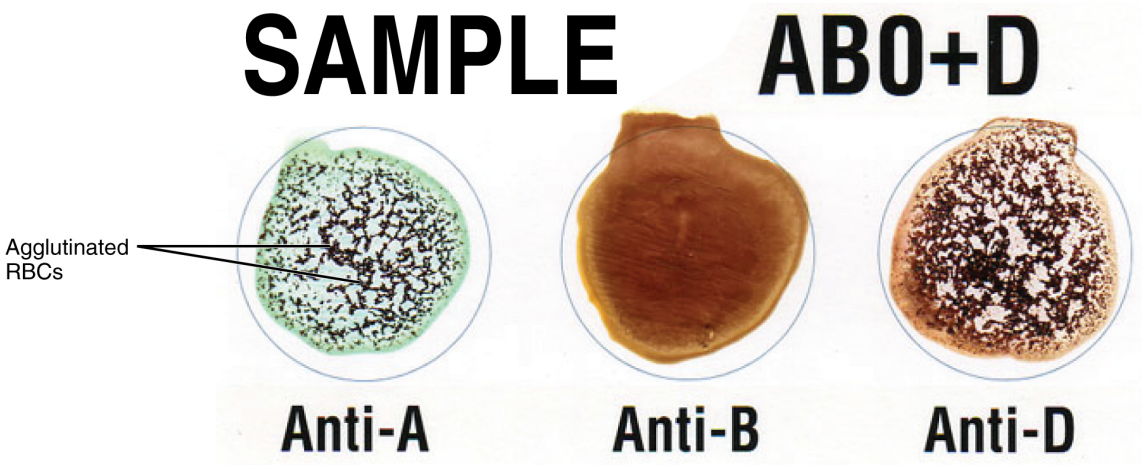

Figure 7.7: This sample of a commercially produced "bedside" card enables quick typing of both a recipient's and donor's blood before transfusion. The card contains three reaction sites or wells. One is coated with an anti-A antibody, one with an anti-B antibody, and one with an anti-D antibody (tests for the presence of Rh factor D). Mixing a drop of blood and saline into each well enables the blood to interact with a preparation of type-specific antibodies, also called anti-seras. Agglutination of RBCs in a given site indicates a positive identification of the blood antigens, in this case A and Rh antigens for blood type A^+. For the purpose of transfusion, the donor's and recipient's blood types must match.

7.4.5 ABO Transfusion Protocols

To avoid transfusion reactions, it is best to transfuse only matching blood types; that is, a type B^+ recipient should ideally receive blood only from a type B^+ donor and so on. That said, in emergency situations, when acute hemorrhage threatens the patient's life, there may not be time for cross matching to identify blood type. In these cases, blood from a **universal donor**—an individual with type O^- blood—may be transfused. Recall that type O erythrocytes do not display A or B antigens. Thus, anti-A or anti-B antibodies that might be circulating in the patient's blood plasma will not encounter any erythrocyte surface antigens on the donated blood and therefore will not be provoked into a response. One problem with this designation of universal donor is if the O^- individual had prior exposure to Rh antigen, Rh antibodies may be present in the donated blood. Also, introducing type O blood into an individual with type A, B, or AB blood will

nevertheless introduce antibodies against both A and B antigens, as these are always circulating in the type O blood plasma. This may cause problems for the recipient, but because the volume of blood transfused is much lower than the volume of the patient's own blood, the adverse effects of the relatively few infused plasma antibodies are typically limited. Rh factor also plays a role. If Rh^- individuals receiving blood have had prior exposure to Rh antigen, antibodies for this antigen may be present in the blood and trigger agglutination to some degree. Although it is always preferable to cross match a patient's blood before transfusing, in a true life-threatening emergency situation, this is not always possible, and these procedures may be implemented.

A patient with blood type AB^+ is known as the **universal recipient**. This patient can theoretically receive any type of blood, because the patient's own blood—having both A and B antigens on the erythrocyte surface—does not produce anti-A or anti-B antibodies. In addition, an Rh^+ patient can receive both Rh^+ and Rh^- blood. However, keep in mind that the donor's blood will contain circulating antibodies, again with possible negative implications. Figure 7.8 (ABO Blood Group) summarizes the blood types and compatibilities.

At the scene of multiple-vehicle accidents, military engagements, and natural or human-caused disasters, many victims may suffer simultaneously from acute hemorrhage, yet type O blood may not be immediately available. In these circumstances, medics may at least try to replace some of the volume of blood that has been lost. This is done by intravenous administration of a saline solution that provides fluids and electrolytes in proportions equivalent to those of normal blood plasma. Research is ongoing to develop a safe and effective artificial blood that would carry out the oxygen-carrying function of blood without the RBCs, enabling transfusions in the field without concern for incompatibility. These blood substitutes normally contain hemoglobin- as well as perfluorocarbon-based oxygen carriers.

ABO Blood Group

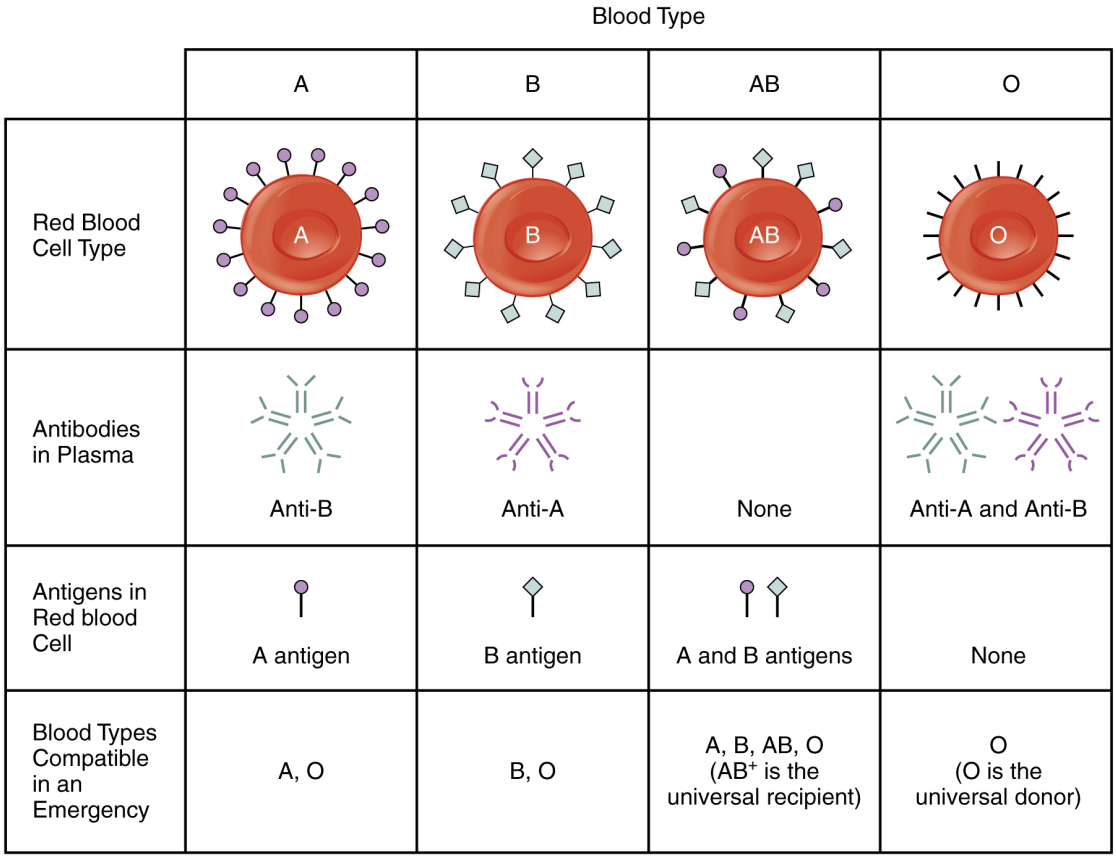

Figure 7.8: This chart summarizes the characteristics of the blood types in the ABO blood group. See the text for more on the concept of a universal donor or recipient.

7.4.6 Chapter Review

Antigens are nonself molecules, usually large proteins, which provoke an immune response. In transfusion reactions, antibodies attach to antigens on the surfaces of erythrocytes and cause agglutination and hemolysis. ABO blood group antigens are designated A and B. People with type A blood have A antigens on their erythrocytes, whereas those with type B blood have B antigens. Those with AB blood have both A and B antigens, and those with type O blood have neither A nor B antigens. The blood plasma contains preformed antibodies against the antigens not present on a person's erythrocytes.

A second group of blood antigens is the Rh group, the most important of which is Rh D. People with Rh^- blood do not have this antigen on their erythrocytes, whereas those who are Rh^+ do. About 85 percent of Americans are Rh^+. When a woman who is Rh^- becomes pregnant with an Rh^+ fetus, her body may begin to produce anti-Rh antibodies. If she subsequently becomes pregnant with a second Rh^+ fetus and is not treated preventively with RhoGAM, the fetus will be at risk for an antigen-antibody reaction, including agglutination and hemolysis. This is known as hemolytic disease of the newborn.

Cross matching to determine blood type is necessary before transfusing blood, unless the patient is experiencing hemorrhage that is an immediate threat to life, in which case type O^- blood may be transfused.

7.4.7 Review Questions

Exercise 7.4.1 *(Solution on p. 171.)*
The process in which antibodies attach to antigens, causing the formation of masses of linked cells, is called _____.

a. sensitization
b. coagulation
c. agglutination
d. hemolysis

Exercise 7.4.2 *(Solution on p. 171.)*
People with ABO blood type O _____.

a. have both antigens A and B on their erythrocytes
b. lack both antigens A and B on their erythrocytes
c. have neither anti-A nor anti-B antibodies circulating in their blood plasma
d. are considered universal recipients

Exercise 7.4.3 *(Solution on p. 171.)*
Hemolytic disease of the newborn is a risk during a subsequent pregnancy in which _____.

a. a type AB mother is carrying a type O fetus
b. a type O mother is carrying a type AB fetus
c. an Rh^+ mother is carrying an Rh^- fetus
d. an Rh^- mother is carrying a second Rh^+ fetus

7.4.8 Critical Thinking Questions

Exercise 7.4.4 *(Solution on p. 171.)*
Following a motor vehicle accident, a patient is rushed to the emergency department with multiple traumatic injuries, causing severe bleeding. The patient's condition is critical, and there is no time for determining his blood type. What type of blood is transfused, and why?

Exercise 7.4.5 *(Solution on p. 171.)*
In preparation for a scheduled surgery, a patient visits the hospital lab for a blood draw. The technician collects a blood sample and performs a test to determine its type. She places a sample of the patient's blood in two wells. To the first well she adds anti-A antibody. To the second she adds anti-B antibody. Both samples visibly agglutinate. Has the technician made an error, or is this a normal response? If normal, what blood type does this indicate?

7.4.9 References

American Red Cross (US). Blood types [Internet]. c2013 [cited 2013 Apr 3]. Available from: http://www.redcrossblood.org/learn-about-blood/blood-types[5] 2013

[5] http://www.redcrossblood.org/learn-about-blood/blood-types

Solutions to Exercises in Chapter 7

to Exercise 7.2.1 (p. 157)
The formed elements include erythrocytes and leukocytes, which are cells (although mature erythrocytes do not have a nucleus); however, the formed elements also include platelets, which are not true cells but cell fragments.

to Exercise 7.3.1 (p. 162)
A

to Exercise 7.3.2 (p. 162)
C

to Exercise 7.3.3 (p. 163)
D

to Exercise 7.3.4 (p. 163)
C

to Exercise 7.3.5 (p. 163)
She is at risk for anemia, because her unusually heavy menstrual bleeding results in excessive loss of erythrocytes each month. At the same time, her vegan diet means that she does not have dietary sources of heme iron. The non-heme iron she consumes in plant foods is not as well absorbed as heme iron.

to Exercise 7.4.1 (p. 170)
C

to Exercise 7.4.2 (p. 170)
B

to Exercise 7.4.3 (p. 170)
D

to Exercise 7.4.4 (p. 170)
In emergency situations, blood type O^- will be infused until cross matching can be done. Blood type O^- is called the universal donor blood because the erythrocytes have neither A nor B antigens on their surface, and the Rh factor is negative.

to Exercise 7.4.5 (p. 170)
The lab technician has not made an error. Blood type AB has both A and B surface antigens, and neither anti-A nor anti-B antibodies circulating in the plasma. When anti-A antibodies (added to the first well) contact A antigens on AB erythrocytes, they will cause agglutination. Similarly, when anti-B antibodies contact B antigens on AB erythrocytes, they will cause agglutination.

Available for free at Connexions <http://cnx.org/content/col11903/1.3>

Chapter 8

Heart

8.1 Introduction to the Cardiovascular System - Heart[1]

Human Heart

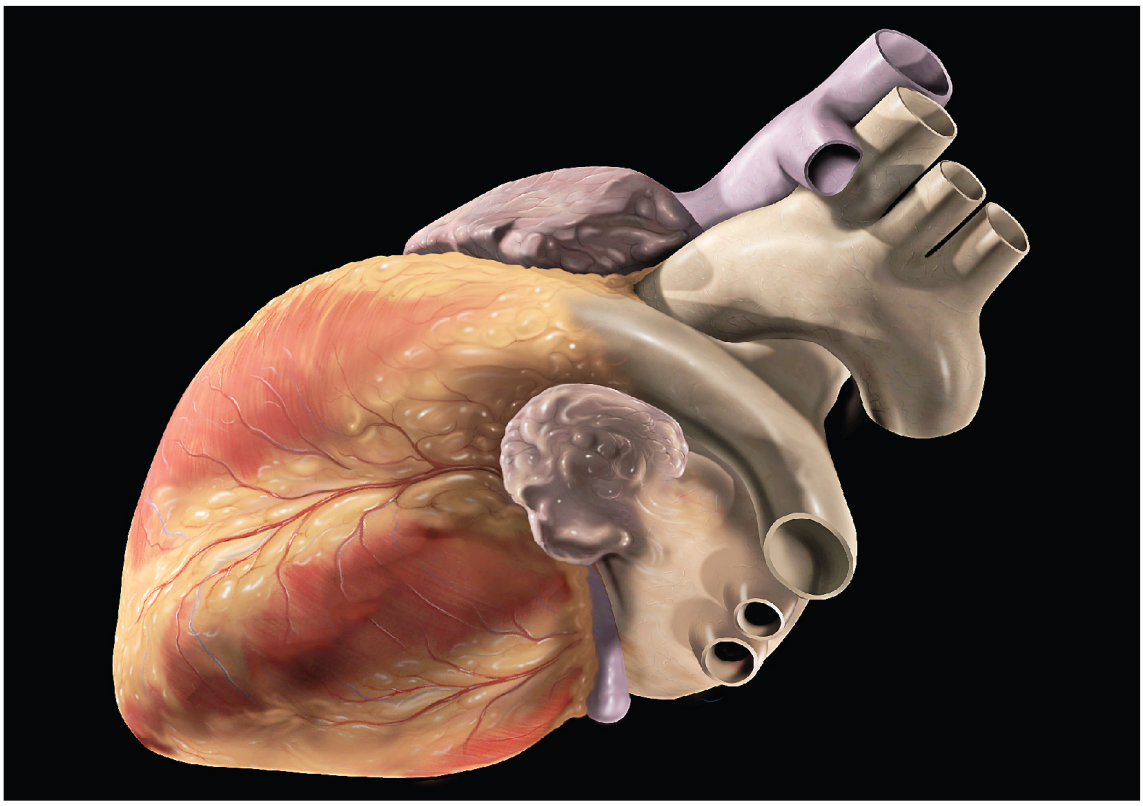

Figure 8.1: This artist's conception of the human heart suggests a powerful engine—not inappropriate for a muscular pump that keeps the body continually supplied with blood. (credit: Patrick J. Lynch)

[1] This content is available online at <http://cnx.org/content/m57992/1.1/>.

NOTE: After studying this chapter, you will be able to:

- Identify and describe the interior and exterior parts of the human heart
- Describe the path of blood through the cardiac circuits
- Describe the size, shape, and location of the heart
- Compare cardiac muscle to skeletal and smooth muscle
- Explain the cardiac conduction system
- Describe the process and purpose of an electrocardiogram
- Explain the cardiac cycle
- Describe the effects of exercise on heart rate
- Identify other factors affecting heart rate

In this chapter, you will explore the remarkable pump that propels the blood into the vessels. There is no single better word to describe the function of the heart other than "pump," since its contraction develops the pressure that ejects blood into the major vessels: the aorta and pulmonary trunk. From these vessels, the blood is distributed to the remainder of the body. Although the connotation of the term "pump" suggests a mechanical device made of steel and plastic, the anatomical structure is a living, sophisticated muscle. As you read this chapter, try to keep these twin concepts in mind: pump and muscle.

Although the term "heart" is an English word, cardiac (heart-related) terminology can be traced back to the Latin term, "kardia." Cardiology is the study of the heart, and cardiologists are the physicians who deal primarily with the heart.

8.2 Heart Anatomy[2]

The vital importance of the heart is obvious. If one assumes an average rate of contraction of 75 contractions per minute, a human heart would contract approximately 108,000 times in one day, more than 39 million times in one year, and nearly 3 billion times during a 75-year lifespan. Each of the major pumping chambers of the heart ejects approximately 70 mL blood per contraction in a resting adult. This would be equal to 5.25 liters of fluid per minute and approximately 14,000 liters per day. Over one year, that would equal 10,000,000 liters or 2.6 million gallons of blood sent through roughly 60,000 miles of vessels. In order to understand how that happens, it is necessary to understand the anatomy and physiology of the heart.

8.2.1 Location of the Heart

The human heart is located within the thoracic cavity and is separated from the other structures by a tough membrane known as the pericardium, or pericardial sac.

[2]This content is available online at <http://cnx.org/content/m57993/1.2/>.

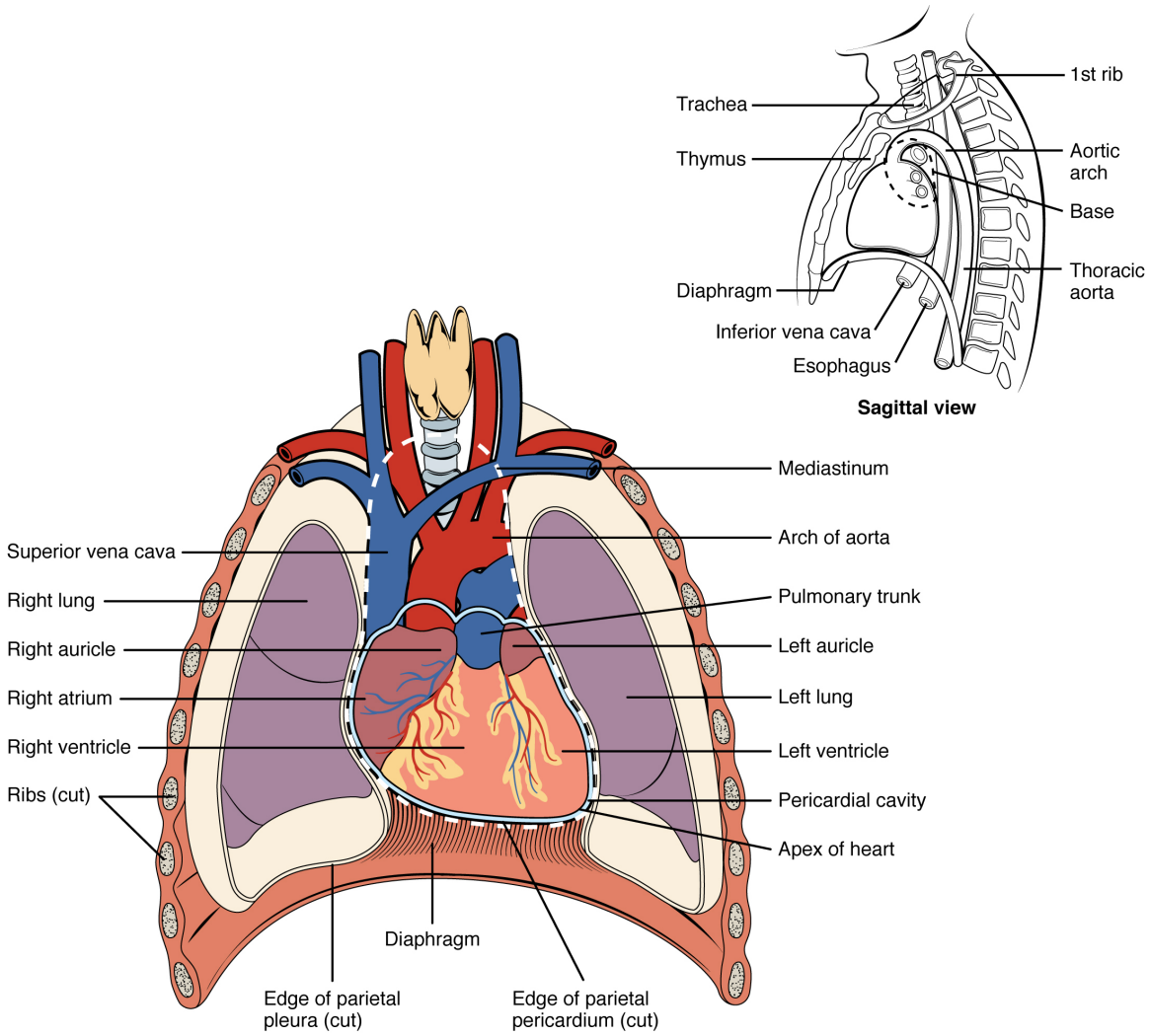

Figure 8.2: The heart is located within the thoracic cavity, medially between the lungs in the mediastinum. It is about the size of a fist, is broad at the top, and tapers toward the base.

: **CPR**

The position of the heart in the torso between the vertebrae and sternum (see Figure 8.2 (Position of the Heart in the Thorax) for the position of the heart within the thorax) allows for individuals to apply an emergency technique known as cardiopulmonary resuscitation (CPR) if the heart of a patient should stop. By applying pressure with the flat portion of one hand on the sternum in the area between the line at T4 and T9 (Figure 8.3 (CPR Technique)), it is possible to manually compress the blood within the heart enough to push some of the blood within it into the pulmonary and systemic circuits. This is particularly critical for the brain, as irreversible damage and death

of neurons occur within minutes of loss of blood flow. Current standards call for compression of the chest at least 5 cm deep and at a rate of 100 compressions per minute, a rate equal to the beat in "Staying Alive," recorded in 1977 by the Bee Gees. If you are unfamiliar with this song, a version is available on www.youtube.com. At this stage, the emphasis is on performing high-quality chest compressions, rather than providing artificial respiration. CPR is generally performed until the patient regains spontaneous contraction or is declared dead by an experienced healthcare professional.

When performed by untrained or overzealous individuals, CPR can result in broken ribs or a broken sternum, and can inflict additional severe damage on the patient. It is also possible, if the hands are placed too low on the sternum, to manually drive the xiphoid process into the liver, a consequence that may prove fatal for the patient. Proper training is essential. This proven life-sustaining technique is so valuable that virtually all medical personnel as well as concerned members of the public should be certified and routinely recertified in its application. CPR courses are offered at a variety of locations, including colleges, hospitals, the American Red Cross, and some commercial companies. They normally include practice of the compression technique on a mannequin.

CPR Technique

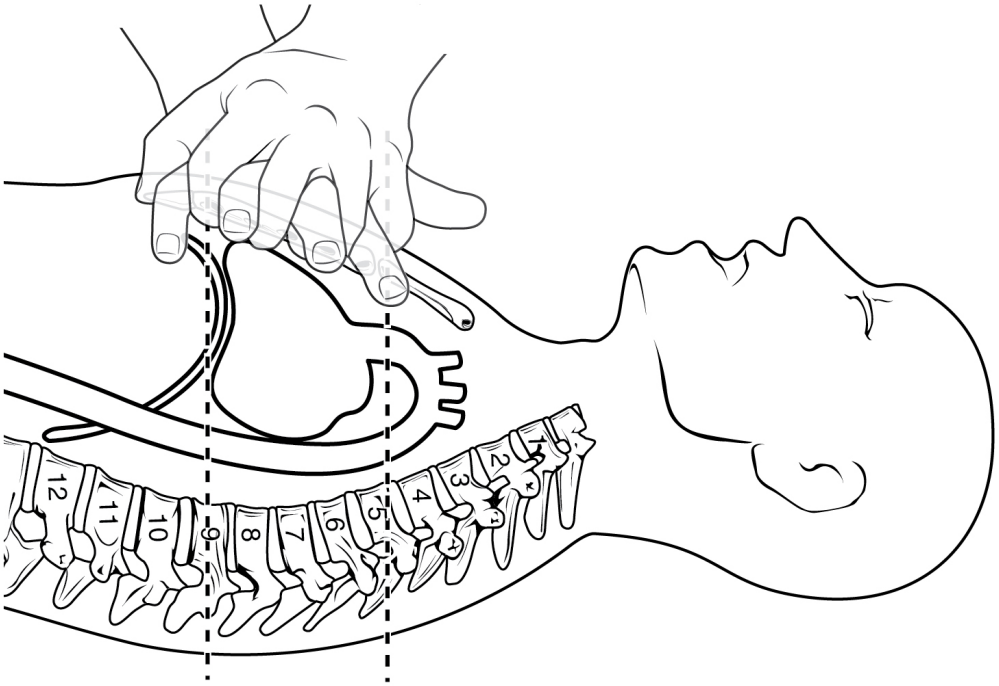

Figure 8.3: If the heart should stop, CPR can maintain the flow of blood until the heart resumes beating. By applying pressure to the sternum, the blood within the heart will be squeezed out of the heart and into the circulation. Proper positioning of the hands on the sternum to perform CPR would be between the lines at T4 and T9.

8.2.2 Shape and Size of the Heart

A typical heart is approximately the size of your fist: 12 cm (5 in) in length, 8 cm (3.5 in) wide, and 6 cm (2.5 in) in thickness. Given the size difference between most members of the sexes, the weight of a female heart is approximately 250–300 grams (9 to 11 ounces), and the weight of a male heart is approximately 300–350 grams (11 to 12 ounces). The heart of a well-trained athlete, especially one specializing in aerobic sports, can be considerably larger than this. Cardiac muscle responds to exercise in a manner similar to that of skeletal muscle. That is, exercise results in the addition of protein myofilaments that increase the size of the individual cells without increasing their numbers, a concept called hypertrophy. Hearts of athletes can pump blood more effectively at lower rates than those of nonathletes. Enlarged hearts are not always a result of exercise; they can result from diseases, such as **hypertrophic cardiomyopathy**.

8.2.3 Chambers and Circulation through the Heart

The human heart consists of four chambers: The left side and the right side each have one **atrium** and one **ventricle**. Each of the upper chambers, the right atrium (plural = atria) and the left atrium, acts as a receiving chamber and contracts to push blood into the lower chambers, the right ventricle and the left ventricle. The ventricles serve as the primary pumping chambers of the heart, propelling blood to the lungs or to the rest of the body.

There are two distinct but linked circuits in the human circulation called the pulmonary and systemic circuits. Although both circuits transport blood and everything it carries, we can initially view the circuits from the point of view of gases. The **pulmonary circuit** transports blood to and from the lungs, where it picks up oxygen and delivers carbon dioxide for exhalation. The **systemic circuit** transports oxygenated blood to virtually all of the tissues of the body and returns relatively deoxygenated blood and carbon dioxide to the heart to be sent back to the pulmonary circulation.

The right ventricle pumps deoxygenated blood into the **pulmonary trunk**, which leads toward the lungs and splits into the left and right **pulmonary arteries**. These vessels in turn branch many times before reaching the **pulmonary capillaries**, where gas exchange occurs: Carbon dioxide exits the blood and oxygen enters. The pulmonary trunk arteries and their branches are the only arteries in the post-natal body that carry relatively deoxygenated blood. Highly oxygenated blood returning from the pulmonary capillaries in the lungs passes through a series of vessels that join together to form the **pulmonary veins**—the only post-natal veins in the body that carry highly oxygenated blood. The pulmonary veins conduct blood into the left atrium, which pumps the blood into the left ventricle, which in turn pumps oxygenated blood into the aorta and on to the many branches of the systemic circuit. Eventually, these vessels will lead to the systemic capillaries, where exchange with the tissue fluid and cells of the body occurs. In this case, oxygen and nutrients exit the systemic capillaries to be used by the cells in their metabolic processes, and carbon dioxide and waste products will enter the blood.

The blood exiting the systemic capillaries is lower in oxygen concentration than when it entered. The capillaries will ultimately unite to form venules, joining to form ever-larger veins, eventually flowing into the two major systemic veins, the **superior vena cava** and the **inferior vena cava**, which return blood to the right atrium. The blood in the superior and inferior venae cavae flows into the right atrium, which pumps blood into the right ventricle. This process of blood circulation continues as long as the individual remains alive. Understanding the flow of blood through the pulmonary and systemic circuits is critical to all health professions (Figure 8.4 (Dual System of the Human Blood Circulation)).

Dual System of the Human Blood Circulation

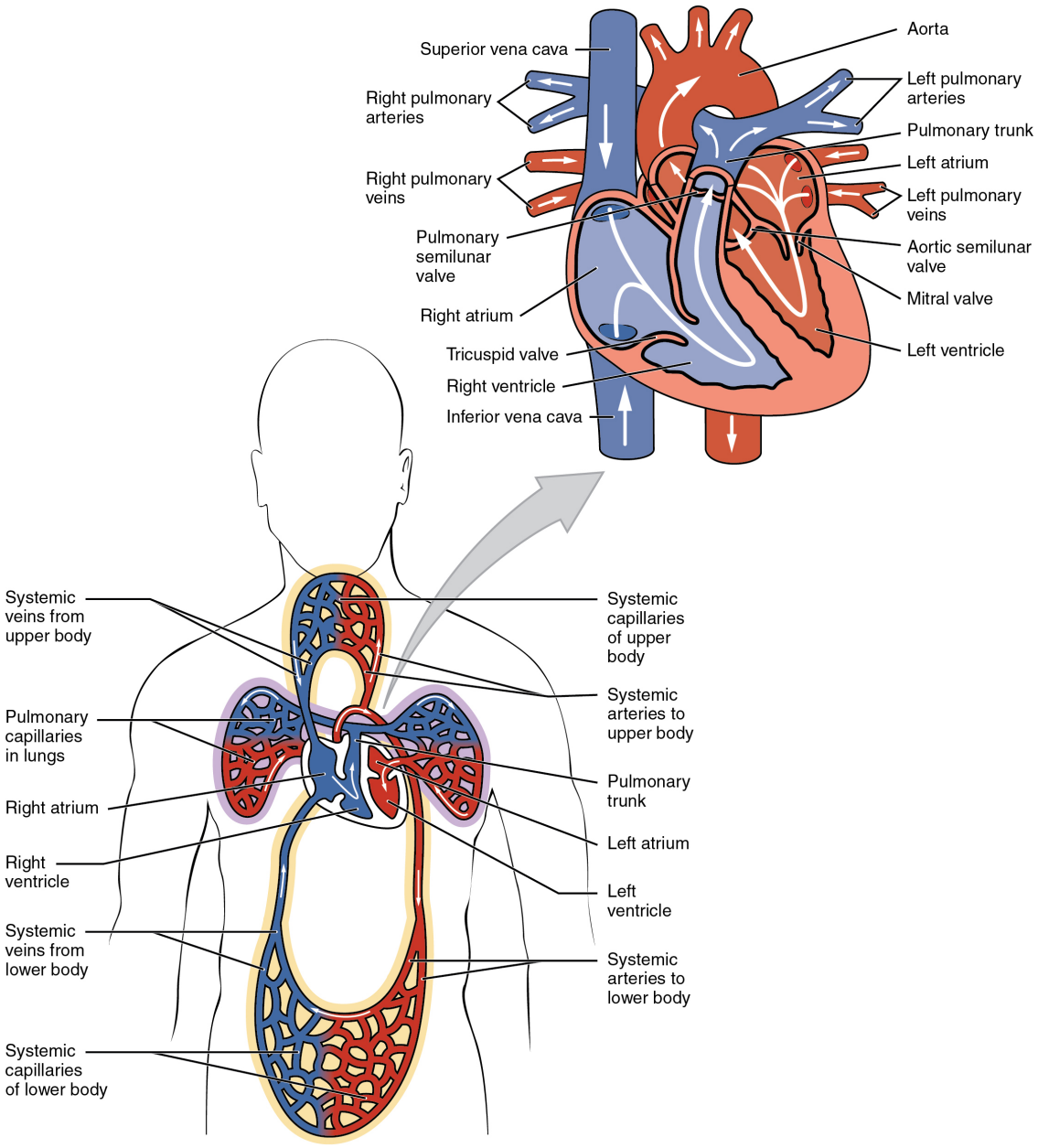

Figure 8.4: Blood flows from the right atrium to the right ventricle, where it is pumped into the pulmonary circuit. The blood in the pulmonary artery branches is low in oxygen but relatively high in carbon dioxide. Gas exchange occurs in the pulmonary capillaries (oxygen into the blood, carbon dioxide out), and blood high in oxygen and low in carbon dioxide is returned to the left atrium. From here, blood enters the left ventricle, which pumps it into the systemic circuit. Following exchange in the systemic capillaries (oxygen and nutrients out of the capillaries and carbon dioxide and wastes in), blood returns to the right atrium and the cycle is repeated.

8.2.4 Membranes, Surface Features, and Layers

8.2.4.1 Layers

The wall of the heart is composed of three layers of unequal thickness. From superficial to deep, these are the epicardium, the myocardium, and the endocardium. The outermost layer of the wall of the heart is also the innermost layer of the pericardium, the epicardium, or the visceral pericardium discussed earlier.

The middle and thickest layer is the **myocardium**, made largely of cardiac muscle cells. It is built upon a framework of collagenous fibers, plus the blood vessels that supply the myocardium and the nerve fibers that help regulate the heart. It is the contraction of the myocardium that pumps blood through the heart and into the major arteries. The muscle pattern is elegant and complex, as the muscle cells swirl and spiral around the chambers of the heart. They form a figure 8 pattern around the atria and around the bases of the great vessels. Deeper ventricular muscles also form a figure 8 around the two ventricles and proceed toward the apex. More superficial layers of ventricular muscle wrap around both ventricles. This complex swirling pattern allows the heart to pump blood more effectively than a simple linear pattern would. Figure 8.5 (Heart Musculature) illustrates the arrangement of muscle cells.

Heart Musculature

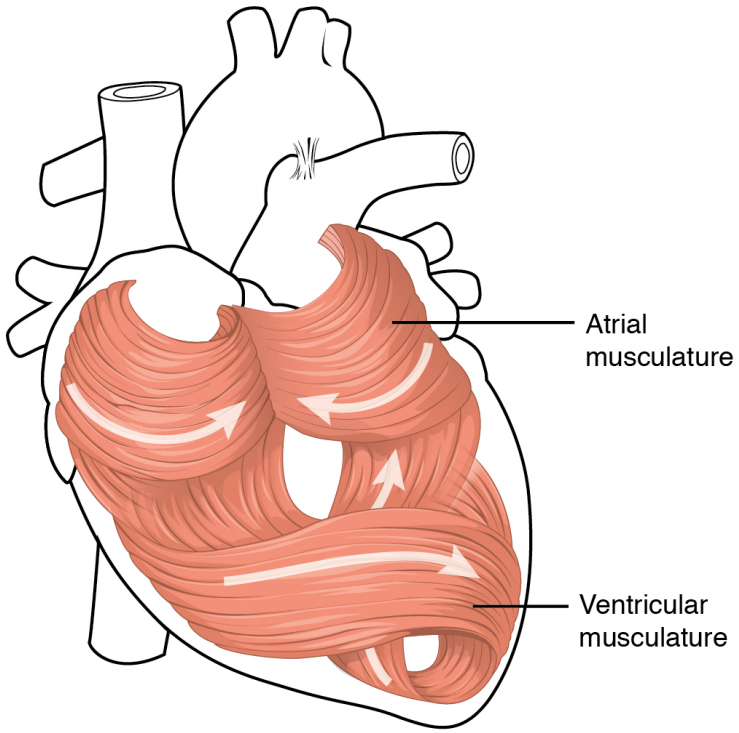

Figure 8.5: The swirling pattern of cardiac muscle tissue contributes significantly to the heart's ability to pump blood effectively.

Although the ventricles on the right and left sides pump the same amount of blood per contraction, the muscle of the left ventricle is much thicker and better developed than that of the right ventricle. In order to overcome the high resistance required to pump blood into the long systemic circuit, the left ventricle must

generate a great amount of pressure. The right ventricle does not need to generate as much pressure, since the pulmonary circuit is shorter and provides less resistance. Figure 8.6 (Differences in Ventricular Muscle Thickness) illustrates the differences in muscular thickness needed for each of the ventricles.

Differences in Ventricular Muscle Thickness

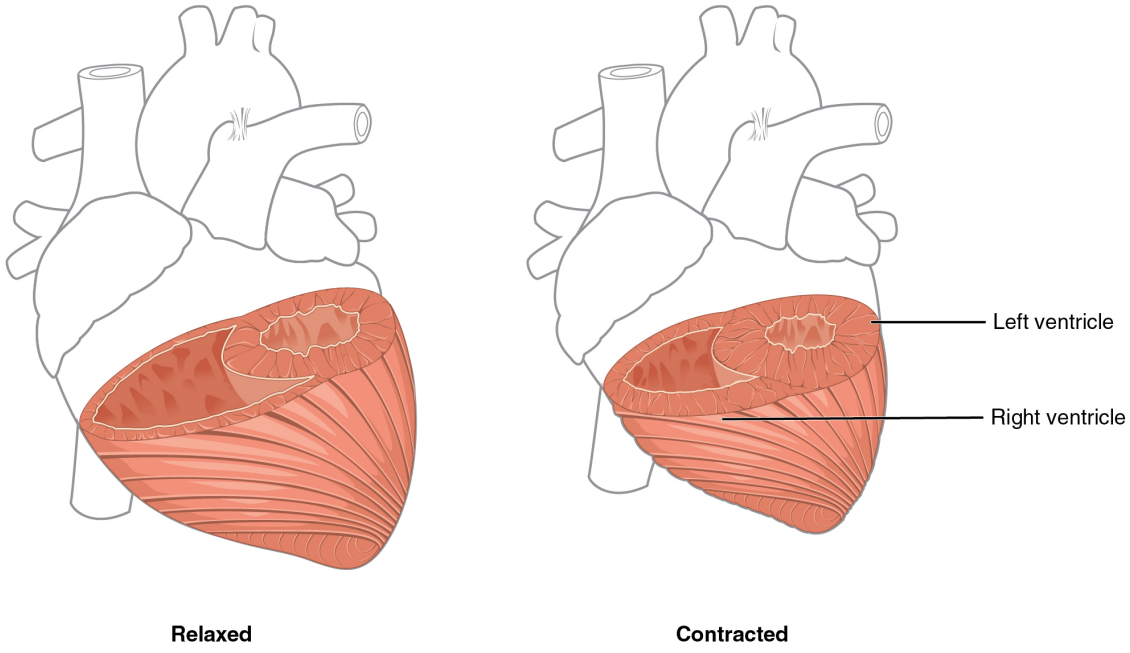

Figure 8.6: The myocardium in the left ventricle is significantly thicker than that of the right ventricle. Both ventricles pump the same amount of blood, but the left ventricle must generate a much greater pressure to overcome greater resistance in the systemic circuit. The ventricles are shown in both relaxed and contracting states. Note the differences in the relative size of the lumens, the region inside each ventricle where the blood is contained.

8.2.5 Internal Structure of the Heart

Recall that the heart's contraction cycle follows a dual pattern of circulation—the pulmonary and systemic circuits—because of the pairs of chambers that pump blood into the circulation. In order to develop a more precise understanding of cardiac function, it is first necessary to explore the internal anatomical structures in more detail.

8.2.5.1 Septa of the Heart

There are four openings that allow blood to move from the atria into the ventricles and from the ventricles into the pulmonary trunk and aorta. Located in each of these openings between the atria and ventricles is a **valve**, a specialized structure that ensures one-way flow of blood. The valves between the atria and ventricles are known generically as **atrioventricular (AV) valves**. The valves at the openings that lead to the pulmonary trunk and aorta are known generically as **semilunar valves**.

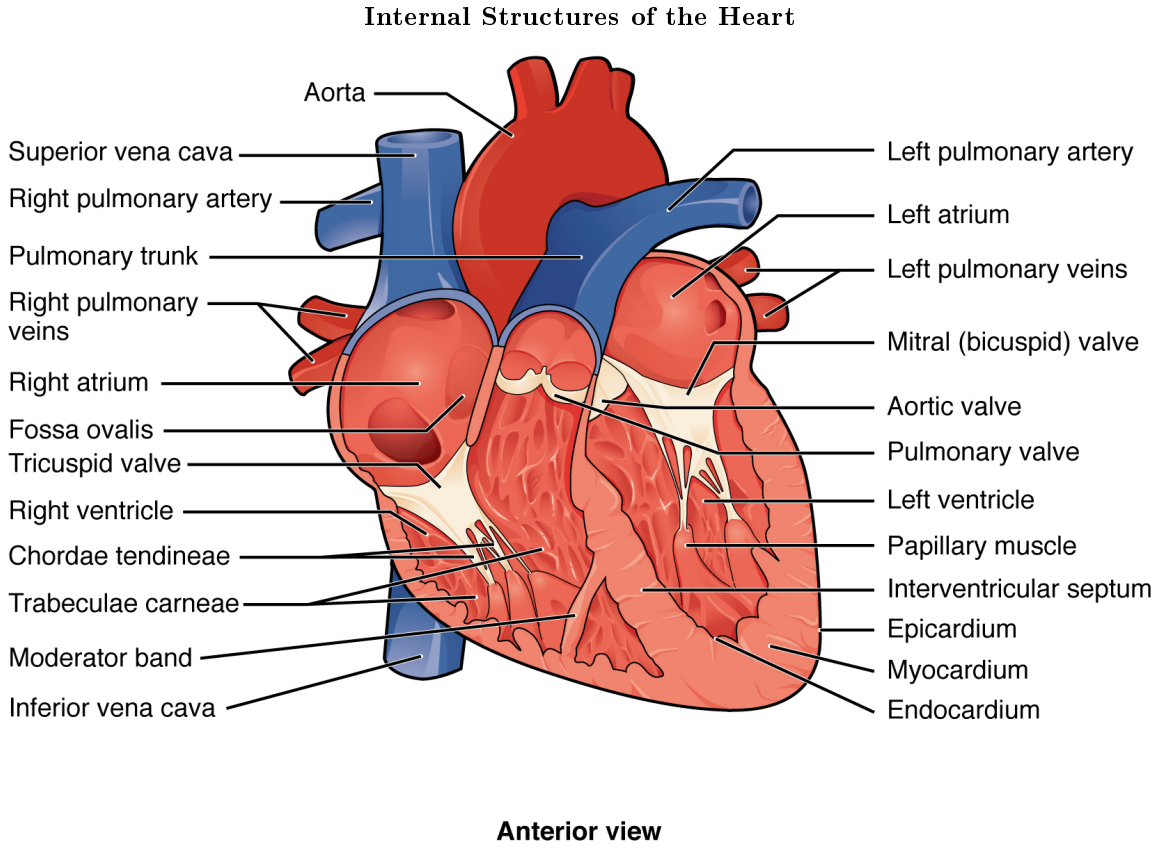

Figure 8.7: This anterior view of the heart shows the four chambers, the major vessels and their early branches, as well as the valves.

8.2.5.2 Right Atrium

The right atrium serves as the receiving chamber for blood returning to the heart from the systemic circulation. The two major systemic veins, the superior and inferior venae cavae, and the large coronary vein called the coronary sinus that drains the heart myocardium empty into the right atrium. The superior vena cava drains blood from regions abover the diaphragm: the head, neck, upper limbs, and the thoracic region. It empties into the superior and posterior portions of the right atrium. The inferior vena cava drains blood from areas below the diaphragm: the lower limbs and abdominal and pelvic region of the body. It, too, empties into the posterior portion of the atria, but is below the opening of the superior vena cava. The majority of the internal heart structures discussed in this and subsequent sections are illustrated in the provided figure.

The atria receive venous blood on a nearly continuous basis, preventing venous flow from stopping while the ventricles are contracting. While most ventricular filling occurs while the atria are relaxed, they do demonstrate a contractile phase and actively pump blood into the ventricles just prior to ventricular contraction. The opening between the atrium and ventricle is guarded by the tricuspid valve.

8.2.5.3 Right Ventricle

The right ventricle receives blood from the right atrium through the tricuspid valve. Each flap of the valve is attached to strong strands of connective tissue, the **chordae tendineae**, literally "tendinous cords," or sometimes more poetically referred to as "heart strings." There are several chordae tendineae associated with each of the flaps. They are composed of approximately 80 percent collagenous fibers with the remainder consisting of elastic fibers and endothelium. They connect each of the flaps to a **papillary muscle**.

When the myocardium of the ventricle contracts, pressure within the ventricular chamber rises. Blood, like any fluid, flows from higher pressure to lower pressure areas, in this case, toward the pulmonary trunk and the atrium. To prevent any potential backflow, the papillary muscles also contract, generating tension on the chordae tendineae. This prevents the flaps of the valves from being forced into the atria and regurgitation of the blood back into the atria during ventricular contraction. Figure 8.8 (Chordae Tendineae and Papillary Muscles) shows papillary muscles and chordae tendineae attached to the tricuspid valve.

Chordae Tendineae and Papillary Muscles

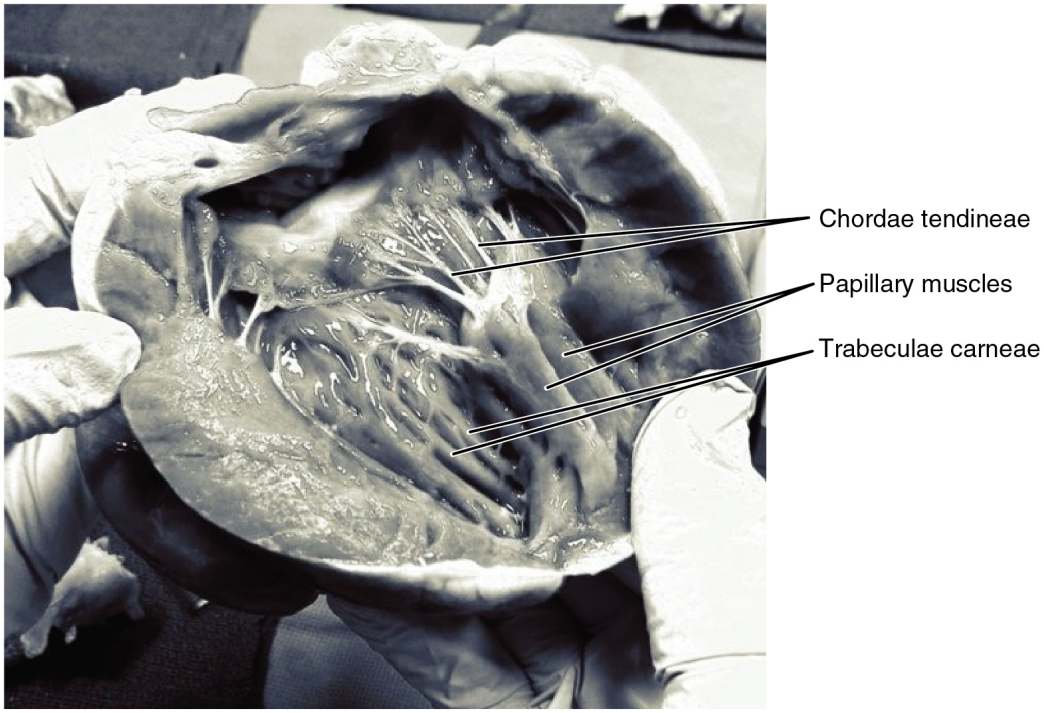

Figure 8.8: In this frontal section, you can see papillary muscles attached to the tricuspid valve on the right as well as the mitral valve on the left via chordae tendineae. (credit: modification of work by "PV KS"/flickr.com)

When the right ventricle contracts, it ejects blood into the pulmonary trunk, which branches into the left and right pulmonary arteries that carry it to each lung. The superior surface of the right ventricle begins to taper as it approaches the pulmonary trunk. At the base of the pulmonary trunk is the pulmonary semilunar valve that prevents backflow from the pulmonary trunk.

8.2.5.4 Left Atrium

After exchange of gases in the pulmonary capillaries, blood returns to the left atrium high in oxygen via one of the four pulmonary veins. Blood flows nearly continuously from the pulmonary veins back into the atrium, which acts as the receiving chamber, and from here through an opening into the left ventricle. Most blood flows passively into the heart while both the atria and ventricles are relaxed, but toward the end of the ventricular relaxation period, the left atrium will contract, pumping blood into the ventricle. This atrial contraction accounts for approximately 20 percent of ventricular filling. The opening between the left atrium and ventricle is guarded by the mitral valve.

8.2.5.5 Left Ventricle

Recall that, although both sides of the heart will pump the same amount of blood, the muscular layer is much thicker in the left ventricle compared to the right (see Figure 8.6 (Differences in Ventricular Muscle Thickness)). The mitral valve is connected to papillary muscles via chordae tendineae.

The left ventricle is the major pumping chamber for the systemic circuit; it ejects blood into the aorta through the aortic semilunar valve.

8.2.5.6 Heart Valve Structure and Function

A transverse section through the heart slightly above the level of the atrioventricular septum reveals all four heart valves along the same plane (Figure 8.9 (Heart Valves)). The valves ensure unidirectional blood flow through the heart. Between the right atrium and the right ventricle is the **right atrioventricular valve**, or **tricuspid valve**. It typically consists of three flaps, or leaflets, made of endocardium reinforced with additional connective tissue. The flaps are connected by chordae tendineae to the papillary muscles, which control the opening and closing of the valves.

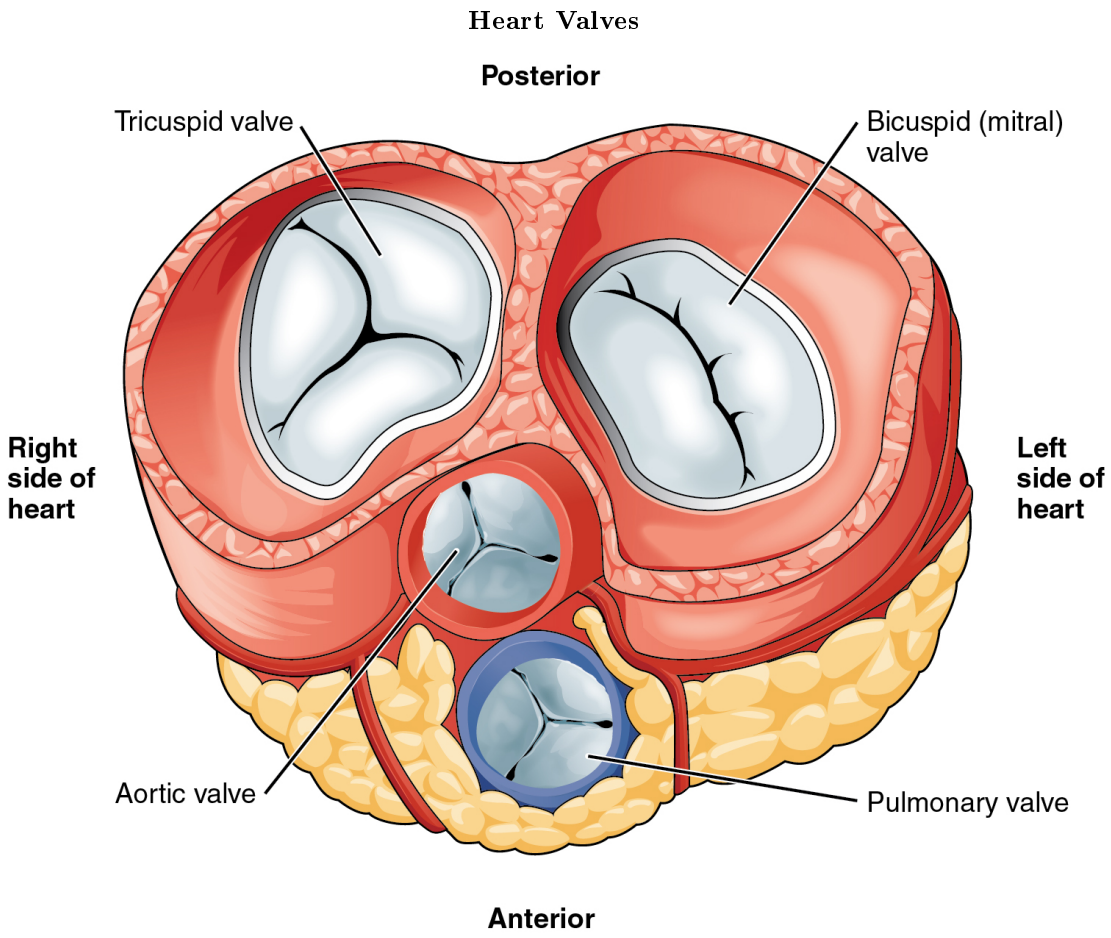

Figure 8.9: With the atria and major vessels removed, all four valves are clearly visible, although it is difficult to distinguish the three separate cusps of the tricuspid valve.

Emerging from the right ventricle at the base of the pulmonary trunk is the pulmonary semilunar valve or the right semilunar valve. The pulmonary valve is comprised of three small flaps of endothelium reinforced with connective tissue. When the ventricle relaxes, the pressure differential causes blood to flow back into the ventricle from the pulmonary trunk. This flow of blood fills the pocket-like flaps of the pulmonary valve, causing the valve to close and producing an audible sound ("Lub"). Unlike the atrioventricular valves, there are no papillary muscles or chordae tendineae associated with the pulmonary valve.

Located at the opening between the left atrium and left ventricle is the **mitral valve**, also called the **bicuspid valve** or the **left atrioventricular valve**. Structurally, this valve consists of two cusps compared to the three cusps of the tricuspid valve. In a clinical setting, the valve is referred to as the mitral valve, rather than the bicuspid valve. The two cusps of the mitral valve are attached by chordae tendineae to two papillary muscles that project from the wall of the ventricle.

At the base of the aorta is the aortic semilunar valve, or the **aortic valve**, which prevents backflow from the aorta. It normally is composed of three flaps. When the ventricle relaxes and blood attempts to flow back into the ventricle from the aorta, blood will fill the cusps of the valve, causing it to close and producing

an audible sound ("dub/dup").

In Figure 8.10 (Blood Flow from the Left Atrium to the Left Ventricle)**a**, the two atrioventricular valves are open and the two semilunar valves are closed. This occurs when both atria and ventricles are relaxed and when the atria contract to pump blood into the ventricles. Figure 8.10 (Blood Flow from the Left Atrium to the Left Ventricle)**b** shows a frontal view. Although only the left side of the heart is illustrated, the process is virtually identical on the right.

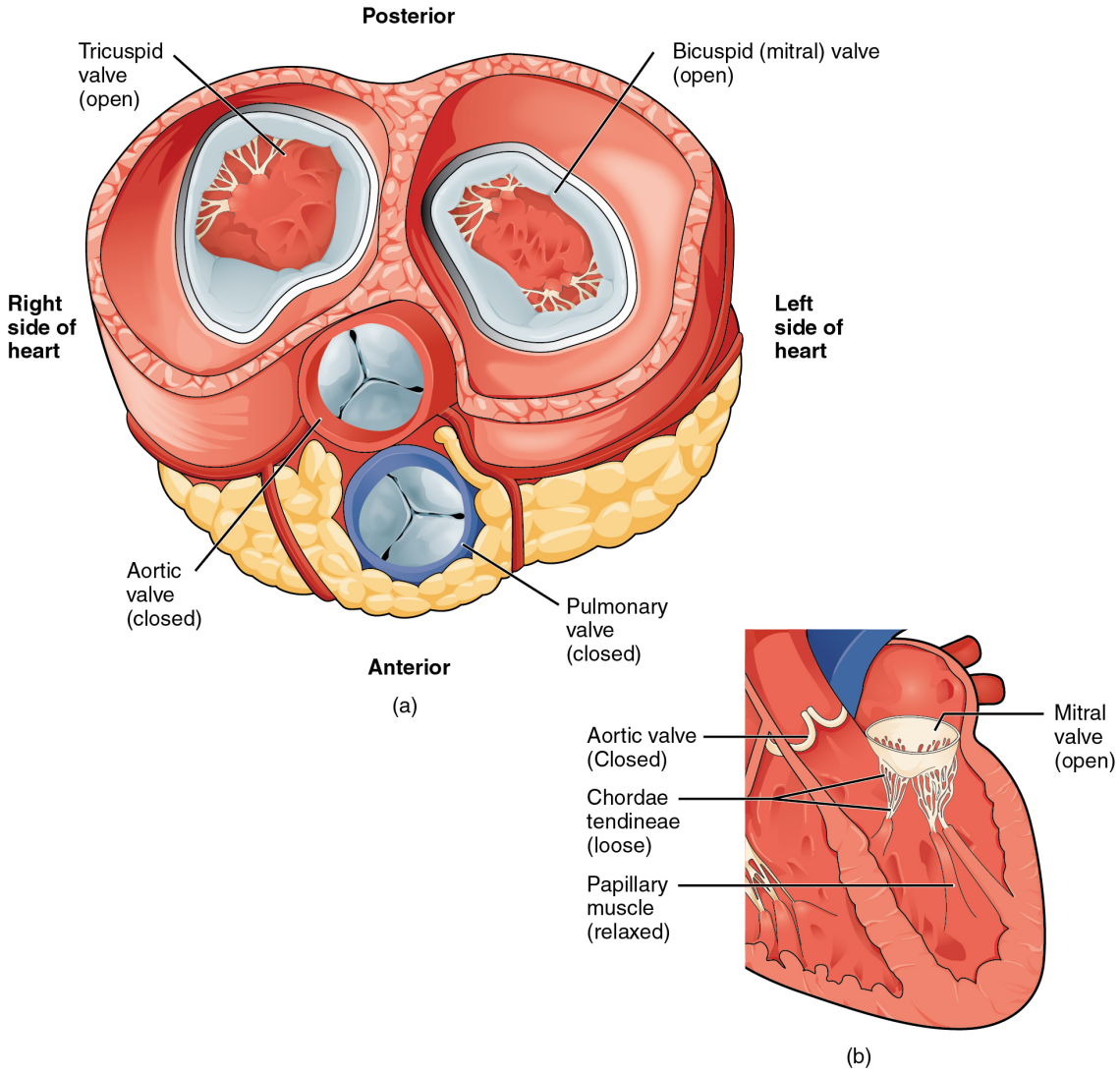

Figure 8.10: (a) A transverse section through the heart illustrates the four heart valves. The two atrioventricular valves are open; the two semilunar valves are closed. The atria and vessels have been removed. (b) A frontal section through the heart illustrates blood flow through the mitral valve. When the mitral valve is open, it allows blood to move from the left atrium to the left ventricle. The aortic semilunar valve is closed to prevent backflow of blood from the aorta to the left ventricle.

Figure 8.11 (Blood Flow from the Left Ventricle into the Great Vessels)**a** shows the atrioventricular valves closed while the two semilunar valves are open. This occurs when the ventricles contract to eject blood into the pulmonary trunk and aorta. Closure of the two atrioventricular valves prevents blood from being forced back into the atria. This stage can be seen from a frontal view in Figure 8.11 (Blood Flow from

the Left Ventricle into the Great Vessels)**b**.

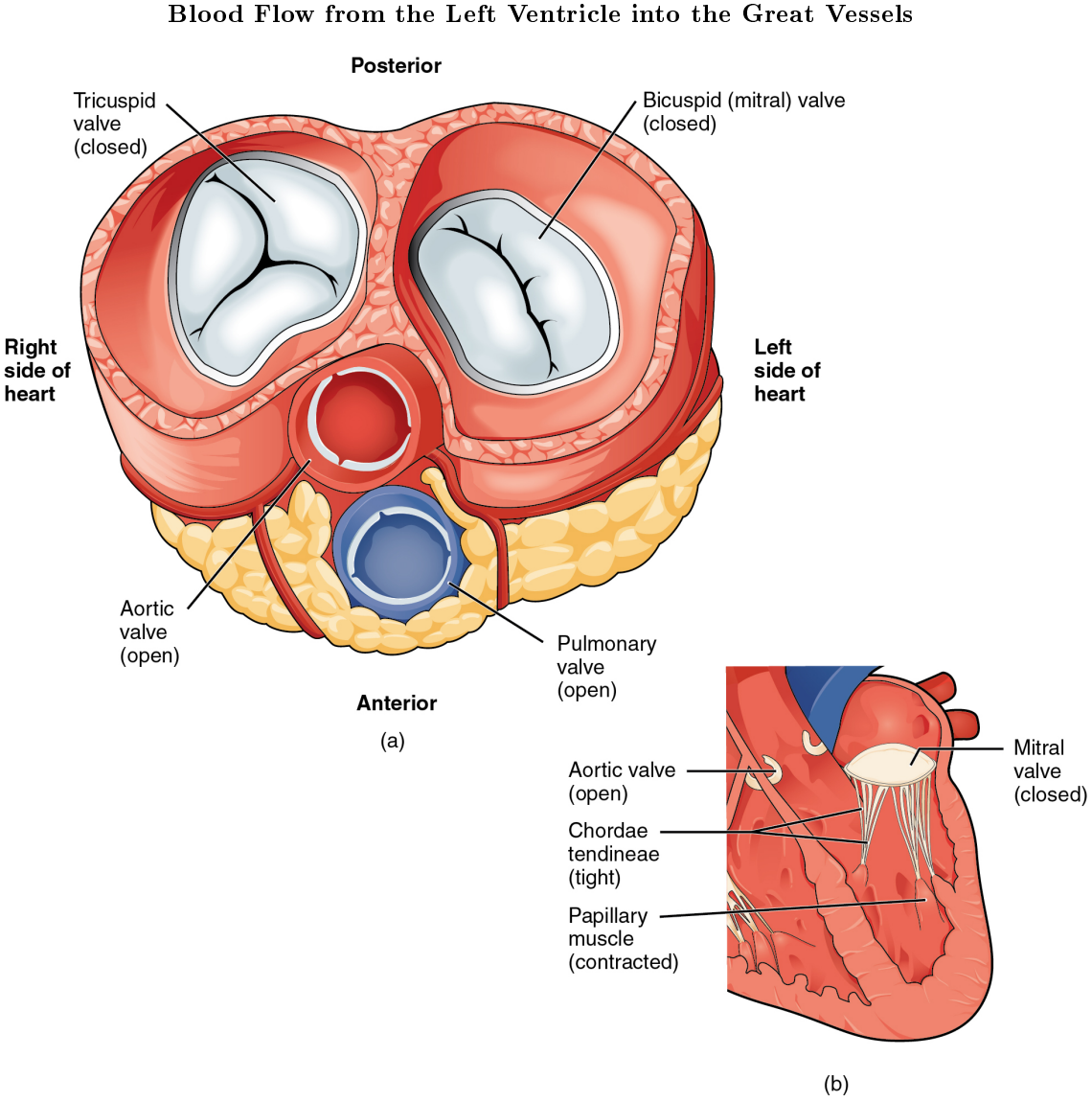

Figure 8.11: (a) A transverse section through the heart illustrates the four heart valves during ventricular contraction. The two atrioventricular valves are closed, but the two semilunar valves are open. The atria and vessels have been removed. (b) A frontal view shows the closed mitral (bicuspid) valve that prevents backflow of blood into the left atrium. The aortic semilunar valve is open to allow blood to be ejected into the aorta.

When the ventricles begin to contract, pressure within the ventricles rises and blood flows toward the area of lowest pressure, which is initially in the atria. This backflow causes the cusps of the tricuspid and

mitral (bicuspid) valves to close. These valves are tied down to the papillary muscles by chordae tendineae. During the relaxation phase of the cardiac cycle, the papillary muscles are also relaxed and the tension on the chordae tendineae is slight (see Figure 8.10 (Blood Flow from the Left Atrium to the Left Ventricle)**b**). However, as the myocardium of the ventricle contracts, so do the papillary muscles. This creates tension on the chordae tendineae (see Figure 8.11 (Blood Flow from the Left Ventricle into the Great Vessels)**b**), helping to hold the cusps of the atrioventricular valves in place and preventing them from being blown back into the atria.

The aortic and pulmonary semilunar valves lack the chordae tendineae and papillary muscles associated with the atrioventricular valves. Instead, they consist of pocket-like folds of endocardium reinforced with additional connective tissue. When the ventricles relax and the change in pressure forces the blood toward the ventricles, the blood presses against these cusps and seals the openings.

: Visit this site[3] to observe an echocardiogram of actual heart valves opening and closing. Although much of the heart has been "removed" from this gif loop so the chordae tendineae are not visible, why is their presence more critical for the atrioventricular valves (tricuspid and mitral) than the semilunar (aortic and pulmonary) valves?

: **Heart Valves**

When heart valves do not function properly, they are often described as incompetent and result in valvular heart disease, which can range from benign to lethal. Some of these conditions are congenital, that is, the individual was born with the defect, whereas others may be attributed to disease processes or trauma. Some malfunctions are treated with medications, others require surgery, and still others may be mild enough that the condition is merely monitored since treatment might trigger more serious consequences.

Valvular disorders are often caused by carditis, or inflammation of the heart. One common trigger for this inflammation is rheumatic fever, or scarlet fever, an autoimmune response to the presence of a bacterium, *Streptococcus pyogenes*, normally a disease of childhood.

While any of the heart valves may be involved in valve disorders, mitral regurgitation is the most common, detected in approximately 2 percent of the population, and the pulmonary semilunar valve is the least frequently involved. When a valve malfunctions, the flow of blood to a region will often be disrupted. The resulting inadequate flow of blood to this region will be described in general terms as an insufficiency. The specific type of insufficiency is named for the valve involved: aortic insufficiency, mitral insufficiency, tricuspid insufficiency, or pulmonary insufficiency.

If one of the cusps of the valve is forced backward by the force of the blood, the condition is referred to as a prolapsed valve. Prolapse may occur if the chordae tendineae are damaged or broken, causing the closure mechanism to fail. The failure of the valve to close properly disrupts the normal one-way flow of blood and results in regurgitation, when the blood flows backward from its normal path. Using a stethoscope, the disruption to the normal flow of blood produces a heart murmur.

[3] http://openstaxcollege.org/l/heartvalve

Stenosis is a condition in which the heart valves become rigid and may calcify over time. The loss of flexibility of the valve interferes with normal function and may cause the heart to work harder to propel blood through the valve, which eventually weakens the heart. Aortic stenosis affects approximately 2 percent of the population over 65 years of age, and the percentage increases to approximately 4 percent in individuals over 85 years. Occasionally, one or more of the chordae tendineae will tear or the papillary muscle itself may die as a component of a myocardial infarction (heart attack). In this case, the patient's condition will deteriorate dramatically and rapidly, and immediate surgical intervention may be required.

Auscultation, or listening to a patient's heart sounds, is one of the most useful diagnostic tools, since it is proven, safe, and inexpensive. The term auscultation is derived from the Latin for "to listen," and the technique has been used for diagnostic purposes as far back as the ancient Egyptians. Valve and septal disorders will trigger abnormal heart sounds. If a valvular disorder is detected or suspected, a test called an echocardiogram, or simply an "echo," may be ordered. Echocardiograms are sonograms of the heart and can help in the diagnosis of valve disorders as well as a wide variety of heart pathologies.

: Visit this site[4] for a free download, including excellent animations and audio of heart sounds.

: **Cardiologist**

Cardiologists are medical doctors that specialize in the diagnosis and treatment of diseases of the heart. After completing 4 years of medical school, cardiologists complete a three-year residency in internal medicine followed by an additional three or more years in cardiology. Following this 10-year period of medical training and clinical experience, they qualify for a rigorous two-day examination administered by the Board of Internal Medicine that tests their academic training and clinical abilities, including diagnostics and treatment. After successful completion of this examination, a physician becomes a board-certified cardiologist. Some board-certified cardiologists may be invited to become a Fellow of the American College of Cardiology (FACC). This professional recognition is awarded to outstanding physicians based upon merit, including outstanding credentials, achievements, and community contributions to cardiovascular medicine.

[4] http://openstaxcollege.org/l/heartsounds

: Visit this site[5] to learn more about cardiologists.

: **Cardiovascular Technologist/Technician**

Cardiovascular technologists/technicians are trained professionals who perform a variety of imaging techniques, such as sonograms or echocardiograms, used by physicians to diagnose and treat diseases of the heart. Nearly all of these positions require an associate degree, and these technicians earn a median salary of $49,410 as of May 2010, according to the U.S. Bureau of Labor Statistics. Growth within the field is fast, projected at 29 percent from 2010 to 2020.

There is a considerable overlap and complementary skills between cardiac technicians and vascular technicians, and so the term cardiovascular technician is often used. Special certifications within the field require documenting appropriate experience and completing additional and often expensive certification examinations. These subspecialties include Certified Rhythm Analysis Technician (CRAT), Certified Cardiographic Technician (CCT), Registered Congenital Cardiac Sonographer (RCCS), Registered Cardiac Electrophysiology Specialist (RCES), Registered Cardiovascular Invasive Specialist (RCIS), Registered Cardiac Sonographer (RCS), Registered Vascular Specialist (RVS), and Registered Phlebology Sonographer (RPhS).

: Visit this site[6] for more information on cardiovascular technologists/technicians.

8.2.6 Coronary Circulation

You will recall that the heart is a remarkable pump composed largely of cardiac muscle cells that are incredibly active throughout life. Like all other cells, a **cardiomyocyte** requires a reliable supply of oxygen and nutrients, and a way to remove wastes, so it needs a dedicated, complex, and extensive coronary circulation. And because of the critical and nearly ceaseless activity of the heart throughout life, this need for a blood supply is even greater than for a typical cell. However, coronary circulation is not continuous; rather, it cycles, reaching a peak when the heart muscle is relaxed and nearly ceasing while it is contracting.

[5] http://openstaxcollege.org/l/cardiologist
[6] http://openstaxcollege.org/l/cardiotech

8.2.6.1 Coronary Arteries and Veins

Coronary arteries supply blood to the myocardium and other components of the heart. The first portion of the aorta after it arises from the left ventricle gives rise to the coronary arteries (right and left), which bring freshly oxygenated blood to the tissues of both sides of the heart. A coronary artery blockage often results in death of the cells (due to myocardial infarction/heart attack) supplied by the particular blood vessel. **Coronary veins** drain the heart and generally parallel the large surface arteries.

: **Heart: Myocardial Infarction**

Myocardial infarction (MI) is the formal term for what is commonly referred to as a heart attack. It normally results from a lack of blood flow (ischemia) and oxygen (hypoxia) to a region of the heart, resulting in death of the cardiac muscle cells. An MI often occurs when a coronary artery is blocked by the buildup of atherosclerotic plaque consisting of lipids, cholesterol and fatty acids, and white blood cells, primarily macrophages. It can also occur when a portion of an unstable atherosclerotic plaque travels through the coronary arterial system and lodges in one of the smaller vessels. The resulting blockage restricts the flow of blood and oxygen to the myocardium and causes death of the tissue. MIs may be triggered by excessive exercise, in which the partially occluded artery is no longer able to pump sufficient quantities of blood, or severe stress, which may induce spasm of the smooth muscle in the walls of the vessel.

In the case of acute MI, there is often sudden pain beneath the sternum called angina pectoris, often radiating down the left arm in males but not in female patients. Until this anomaly between the sexes was discovered, many female patients suffering MIs were misdiagnosed and sent home. In addition, patients typically present with difficulty breathing and shortness of breath, irregular heartbeat, nausea and vomiting, sweating, anxiety, and fainting, although not all of these symptoms may be present. Many of the symptoms are shared with other medical conditions, including anxiety attacks and simple indigestion, so differential diagnosis is critical. It is estimated that between 22 and 64 percent of MIs present without any symptoms.

Immediate treatments for MI are essential and include administering supplemental oxygen, aspirin that helps to break up clots, and nitroglycerine administered sublingually (under the tongue) to facilitate its absorption. Despite its unquestioned success in treatments and use since the 1880s, the mechanism of nitroglycerine is still incompletely understood but is believed to involve the release of nitric oxide, a known vasodilator, and endothelium-derived releasing factor, which also relaxes the smooth muscle in the tunica media of coronary vessels. Longer-term treatments include injections of thrombolytic agents such as streptokinase that dissolve the clot, the anticoagulant heparin, balloon angioplasty and stents to open blocked vessels, and bypass surgery to allow blood to pass around the site of blockage. If the damage is extensive, coronary replacement with a donor heart or coronary assist device, a sophisticated mechanical device that supplements the pumping activity of the heart, may be employed. Despite the attention, development of artificial hearts to augment the severely limited supply of heart donors has proven less than satisfactory but will likely improve in the future.

8.2.6.2 Coronary Artery Disease

: Coronary artery disease is the leading cause of death worldwide. It occurs when the buildup of plaque—a fatty material including cholesterol, connective tissue, white blood cells, and some smooth muscle cells—within the walls of the arteries obstructs the flow of blood and decreases the flexibility or compliance of the vessels. This condition is called atherosclerosis, a hardening of the arteries that involves the accumulation of plaque. As the coronary blood vessels become occluded, the flow of blood to the tissues will be restricted, a condition called ischemia that causes the cells to receive insufficient amounts of oxygen, called hypoxia. Figure 8.12 (Atherosclerotic Coronary Arteries) shows the blockage of coronary arteries highlighted by the injection of dye. Some individuals with coronary artery disease report pain radiating from the chest called angina

pectoris, but others remain asymptomatic. If untreated, coronary artery disease can lead to MI or a heart attack.

Atherosclerotic Coronary Arteries

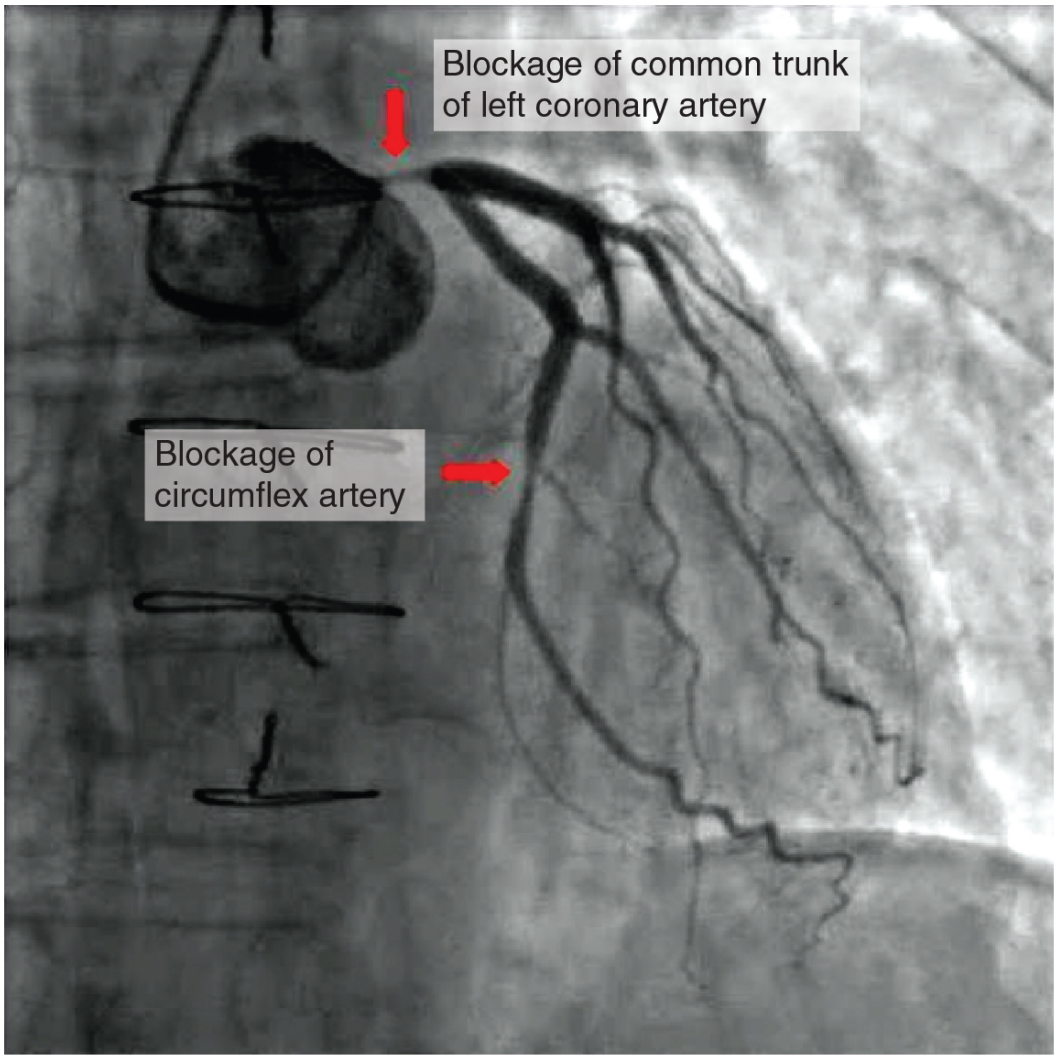

Figure 8.12: In this coronary angiogram (X-ray), the dye makes visible two occluded coronary arteries. Such blockages can lead to decreased blood flow (ischemia) and insufficient oxygen (hypoxia) delivered to the cardiac tissues. If uncorrected, this can lead to cardiac muscle death (myocardial infarction).

The disease progresses slowly and often begins in children and can be seen as fatty "streaks" in the vessels. It then gradually progresses throughout life. Well-documented risk factors include smoking, family history, hypertension, obesity, diabetes, high alcohol consumption, lack of exercise, stress, and hyperlipidemia or high circulating levels of lipids in the blood. Treatments may include medication, changes to diet and exercise, angioplasty with a balloon catheter, insertion of a stent, or coronary bypass procedure.

Angioplasty is a procedure in which the occlusion is mechanically widened with a balloon. A specialized catheter with an expandable tip is inserted into a superficial vessel, normally in the leg, and then directed to the site of the occlusion. At this point, the balloon is inflated to compress the plaque material and to open the vessel to increase blood flow. Then, the balloon is deflated and retracted. A stent consisting of a specialized mesh is typically inserted at the site of occlusion to reinforce the weakened and damaged walls. Stent insertions have been routine in cardiology for more than 40 years.

Coronary bypass surgery may also be performed. This surgical procedure grafts a replacement vessel obtained from another, less vital portion of the body to bypass the occluded area. This procedure is clearly effective in treating patients experiencing a MI, but overall does not increase longevity. Nor does it seem advisable in patients with stable although diminished cardiac capacity since frequently loss of mental acuity occurs following the procedure. Long-term changes to behavior, emphasizing diet and exercise plus a medicine regime tailored to lower blood pressure, lower cholesterol and lipids, and reduce clotting are equally as effective.

8.2.7 Chapter Review

The heart resides within the pericardial sac. The walls of the heart are composed of three layers of tissue, including a thick myocardium. The human heart consists of a pair of atria, which receive blood and pump it into a pair of ventricles, which pump blood into the vessels. The right atrium receives systemic blood relatively low in oxygen and pumps it into the right ventricle, which pumps it into the pulmonary circuit. Exchange of oxygen and carbon dioxide occurs in the lungs, and blood high in oxygen returns to the left atrium, which pumps blood into the left ventricle, which in turn pumps blood into the aorta and the remainder of the systemic circuit. The two openings between the atria and ventricles are guarded by the atrioventricular valves, the right tricuspid valve and the left mitral valve, which prevent the backflow of blood when the ventricles contract. Each is attached to chordae tendineae that extend to the papillary muscles, which are extensions of the myocardium, to prevent the valves from being blown back into the atria. The pulmonary semilunar valve is located at the base of the pulmonary trunk, and the left semilunar valve is located at the base of the aorta. The right and left coronary arteries are the first to branch off the aorta. Cardiac veins parallel the cardiac arteries and eventually drain into the right atrium.

8.2.8 Review Questions

Exercise 8.2.1 *(Solution on p. 215.)*

Which of the following is not important in preventing backflow of blood?

a. chordae tendineae
b. papillary muscles
c. AV valves
d. endocardium

Exercise 8.2.2 *(Solution on p. 215.)*

Which valve separates the left atrium from the left ventricle?

a. mitral
b. tricuspid
c. pulmonary
d. aortic

Exercise 8.2.3 *(Solution on p. 215.)*

Which of the following lists the valves in the order through which the blood flows from the vena cava through the heart?

a. tricuspid, pulmonary semilunar, bicuspid, aortic semilunar
b. mitral, pulmonary semilunar, bicuspid, aortic semilunar
c. aortic semilunar, pulmonary semilunar, tricuspid, bicuspid
d. bicuspid, aortic semilunar, tricuspid, pulmonary semilunar

Exercise 8.2.4 *(Solution on p. 215.)*
Which chamber initially receives blood from the systemic circuit?

a. left atrium
b. left ventricle
c. right atrium
d. right ventricle

Exercise 8.2.5 *(Solution on p. 215.)*
The myocardium would be the thickest in the _____.

a. left atrium
b. left ventricle
c. right atrium
d. right ventricle

8.2.9 Critical Thinking Questions

Exercise 8.2.6 *(Solution on p. 215.)*
Describe how the valves keep the blood moving in one direction.

Exercise 8.2.7 *(Solution on p. 215.)*
Why is the pressure in the pulmonary circulation lower than in the systemic circulation?

8.3 Cardiac Muscle and Electrical Activity[7]

Recall that cardiac muscle shares a few characteristics with both skeletal muscle and smooth muscle, but it has some unique properties of its own. Not the least of these exceptional properties is its ability to initiate an electrical potential at a fixed rate that spreads rapidly from cell to cell to trigger the contraction mechanism. This property is known as **autorhythmicity**. Neither smooth nor skeletal muscle can do this. Even though cardiac muscle has autorhythmicity, heart rate is modulated by the endocrine and nervous systems.

8.3.1 Structure of Cardiac Muscle

Compared to the giant cylinders of skeletal muscle, cardiac muscle cells, or cardiomyocytes, are considerably shorter with much smaller diameters. Cardiac muscle also demonstrates striations, the alternating pattern of dark A bands and light I bands attributed to the precise arrangement of the myofilaments and fibrils that are organized in sarcomeres along the length of the cell (Figure 8.13 (Cardiac Muscle)**a**). These contractile elements are virtually identical to skeletal muscle. T (transverse) tubules penetrate from the surface plasma membrane, the sarcolemma, to the interior of the cell, allowing the electrical impulse to reach the interior. The T tubules are only found at the Z discs, whereas in skeletal muscle, they are found at the junction of the A and I bands. Therefore, there are one-half as many T tubules in cardiac muscle as in skeletal muscle. In addition, the sarcoplasmic reticulum stores few calcium ions, so most of the calcium ions must come from

[7] This content is available online at <http://cnx.org/content/m57994/1.2/>.

outside the cells. The result is a slower onset of contraction. Mitochondria are plentiful, providing energy for the contractions of the heart. Typically, cardiomyocytes have a single, central nucleus, but two or more nuclei may be found in some cells.

Cardiac muscle cells branch freely. A junction between two adjoining cells is marked by a critical structure called an **intercalated disc**, which helps support the synchronized contraction of the muscle (Figure 8.13 (Cardiac Muscle)**b**). The importance of strongly binding these cells together is necessitated by the forces exerted by contraction.

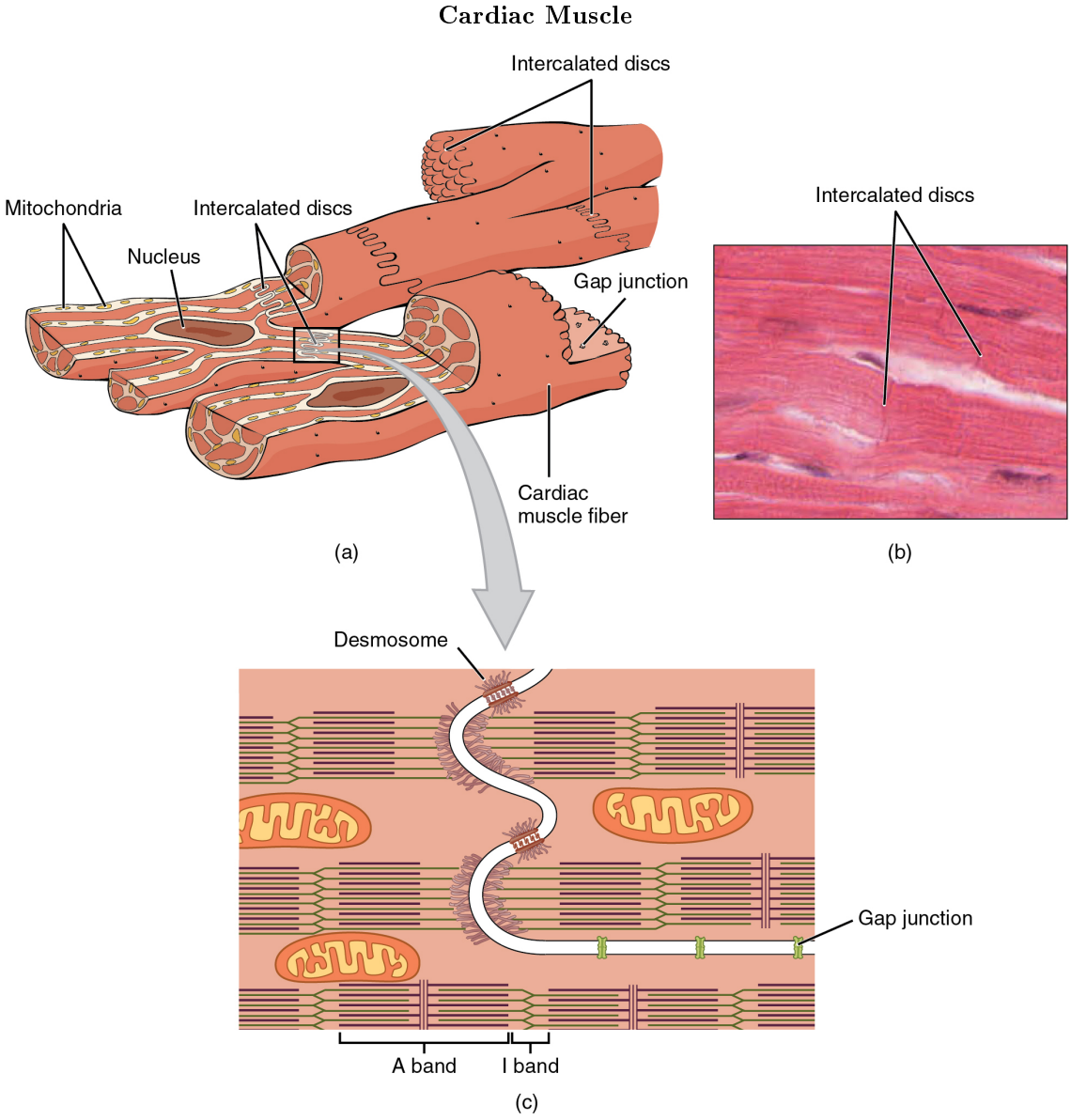

Figure 8.13: (a) Cardiac muscle cells have intercalated discs that are found at the junction of different cardiac muscle cells. (b) A photomicrograph of cardiac muscle cells shows the nuclei and intercalated discs. (Micrograph provided by the Regents of the University of Michigan Medical School ©2012)

: **Repair and Replacement**

Damaged cardiac muscle cells have extremely limited abilities to repair themselves or to replace dead cells via mitosis. Recent evidence indicates that at least some stem cells remain within the heart that continue to divide and at least potentially replace these dead cells. However, newly formed or

repaired cells are rarely as functional as the original cells, and cardiac function is reduced. In the event of a heart attack or MI, dead cells are often replaced by patches of scar tissue. Autopsies performed on individuals who had successfully received heart transplants show some proliferation of original cells. If researchers can unlock the mechanism that generates new cells and restore full mitotic capabilities to heart muscle, the prognosis for heart attack survivors will be greatly enhanced.

8.3.2 Conduction System of the Heart

If embryonic heart cells are separated into a Petri dish and kept alive, each is capable of generating its own electrical impulse followed by contraction. When two independently beating embryonic cardiac muscle cells are placed together, the cell with the higher inherent rate sets the pace, and the impulse spreads from the faster to the slower cell to trigger a contraction. As more cells are joined together, the fastest cell continues to assume control of the rate. A fully developed adult heart maintains the capability of generating its own electrical impulse, triggered by the fastest cells, as part of the cardiac conduction system. The components of the cardiac conduction system include the sinoatrial (SA) node, the atrioventricular (AV) node, the atrioventricular bundle, the atrioventricular bundle branches, and the Purkinje fibers (Figure 8.14 (Conduction System of the Heart)).

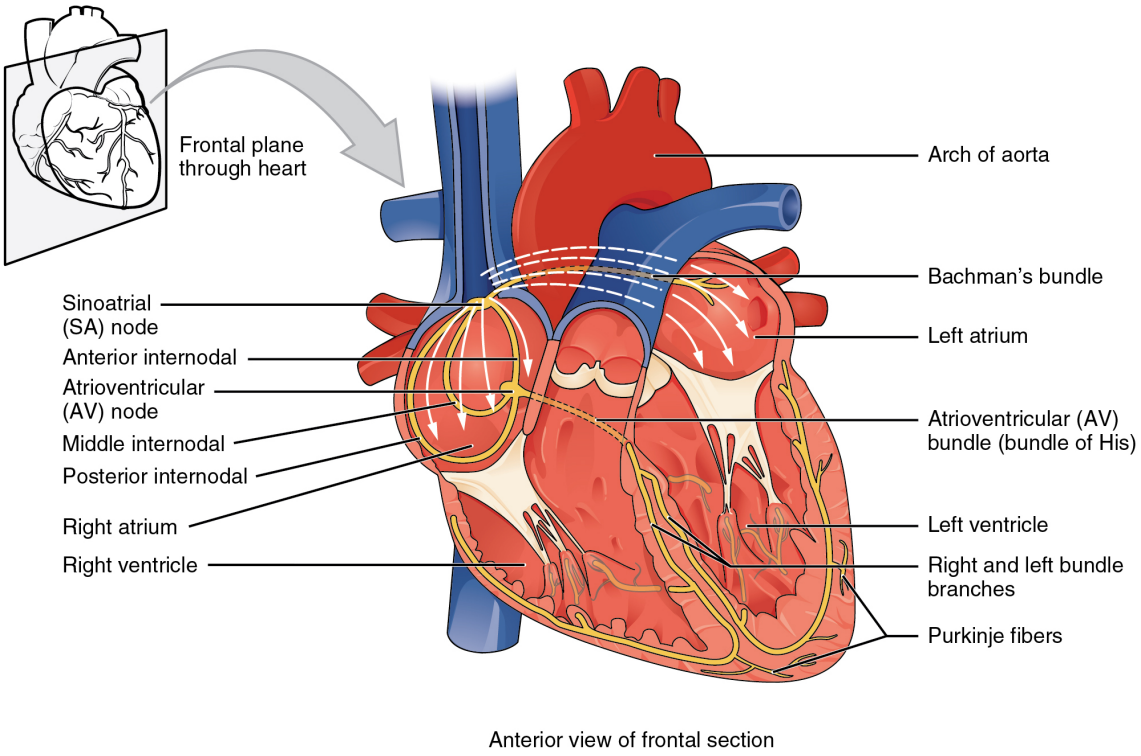

Figure 8.14: Specialized conducting components of the heart include the sinoatrial (SA) node, the atrioventricular (AV) node, the atrioventricular bundle, the right and left bundle branches, and the Purkinje fibers.

8.3.2.1 Sinoatrial (SA) Node

Normal cardiac rhythm is established by the **sinoatrial (SA) node**, a specialized clump of myocardial conducting cells located in the superior and posterior walls of the right atrium in close proximity to the opening of the superior vena cava. The SA node is known as the **pacemaker** of the heart. It initiates the **sinus rhythm**, or normal electrical pattern followed by contraction of the heart.

This impulse spreads from its initiation in the SA node throughout the atria to the atrioventricular (AV) node. The impulse takes approximately 50 ms (milliseconds) to travel between these two nodes. The connective tissue of the cardiac skeleton prevents the impulse from spreading into the myocardial cells in the ventricles except at the atrioventricular node. Figure 8.15 (Cardiac Conduction) illustrates the initiation of the impulse in the SA node that then spreads the impulse throughout the atria to the atrioventricular node.

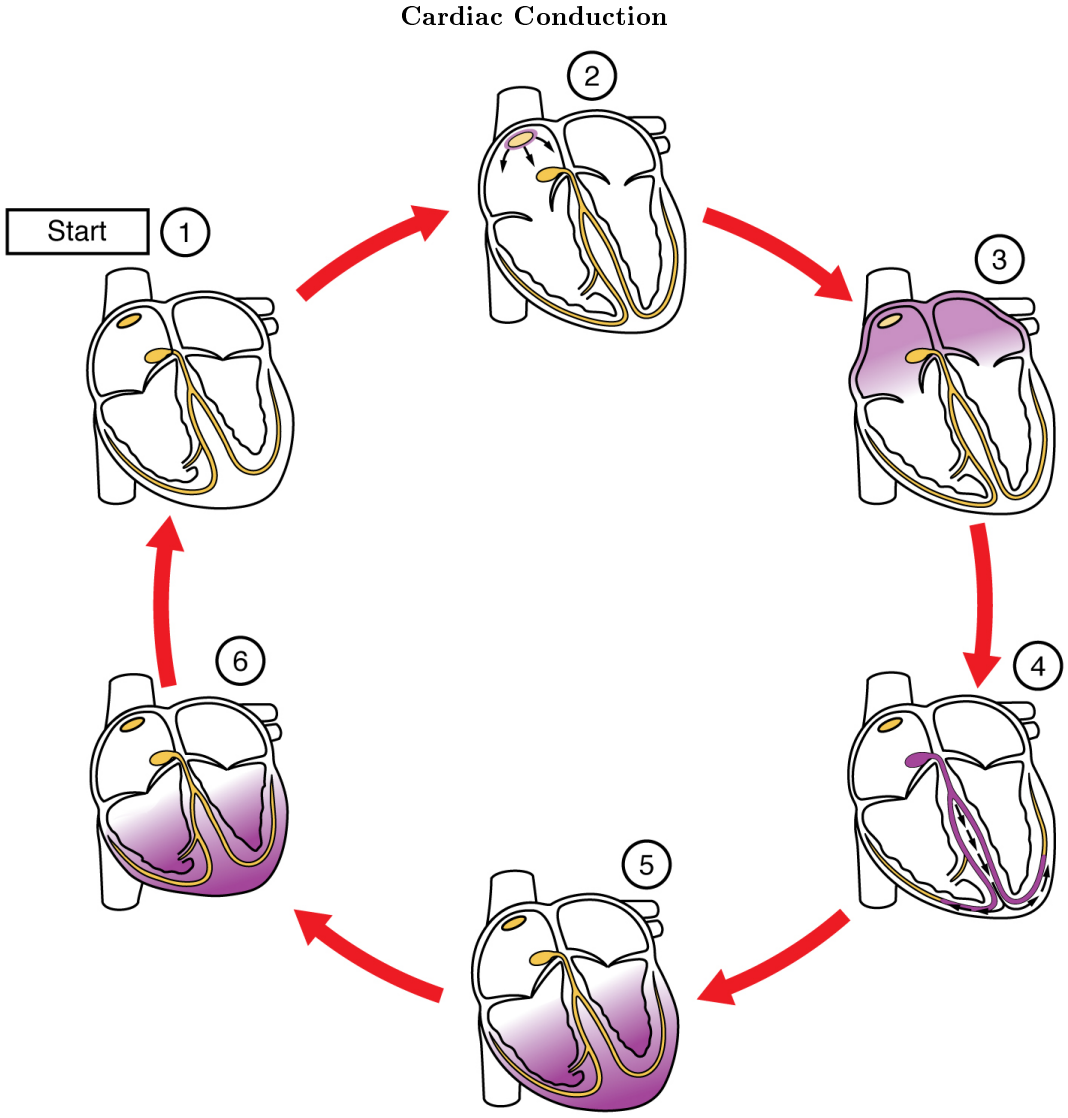

Figure 8.15: (1) The sinoatrial (SA) node and the remainder of the conduction system are at rest. (2) The SA node initiates the action potential, which sweeps across the atria. (3) After reaching the atrioventricular node, there is a delay of approximately 100 ms that allows the atria to complete pumping blood before the impulse is transmitted to the atrioventricular bundle. (4) Following the delay, the impulse travels through the atrioventricular bundle and bundle branches to the Purkinje fibers. (5) The impulse spreads to the contractile fibers of the ventricle. (6) Ventricular contraction begins.

8.3.2.2 Atrioventricular (AV) Node

The **atrioventricular (AV) node** is a second clump of specialized conductive cells, located in the lower portion of the right atrium within the atrioventricular wall. There is a critical pause before the AV node

initiates an impulse and transmits it to the atrioventricular bundle (see Figure 8.15 (Cardiac Conduction), step 3).

8.3.2.3 Atrioventricular Bundle (Bundle of His), Bundle Branches, and Purkinje Fibers

Arising from the AV node, the **atrioventricular bundle**, proceeds through the septum before dividing into two **atrioventricular bundle branches**, commonly called the left and right bundle branches. The left bundle branch supplies the left ventricle, and the right bundle branch the right ventricle. Both bundle branches descend and reach the apex of the heart where they connect with the Purkinje fibers (see Figure 8.15 (Cardiac Conduction), step 4).

The **Purkinje fibers** are additional myocardial conductive fibers that spread the impulse to the myocardial contractile cells in the ventricles. Since the electrical stimulus begins at the apex, the contraction also begins at the apex and travels toward the base of the heart, similar to squeezing a tube of toothpaste from the bottom. This allows the blood to be pumped out of the ventricles and into the aorta and pulmonary trunk.

8.3.3 Electrocardiogram

By careful placement of surface electrodes on the body, it is possible to record the complex, compound electrical signal of the heart. This tracing of the electrical signal is the **electrocardiogram (ECG)**, also commonly abbreviated EKG (K coming kardiology, from the German term for cardiology). Careful analysis of the ECG reveals a detailed picture of both normal and abnormal heart function, and is an indispensable clinical diagnostic tool. The standard electrocardiograph (the instrument that generates an ECG) uses 3, 5, or 12 leads. The greater the number of leads an electrocardiograph uses, the more information the ECG provides. The term "lead" may be used to refer to the cable from the electrode to the electrical recorder, but it typically describes the voltage difference between two of the electrodes. The 12-lead electrocardiograph uses 10 electrodes placed in standard locations on the patient's skin (Figure 8.16 (Standard Placement of ECG Leads)). In continuous ambulatory electrocardiographs, the patient wears a small, portable, battery-operated device known as a Holter monitor, that continuously monitors heart electrical activity, typically for a period of 24 hours during the patient's normal routine.

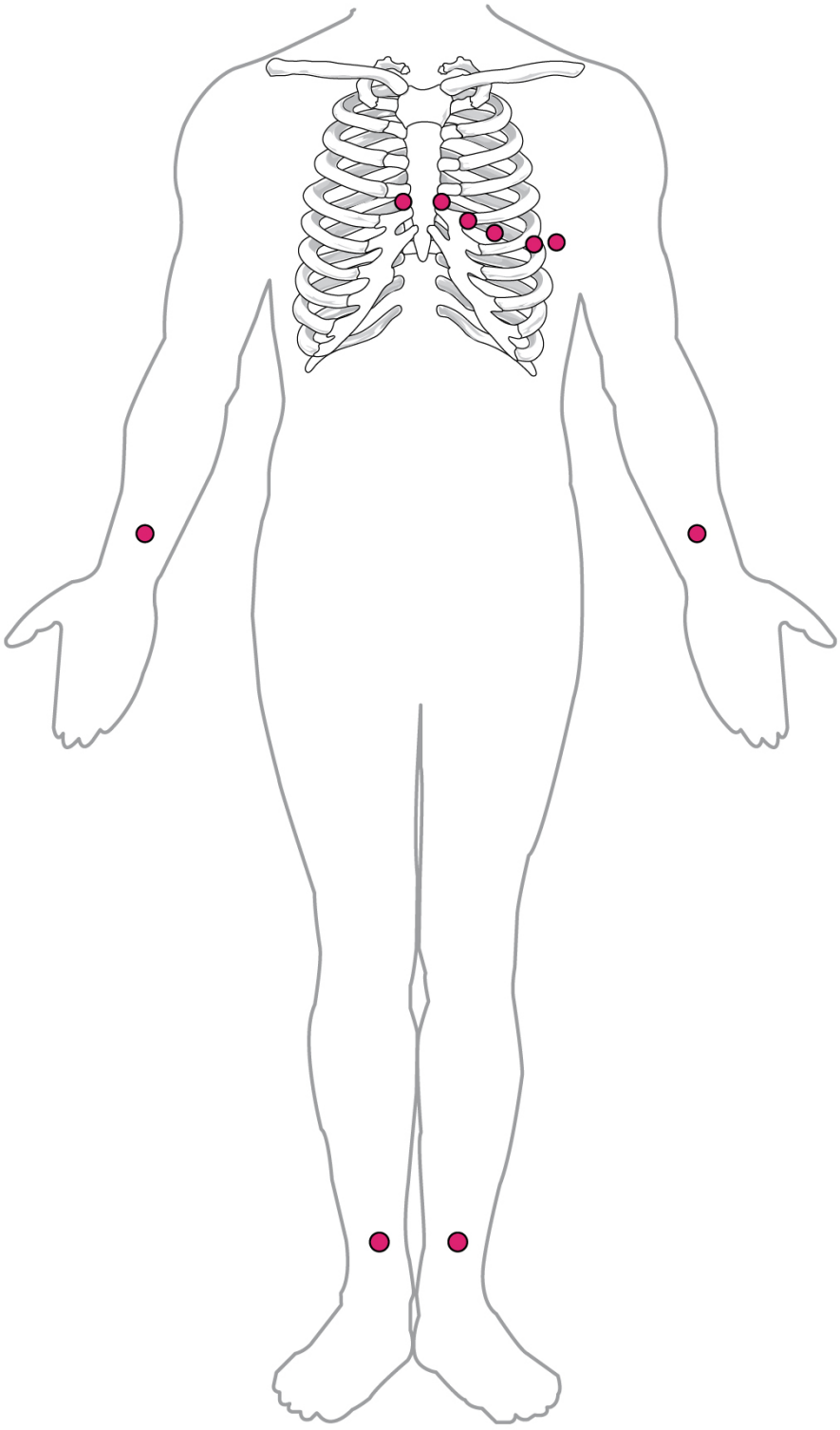

Figure 8.16: In a 12-lead ECG, six electrodes are placed on the chest, and four electrodes are placed on the limbs. Available for free at Connexions <http://cnx.org/content/col11903/1.3>

A normal ECG tracing is presented in Figure 8.17 (Electrocardiogram). Each component, segment, and interval is labeled and corresponds to important electrical events, demonstrating the relationship between these events and contraction in the heart.

There are five prominent points on the ECG: the P wave, the QRS complex, and the T wave. The small **P wave** represents the depolarization of the atria. The atria begin contracting approximately 25 ms after the start of the P wave. The large **QRS complex** represents the depolarization of the ventricles, which requires a much stronger electrical signal because of the larger size of the ventricular cardiac muscle. The ventricles begin to contract as the QRS reaches the peak of the R wave. Lastly, the **T wave** represents the repolarization of the ventricles. The repolarization of the atria occurs during the QRS complex, which masks it on an ECG.

: Visit this site[8] for a more detailed analysis of ECGs.

[8] http://openstaxcollege.org/l/ECG

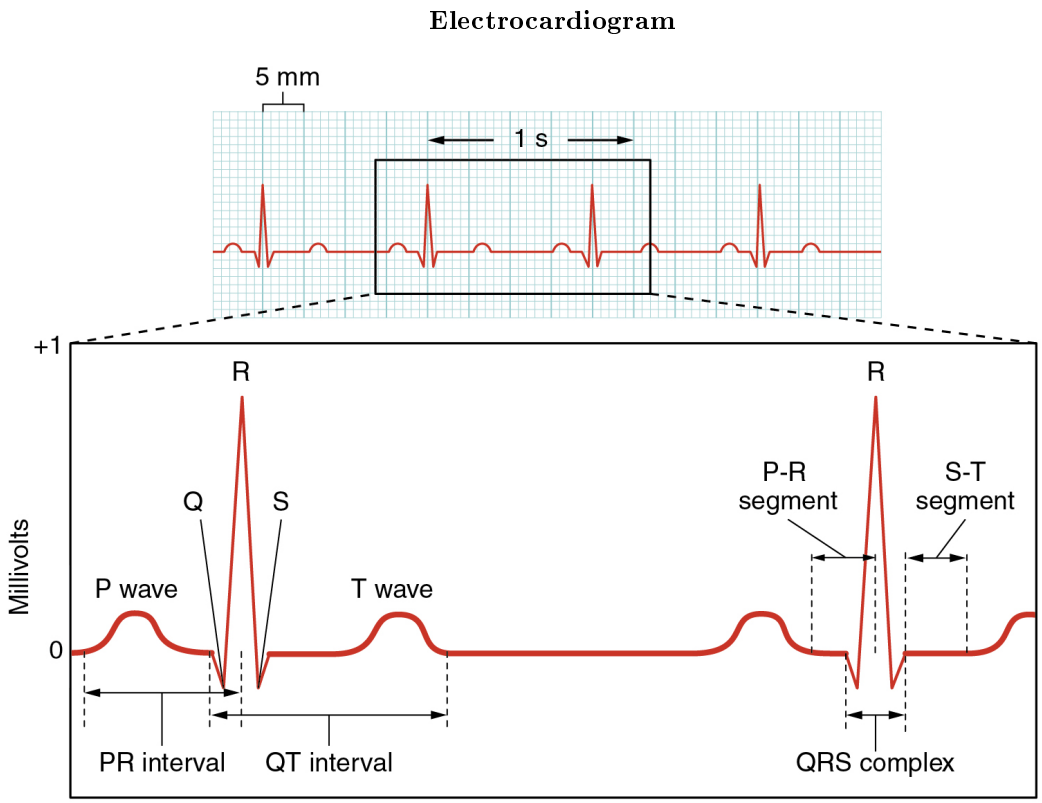

Figure 8.17: A normal tracing shows the P wave, QRS complex, and T wave. Additional segments and intervals are also shown.

ECG Tracing Correlated to the Cardiac Cycle

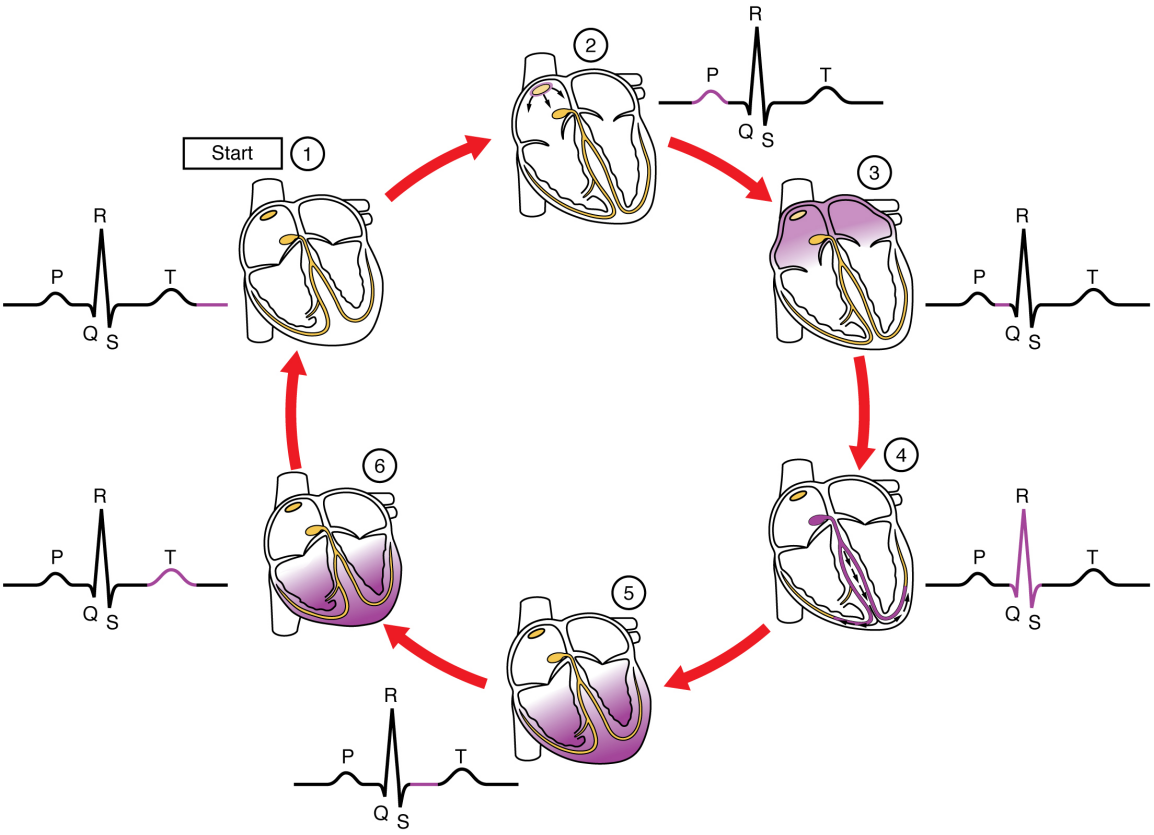

Figure 8.18: This diagram correlates an ECG tracing with the electrical and mechanical events of a heart contraction. Each segment of an ECG tracing corresponds to one event in the cardiac cycle.

: While interpretation of an ECG is possible and extremely valuable after some training, a full understanding of the complexities and intricacies generally requires several years of experience. In general, the size of the electrical variations, the duration of the events, and detailed analysis provide the most comprehensive picture of cardiac function. For example, an amplified P wave may indicate enlargement of the atria and an enlarged Q wave may indicate a MI (Myocardial Infarction). T waves often appear flatter when insufficient oxygen is being delivered to the myocardium.

As useful as analyzing these electrical recordings may be, there are limitations. For example, not all areas suffering a MI may be obvious on the ECG. Additionally, it will not reveal the effectiveness of the pumping, which requires further testing, such as an ultrasound test called an echocardiogram or nuclear medicine imaging. Common abnormalities that may be detected by the ECGs are shown in Figure 8.19 (Common ECG Abnormalities).

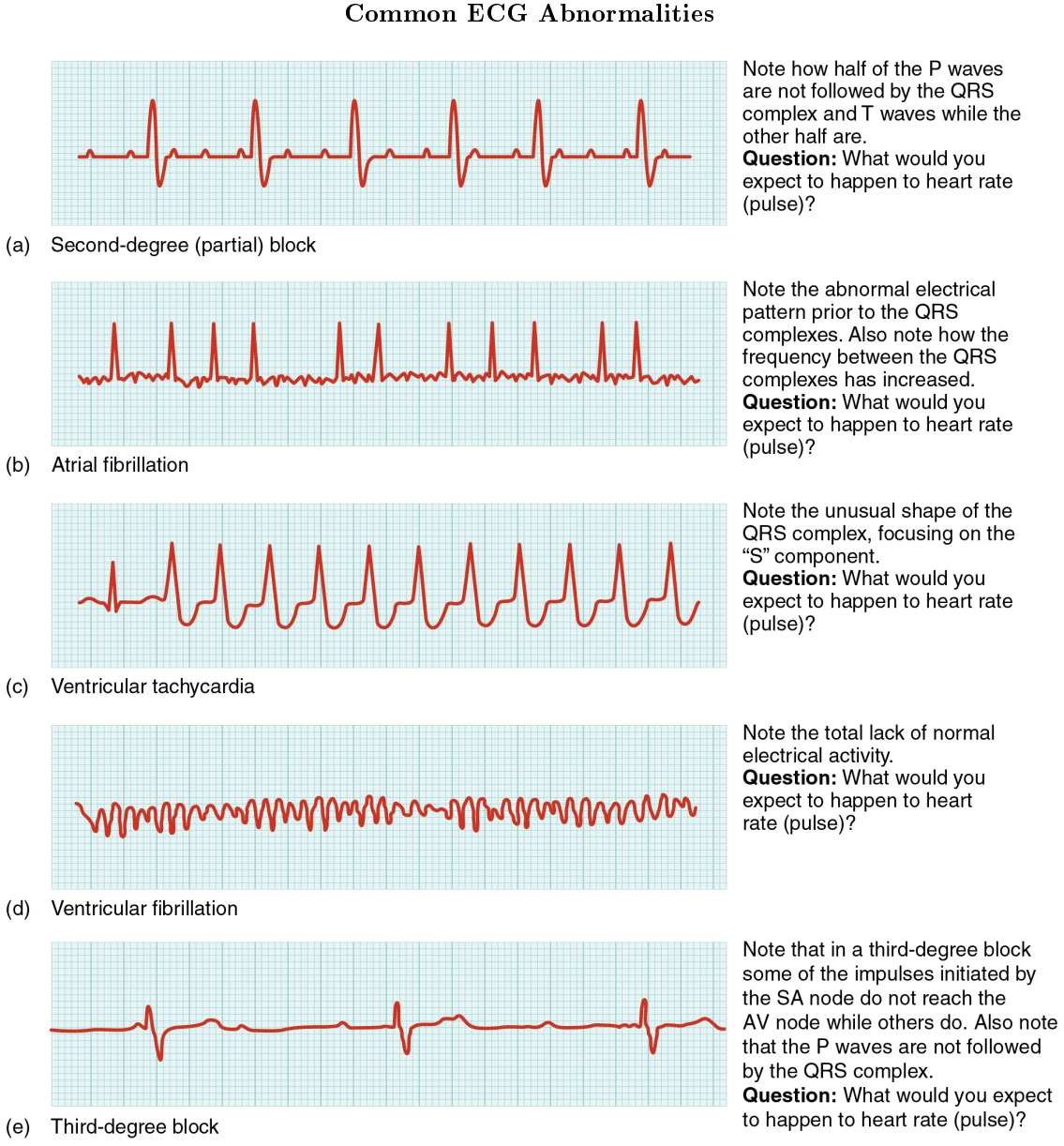

Figure 8.19: (a) In a second-degree or partial block, one-half of the P waves are not followed by the QRS complex and T waves while the other half are. (b) In atrial fibrillation, the electrical pattern is abnormal prior to the QRS complex, and the frequency between the QRS complexes has increased. (c) In ventricular tachycardia, the shape of the QRS complex is abnormal. (d) In ventricular fibrillation, there is no normal electrical activity. (e) In a third-degree block, there is no correlation between atrial activity (the P wave) and ventricular activity (the QRS complex).

: **External Automated Defibrillators**

In the event that the electrical activity of the heart is severely disrupted, cessation of electrical activity or fibrillation may occur. In fibrillation, the heart beats in a wild, uncontrolled manner,

which prevents it from being able to pump effectively. Atrial fibrillation (see Figure 8.19 (Common ECG Abnormalities)**b**) is a serious condition, but as long as the ventricles continue to pump blood, the patient's life may not be in immediate danger. Ventricular fibrillation (see Figure 8.19 (Common ECG Abnormalities)**d**) is a medical emergency that requires life support, because the ventricles are not effectively pumping blood. In a hospital setting, it is often described as "code blue." If untreated for as little as a few minutes, ventricular fibrillation may lead to brain death. The most common treatment is defibrillation, which uses special paddles to apply a charge to the heart from an external electrical source in an attempt to establish a normal sinus rhythm (Figure 8.20 (Defibrillators)). A defibrillator effectively stops the heart so that the SA node can trigger a normal conduction cycle. Because of their effectiveness in reestablishing a normal sinus rhythm, external automated defibrillators (EADs) are being placed in areas frequented by large numbers of people, such as schools, restaurants, and airports. These devices contain simple and direct verbal instructions that can be followed by nonmedical personnel in an attempt to save a life.

Defibrillators

Figure 8.20: (a) An external automatic defibrillator can be used by nonmedical personnel to reestablish a normal sinus rhythm in a person with fibrillation. (b) Defibrillator paddles are more commonly used in hospital settings. (credit b: "widerider107"/flickr.com)

When arrhythmias become a chronic problem, the heart maintains a junctional rhythm, which originates in the AV node. In order to speed up the heart rate and restore full sinus rhythm, a cardiologist can implant an **artificial pacemaker**, which delivers electrical impulses to the heart muscle to ensure that the heart continues to contract and pump blood effectively. These artificial pacemakers are programmable by the cardiologists and can either provide stimulation temporarily upon demand or on a continuous basis. Some devices also contain built-in defibrillators.

8.3.4 Chapter Review

The heart is regulated by both neural and endocrine (i.e. hormonal) control, yet it is capable of initiating its own action potential followed by muscular contraction. The conductive cells within the heart establish the heart rate and transmit it through the myocardium. The contractile cells contract and propel the blood. The normal path of transmission for the conductive cells is the sinoatrial (SA) node, atrioventricular (AV) node, atrioventricular (AV) bundle, bundle branches, and Purkinje fibers. Recognizable points on the ECG include

the P wave that corresponds to atrial depolarization (i.e. contraction), the QRS complex that corresponds to ventricular depolarization, and the T wave that corresponds to ventricular repolarization (relaxation).

8.3.5 Review Questions

Exercise 8.3.1 *(Solution on p. 215.)*
Which of the following is unique to cardiac muscle cells?

a. Only cardiac muscle contains a sarcoplasmic reticulum.
b. Only cardiac muscle has gap junctions.
c. Only cardiac muscle is capable of autorhythmicity
d. Only cardiac muscle has a high concentration of mitochondria.

Exercise 8.3.2 *(Solution on p. 215.)*
Which portion of the ECG corresponds to repolarization (i.e. relaxation) of the atria?

a. P wave
b. QRS complex
c. T wave
d. none of the above: atrial repolarization is masked by ventricular depolarization

8.3.6 Critical Thinking Questions

Exercise 8.3.3 *(Solution on p. 215.)*
How does the delay of the impulse at the atrioventricular node contribute to cardiac function?

8.4 Cardiac Cycle[9]

The period of time that begins with contraction of the atria and ends with ventricular relaxation is known as the **cardiac cycle** (Figure 8.21 (Overview of the Cardiac Cycle)). The period of contraction that the heart undergoes while it pumps blood into circulation is called **systole**. The period of relaxation that occurs as the chambers fill with blood is called **diastole**. Both the atria and ventricles undergo systole and diastole, and it is essential that these components be carefully regulated and coordinated to ensure blood is pumped efficiently to the body.

[9] This content is available online at <http://cnx.org/content/m57995/1.2/>.

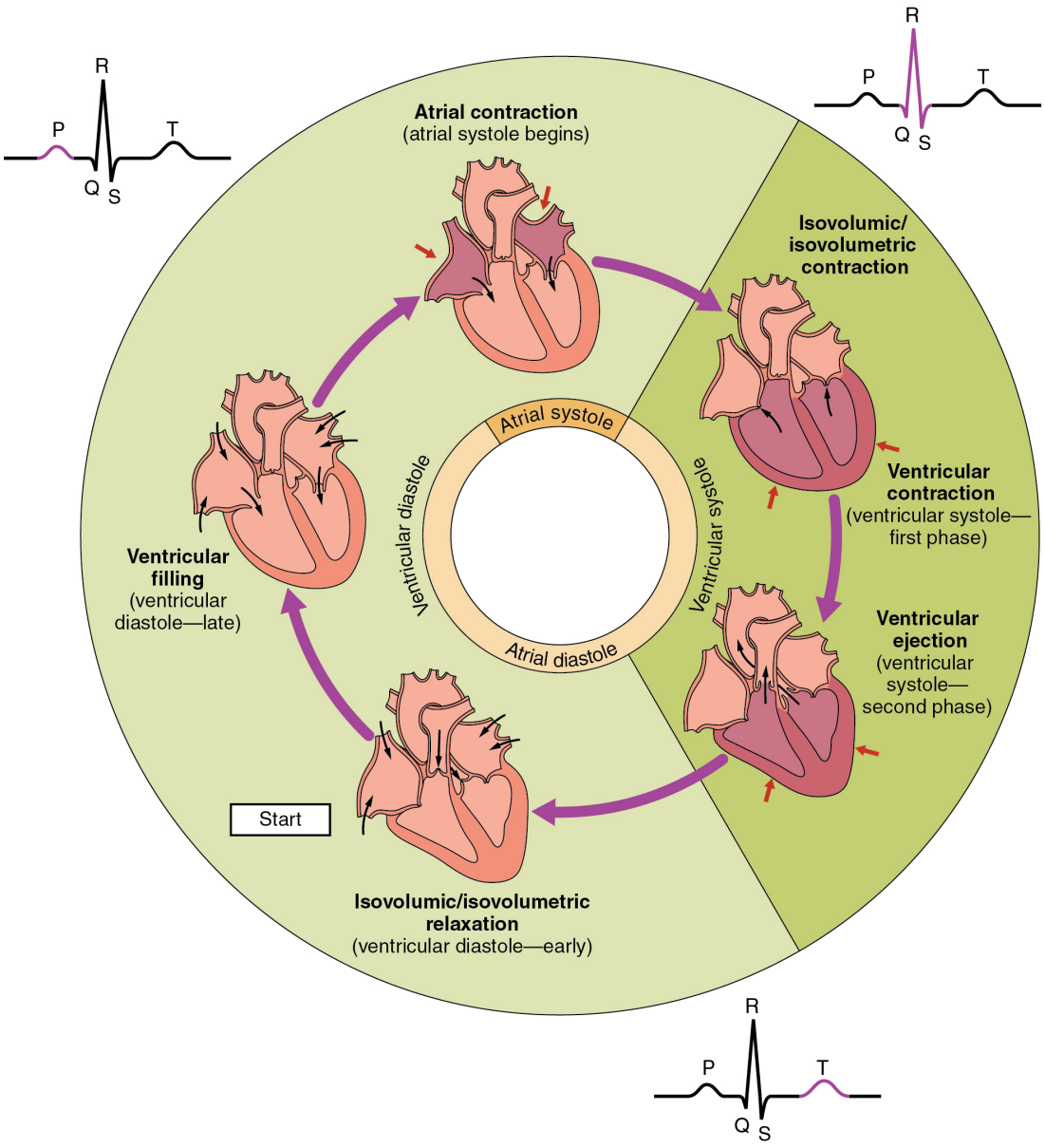

Figure 8.21: The cardiac cycle begins with atrial systole and progresses to ventricular systole, atrial diastole, and ventricular diastole, when the cycle begins again. Correlations to the ECG are highlighted.

8.4.1 Pressures and Flow

Fluids, whether gases or liquids, are materials that flow according to pressure gradients—that is, they move from regions that are higher in pressure to regions that are lower in pressure. Accordingly, when the heart chambers are relaxed (diastole), blood will flow into the atria from the veins, which are higher in pressure. As blood flows into the atria, the pressure will rise, so the blood will initially move passively from the atria into the ventricles. When the action potential triggers the muscles in the atria to contract (atrial systole), the pressure within the atria rises further, pumping blood into the ventricles. During ventricular systole, pressure rises in the ventricles, pumping blood into the pulmonary trunk from the right ventricle and into the aorta from the left ventricle. Again, as you consider this flow and relate it to the conduction pathway, the elegance of the system should become apparent.

8.4.2 Phases of the Cardiac Cycle

At the beginning of the cardiac cycle, both the atria and ventricles are relaxed (diastole). Blood is flowing into the right atrium from the superior and inferior venae cavae and the coronary sinus. Blood flows into the left atrium from the four pulmonary veins. The two atrioventricular valves, the tricuspid and mitral valves, are both open, so blood flows unimpeded from the atria and into the ventricles. Approximately 70–80 percent of ventricular filling occurs by this method. The two semilunar valves, the pulmonary and aortic valves, are closed, preventing backflow of blood into the right and left ventricles from the pulmonary trunk on the right and the aorta on the left.

8.4.2.1 Atrial Systole and Diastole

Contraction of the atria follows depolarization, represented by the P wave of the ECG. As the atrial muscles contract from the superior portion of the atria toward the atrioventricular septum, pressure rises within the atria and blood is pumped into the ventricles through the open atrioventricular (tricuspid, and mitral or bicuspid) valves. At the start of atrial systole, the ventricles are normally filled with approximately 70–80 percent of their capacity due to inflow during diastole. Atrial contraction, also referred to as the "atrial kick," contributes the remaining 20–30 percent of filling (see Figure 8.21 (Overview of the Cardiac Cycle)). Atrial systole ends prior to ventricular systole, as the atrial muscle returns to diastole.

8.4.2.2 Ventricular Systole

Ventricular systole (see Figure 8.21 (Overview of the Cardiac Cycle)) follows the depolarization of the ventricles and is represented by the QRS complex in the ECG. It may be conveniently divided into two phases, lasting a total of 270 ms. At the end of atrial systole and just prior to atrial contraction, the ventricles contain approximately 130 mL blood in a resting adult in a standing position. This volume is known as the **end diastolic volume (EDV)** or **preload**.

Initially, as the muscles in the ventricle contract, the pressure of the blood within the chamber rises, but it is not yet high enough to open the semilunar (pulmonary and aortic) valves and be ejected from the heart. However, blood pressure quickly rises above that of the atria that are now relaxed and in diastole. This increase in pressure causes blood to flow back toward the atria, closing the tricuspid and mitral valves.

In the second phase of ventricular systole, the contraction of the ventricular muscle has raised the pressure within the ventricle to the point that it is greater than the pressures in the pulmonary trunk and the aorta. Blood is pumped from the heart, pushing open the pulmonary and aortic semilunar valves. Pressure generated by the left ventricle will be appreciably greater than the pressure generated by the right ventricle, since the existing pressure in the aorta will be so much higher. Nevertheless, both ventricles pump the same amount of blood.

8.4.2.3 Ventricular Diastole

Ventricular relaxation, or diastole, follows repolarization of the ventricles and is represented by the T wave of the ECG.

During the early phase of ventricular diastole, as the ventricular muscle relaxes, pressure on the remaining blood within the ventricle begins to fall. When pressure within the ventricles drops below pressure in both the pulmonary trunk and aorta, blood flows back toward the heart. The semilunar valves close to prevent backflow into the heart.

In the second phase of ventricular diastole, as the ventricular muscle relaxes, pressure on the blood within the ventricles drops even further. Eventually, it drops below the pressure in the atria. When this occurs, blood flows from the atria into the ventricles, pushing open the tricuspid and mitral valves. As pressure drops within the ventricles, blood flows from the major veins into the relaxed atria and from there into the ventricles. Both chambers are in diastole, the atrioventricular valves are open, and the semilunar valves remain closed (see Figure 8.21 (Overview of the Cardiac Cycle)). The cardiac cycle is complete.

Figure 8.22 (Relationship between the Cardiac Cycle and ECG) illustrates the relationship between the cardiac cycle and the ECG.

Relationship between the Cardiac Cycle and ECG

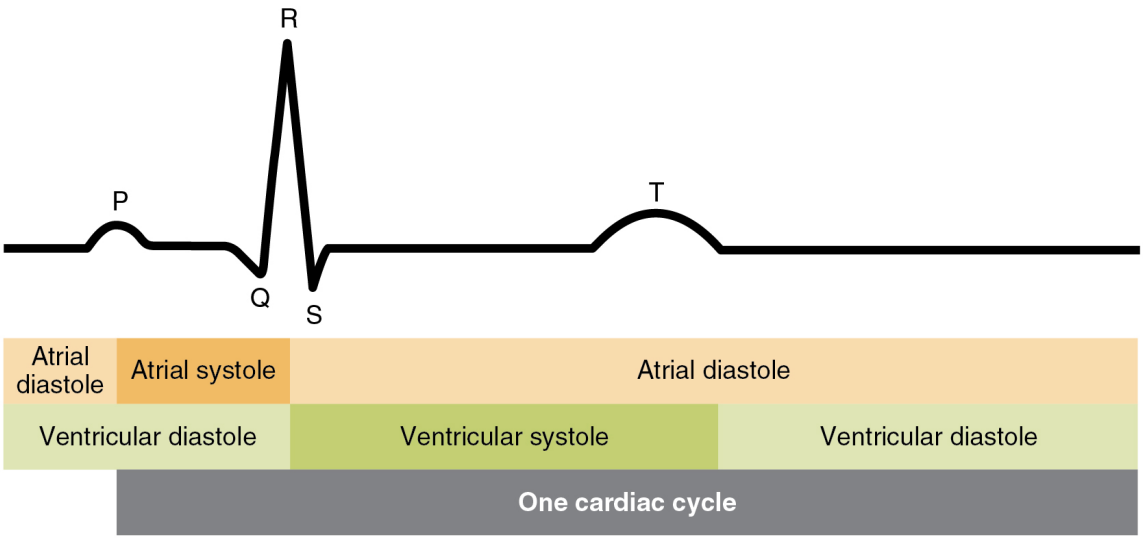

Figure 8.22: Initially, both the atria and ventricles are relaxed (diastole). The P wave represents depolarization of the atria and is followed by atrial contraction (systole). Atrial systole extends until the QRS complex, at which point, the atria relax. The QRS complex represents depolarization of the ventricles and is followed by ventricular contraction. The T wave represents the repolarization of the ventricles and marks the beginning of ventricular relaxation.

8.4.3 Heart Sounds

One of the simplest, yet effective, diagnostic techniques applied to assess the state of a patient's heart is auscultation using a stethoscope.

In a normal, healthy heart, there are only two audible **heart sounds**: Lub and Dup (or Dub). "Lub," or first heart sound is the sound created by the closing of the atrioventricular valves during ventricular contraction . The second heart sound,"Dup" (or "Dub") is the sound of the closing of the semilunar valves during ventricular diastole.

The term **murmur** is used to describe an unusual sound coming from the heart that is caused by the turbulent flow of blood. Murmurs are graded on a scale of 1 to 6, with 1 being the most common, the most difficult sound to detect, and the least serious. The most severe is a 6. Specialized electronic stethoscopes are used to record both normal and abnormal sounds.

When using a stethoscope to listen to the heart sounds, called asculation, it is common practice for the clinician to ask the patient to breathe deeply. This procedure not only allows for listening to airflow, but it may also amplify heart murmurs. Inhalation increases blood flow into the right side of the heart and may increase the amplitude of right-sided heart murmurs. Expiration partially restricts blood flow into the left side of the heart and may amplify left-sided heart murmurs. Figure 8.23 (Stethoscope Placement for Auscultation) indicates proper placement of the bell of the stethoscope to facilitate hearing the sounds.

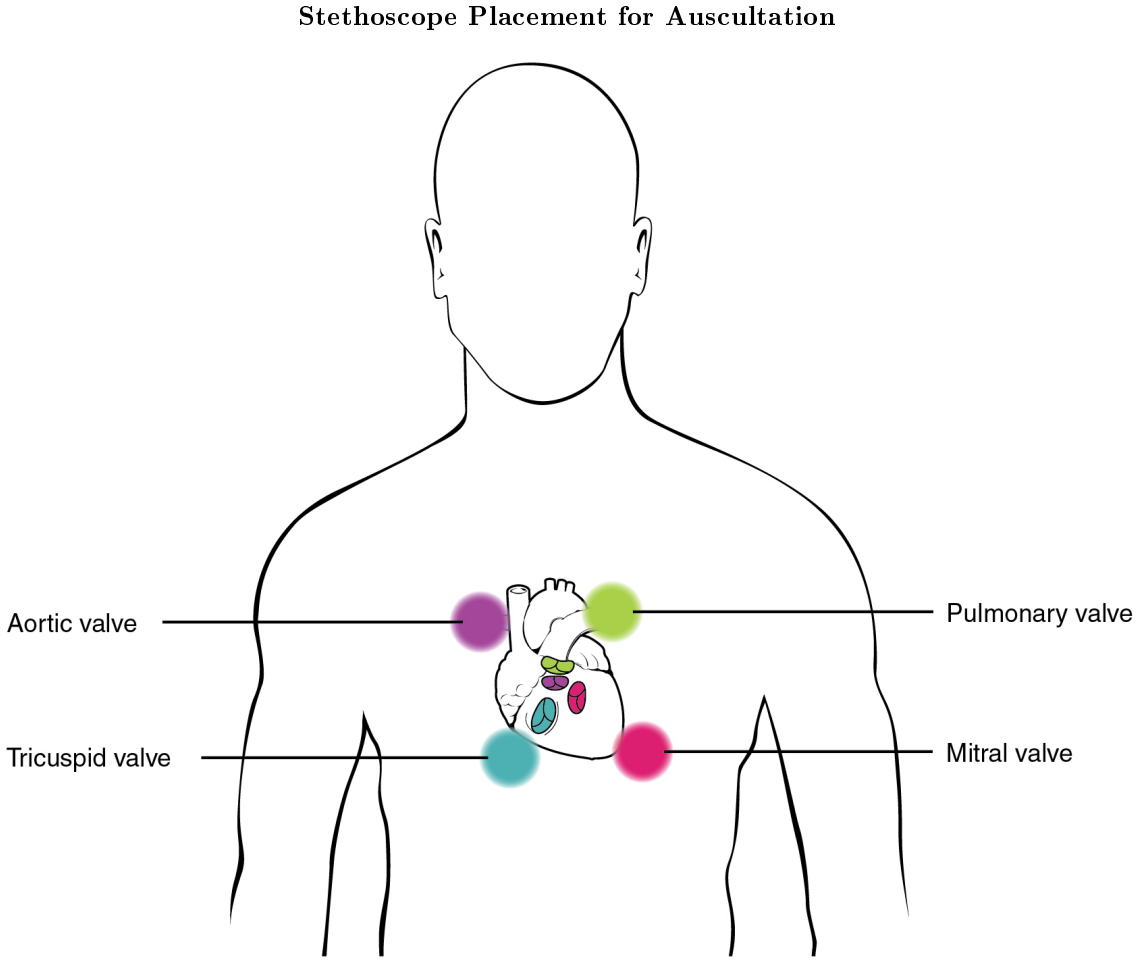

Figure 8.23: Proper placement of the bell of the stethoscope facilitates auscultation. At each of the four locations on the chest, a different valve can be heard.

8.4.4 Chapter Review

The cardiac cycle comprises a complete relaxation and contraction of both the atria and ventricles, and lasts approximately 0.8 seconds. Beginning with all chambers in diastole, blood flows passively from the veins into the atria and past the atrioventricular valves into the ventricles. The atria begin to contract (atrial systole), following depolarization of the atria, and pump blood into the ventricles. The ventricles begin to contract (ventricular systole), raising pressure within the ventricles. When ventricular pressure rises above the pressure in the atria, blood flows toward the atria, producing the first heart sound, lub. As pressure in the ventricles rises above two major arteries, blood pushes open the two semilunar valves and moves into the pulmonary trunk and aorta in the ventricular ejection phase. Following ventricular repolarization, the ventricles begin to relax (ventricular diastole), and pressure within the ventricles drops. As ventricular pressure drops, there is a tendency for blood to flow back into the atria from the major arteries, closing

the two semilunar valves. The second heart sound, dub (or dup) , occurs when the semilunar valves close. When the pressure falls below that of the atria, blood moves from the atria into the ventricles, opening the atrioventricular valves and marking one complete heart cycle. The valves prevent backflow of blood. Failure of the valves to operate properly produces turbulent blood flow within the heart; the resulting heart murmur can often be heard with a stethoscope.

8.4.5 Review Questions

Exercise 8.4.1 *(Solution on p. 215.)*

Most blood enters the ventricle during _ _ _ _ _ _ _ _.

a. atrial systole
b. atrial diastole
c. ventricular systole
d. isovolumic contraction

Exercise 8.4.2 *(Solution on p. 215.)*

The first heart sound represents which portion of the cardiac cycle?

a. atrial systole
b. ventricular systole
c. closing of the atrioventricular valves
d. closing of the semilunar valves

Exercise 8.4.3 *(Solution on p. 215.)*

Ventricular relaxation immediately follows _ _ _ _ _ _ _ _.

a. atrial depolarization
b. ventricular repolarization
c. ventricular depolarization
d. atrial repolarization

8.4.6 Critical Thinking Questions

Exercise 8.4.4 *(Solution on p. 215.)*

Describe one cardiac cycle, beginning with both atria and ventricles relaxed.

Solutions to Exercises in Chapter 8

to Exercise 8.2.1 (p. 194)
D
to Exercise 8.2.2 (p. 194)
A
to Exercise 8.2.3 (p. 194)
A
to Exercise 8.2.4 (p. 195)
C
to Exercise 8.2.5 (p. 195)
B
to Exercise 8.2.6 (p. 195)
When the ventricles contract and pressure begins to rise in the ventricles, there is an initial tendency for blood to flow back (regurgitate) to the atria. However, the papillary muscles also contract, placing tension on the chordae tendineae and holding the atrioventricular valves (tricuspid and mitral) in place to prevent the valves from prolapsing and being forced back into the atria. The semilunar valves (pulmonary and aortic) lack chordae tendineae and papillary muscles, but do not face the same pressure gradients as do the atrioventricular valves. As the ventricles relax and pressure drops within the ventricles, there is a tendency for the blood to flow backward. However, the valves, consisting of reinforced endothelium and connective tissue, fill with blood and seal off the opening preventing the return of blood.
to Exercise 8.2.7 (p. 195)
The pulmonary circuit consists of blood flowing to and from the lungs, whereas the systemic circuit carries blood to and from the entire body. The systemic circuit is far more extensive, consisting of far more vessels and offers much greater resistance to the flow of blood, so the heart must generate a higher pressure to overcome this resistance. This can be seen in the thickness of the myocardium in the ventricles.
to Exercise 8.3.1 (p. 208)
C
to Exercise 8.3.2 (p. 208)
D
to Exercise 8.3.3 (p. 208)
It ensures sufficient time for the atrial muscle to contract and pump blood into the ventricles prior to the impulse being conducted into the lower chambers.
to Exercise 8.4.1 (p. 214)
B
to Exercise 8.4.2 (p. 214)
C
to Exercise 8.4.3 (p. 214)
B
to Exercise 8.4.4 (p. 214)
The cardiac cycle comprises a complete relaxation and contraction of both the atria and ventricles, and lasts approximately 0.8 seconds. Beginning with all chambers in diastole, blood flows passively from the veins into the atria and past the atrioventricular valves into the ventricles. The atria begin to contract following depolarization of the atria and pump blood into the ventricles. The ventricles begin to contract, raising pressure within the ventricles. When ventricular pressure rises above the pressure in the two major arteries, blood pushes open the two semilunar valves and moves into the pulmonary trunk and aorta in the ventricular ejection phase. Following ventricular repolarization, the ventricles begin to relax, and pressure within the ventricles drops. When the pressure falls below that of the atria, blood moves from the atria into the ventricles, opening the atrioventricular valves and marking one complete heart cycle.

Chapter 9

Blood Vessels

9.1 Introduction to the Cardiovascular System - Blood Vessels and Circulation[1]

Blood Vessels

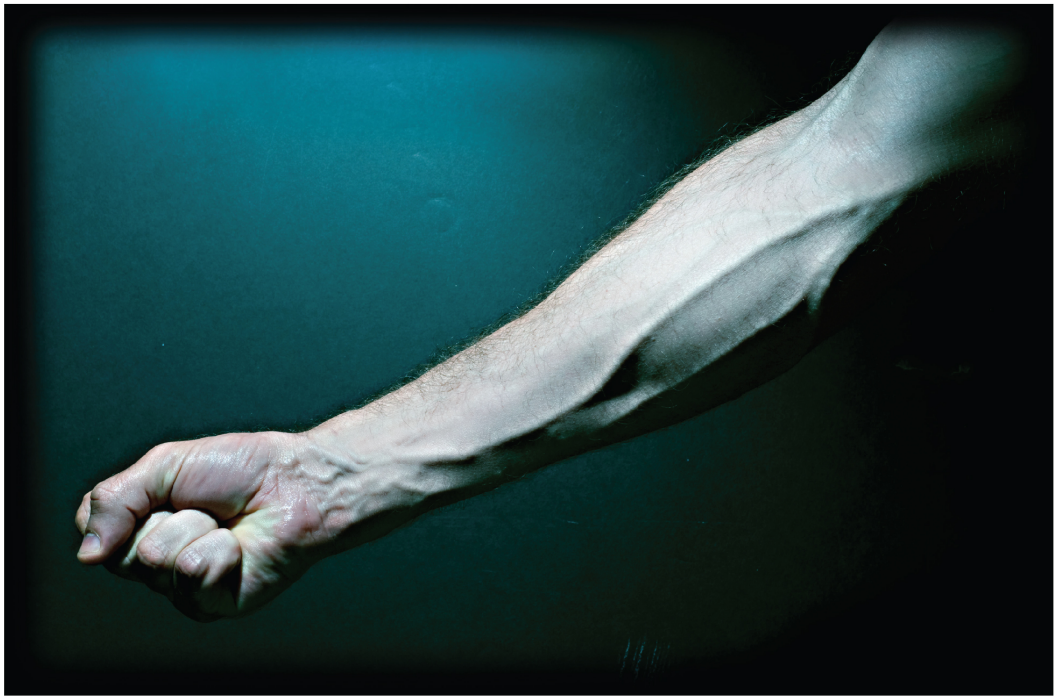

Figure 9.1: While most blood vessels are located deep from the surface and are not visible, the superficial veins of the upper limb provide an indication of the extent, prominence, and importance of these structures to the body. (credit: Colin Davis)

[1] This content is available online at <http://cnx.org/content/m57996/1.2/>.

NOTE: After studying this chapter, you will be able to:

- Compare and contrast the anatomical structure of arteries, arterioles, capillaries, venules, and veins
- Accurately describe the forces that account for capillary exchange
- Describe the interaction of the cardiovascular system with other body systems
- Identify and describe the hepatic portal system

In this chapter, you will learn about the vascular part of the cardiovascular system, that is, the vessels that transport blood throughout the body and provide the physical site where gases, nutrients, and other substances are exchanged with body cells. When vessel functioning is reduced, blood-borne substances do not circulate effectively throughout the body. As a result, tissue injury occurs, metabolism is impaired, and the functions of every bodily system are threatened.

9.2 Structure and Function of Blood Vessels[2]

Blood is carried through the body via blood vessels. An artery is a blood vessel that carries blood away from the heart, where it branches into ever-smaller vessels. Eventually, the smallest arteries, vessels called arterioles, further branch into tiny capillaries, where nutrients and wastes are exchanged, and then combine with other vessels that exit capillaries to form venules, small blood vessels that carry blood to a vein, a larger blood vessel that returns blood to the heart.

Arteries and veins transport blood in two distinct circuits: the systemic circuit and the pulmonary circuit (Figure 9.2 (Cardiovascular Circulation)). Systemic arteries provide blood rich in oxygen to the body's tissues. The blood returned to the heart through systemic veins has less oxygen, since much of the oxygen carried by the arteries has been delivered to the cells. In contrast, in the pulmonary circuit, arteries carry blood low in oxygen exclusively to the lungs for gas exchange. Pulmonary veins then return freshly oxygenated blood from the lungs to the heart to be pumped back out into systemic circulation. Although arteries and veins differ structurally and functionally, they share certain features.

[2]This content is available online at <http://cnx.org/content/m57997/1.2/>.

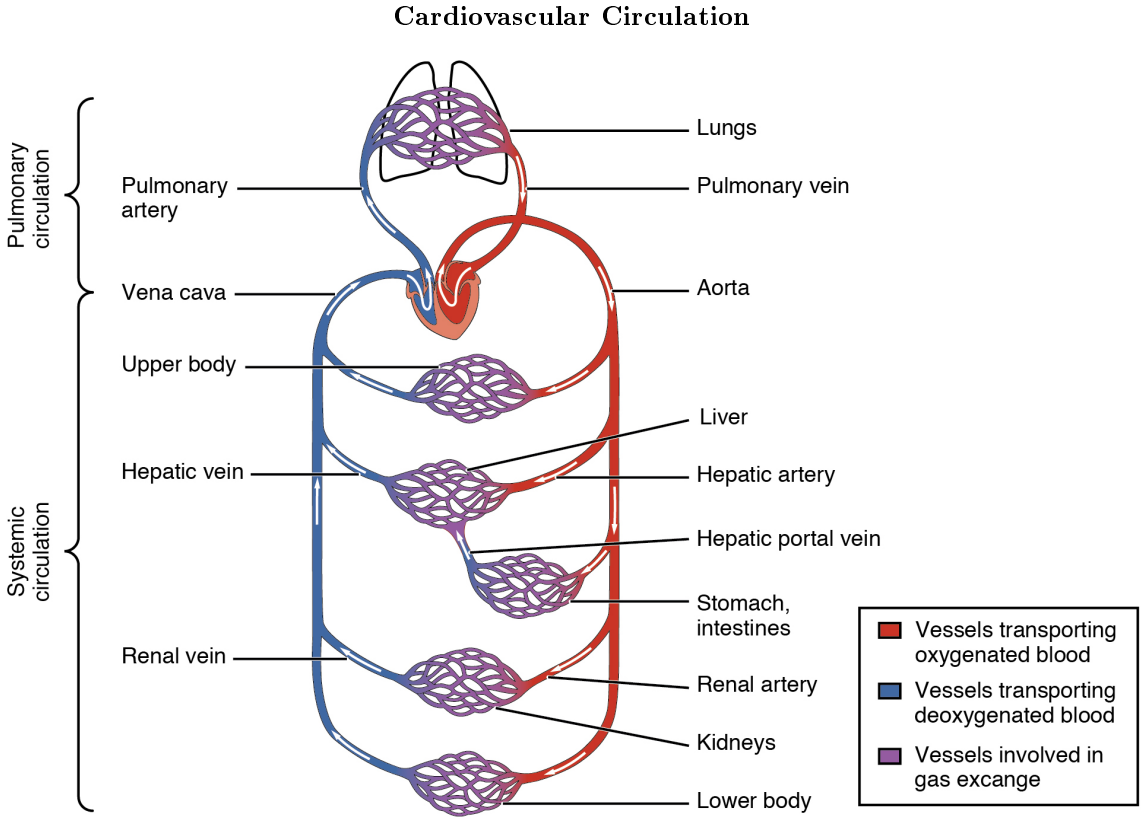

Figure 9.2: The pulmonary circuit moves blood from the right side of the heart to the lungs and back to the heart. The systemic circuit moves blood from the left side of the heart to the head and body and returns it to the right side of the heart to repeat the cycle. The arrows indicate the direction of blood flow, and the colors show the relative levels of oxygen concentration.

9.2.1 Shared Structures

Different types of blood vessels vary slightly in their structures, but they share the same general features. Arteries and arterioles have thicker walls than veins and venules because they are closer to the heart and receive blood that is surging at a far greater pressure (Figure 9.3 (Structure of Blood Vessels)). Each type of vessel has a **lumen**—a hollow passageway through which blood flows. Arteries have smaller lumens than veins, a characteristic that helps to maintain the pressure of blood moving through the system. Together, their thicker walls and smaller diameters give arterial lumens a more rounded appearance in cross section than the lumens of veins.

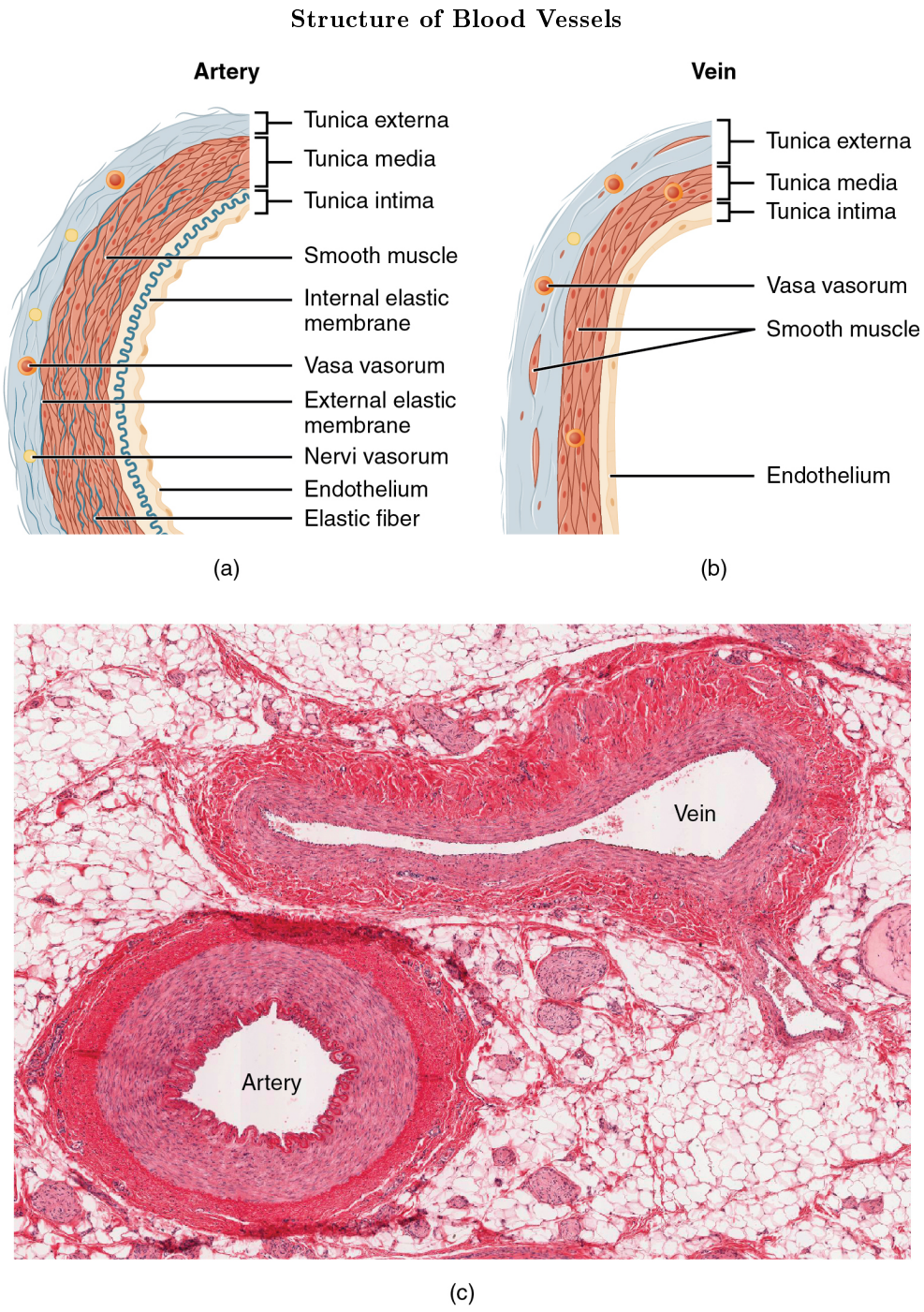

Figure 9.3: (a) Arteries and (b) veins share the same general features, but the walls of arteries are much thicker because of the higher pressure of the blood that flows through them. (c) A micrograph shows the relative differences in thickness. LM × 160. (Micrograph provided by the Regents of the University of Michigan Medical School ©2012)

By the time blood has passed through capillaries and entered venules, the pressure initially exerted upon it by heart contractions has diminished. In other words, in comparison to arteries, venules and veins withstand a much lower pressure from the blood that flows through them. Their walls are considerably thinner and their lumens are correspondingly larger in diameter, allowing more blood to flow with less vessel resistance. In addition, many veins of the body, particularly those of the limbs, contain valves that assist the unidirectional flow of blood toward the heart. This is critical because blood flow becomes sluggish in the extremities, as a result of the lower pressure and the effects of gravity.

9.2.2 Capillaries

A **capillary** is a microscopic channel that supplies blood to the tissues themselves. Exchange of gases and other substances occurs in the capillaries between the blood and the surrounding cells and their tissue fluid (interstitial fluid). The diameter of a capillary lumen ranges from 5–10 micrometers; the smallest are just barely wide enough for an erythrocyte to squeeze through.

9.2.3 Chapter Review

Blood pumped by the heart flows through a series of vessels known as arteries, arterioles, capillaries, venules, and veins before returning to the heart. Arteries transport blood away from the heart and branch into smaller vessels, forming arterioles. Arterioles distribute blood to capillary beds, the sites of exchange with the body tissues. Capillaries lead back to small vessels known as venules that flow into the larger veins and eventually back to the heart.

The arterial system is a relatively high-pressure system, so arteries have thick walls with more elastic fibers that appear round in cross section. The venous system is a lower-pressure system, containing veins that have larger lumens and thinner walls. They often appear flattened.

9.2.4 Review Questions

Exercise 9.2.1 *(Solution on p. 223.)*

Closer to the heart, arteries would be expected to have a higher percentage of _____ to help deal with the increased pressure.

a. endothelium
b. smooth muscle fibers
c. elastic fibers
d. collagenous fibers

Exercise 9.2.2 *(Solution on p. 223.)*

Which of the following best describes veins?

a. thick walled, small lumens, low pressure, lack valves
b. thin walled, large lumens, low pressure, have valves
c. thin walled, small lumens, high pressure, have valves
d. thick walled, large lumens, high pressure, lack valves

9.2.5 Critical Thinking Questions

Exercise 9.2.3 *(Solution on p. 223.)*

Cocaine use causes vasoconstriction. Is this likely to increase or decrease blood pressure, and why?

Solutions to Exercises in Chapter 9

to Exercise 9.2.1 (p. 222)
C
to Exercise 9.2.2 (p. 222)
B
to Exercise 9.2.3 (p. 222)
Vasoconstriction causes the lumens of blood vessels to narrow. This increases the pressure of the blood flowing within the vessel.

Available for free at Connexions <http://cnx.org/content/col11903/1.3>

Chapter 10

Respiratory System

10.1 Introduction to the Respiratory System[1]

Mountain Climbers

Figure 10.1: The thin air at high elevations can strain the human respiratory system. (credit: "borte-scristian"/flickr.com)

[1] This content is available online at <http://cnx.org/content/m57998/1.1/>.

NOTE: After studying this chapter, you will be able to:

- List the structures of the respiratory system
- List the major functions of the respiratory system
- Outline the forces that allow for air movement into and out of the lungs
- Outline the process of gas exchange
- Summarize the process of oxygen and carbon dioxide transport within the respiratory system
- Discuss how the respiratory system responds to exercise

Hold your breath. Really! See how long you can hold your breath as you continue reading...How long can you do it? Chances are you are feeling uncomfortable already. A typical human cannot survive without breathing for more than 3 minutes, and even if you wanted to hold your breath longer, your autonomic nervous system would take control. This is because every cell in the body needs to run the oxidative stages of cellular respiration, the process by which energy is produced in the form of adenosine triphosphate (ATP). For oxidative phosphorylation to occur, oxygen is used as a reactant and carbon dioxide is released as a waste product. You may be surprised to learn that although oxygen is a critical need for cells, it is actually the accumulation of carbon dioxide that primarily drives your need to breathe. Carbon dioxide is exhaled and oxygen is inhaled through the respiratory system, which includes muscles to move air into and out of the lungs, passageways through which air moves, and microscopic gas exchange surfaces covered by capillaries. The circulatory system transports gases from the lungs to tissues throughout the body and vice versa. A variety of diseases can affect the respiratory system, such as asthma, emphysema, chronic obstruction pulmonary disorder (COPD), and lung cancer. All of these conditions affect the gas exchange process and result in labored breathing and other difficulties.

10.2 Organs and Structures of the Respiratory System[2]

The major organs of the respiratory system function primarily to provide oxygen to body tissues for cellular respiration, remove the waste product carbon dioxide, and help to maintain acid-base balance. Portions of the respiratory system are also used for non-vital functions, such as sensing odors, speech production, and coughing (Figure 10.2 (Major Respiratory Structures)).

[2]This content is available online at <http://cnx.org/content/m57999/1.2/>.

Major Respiratory Structures

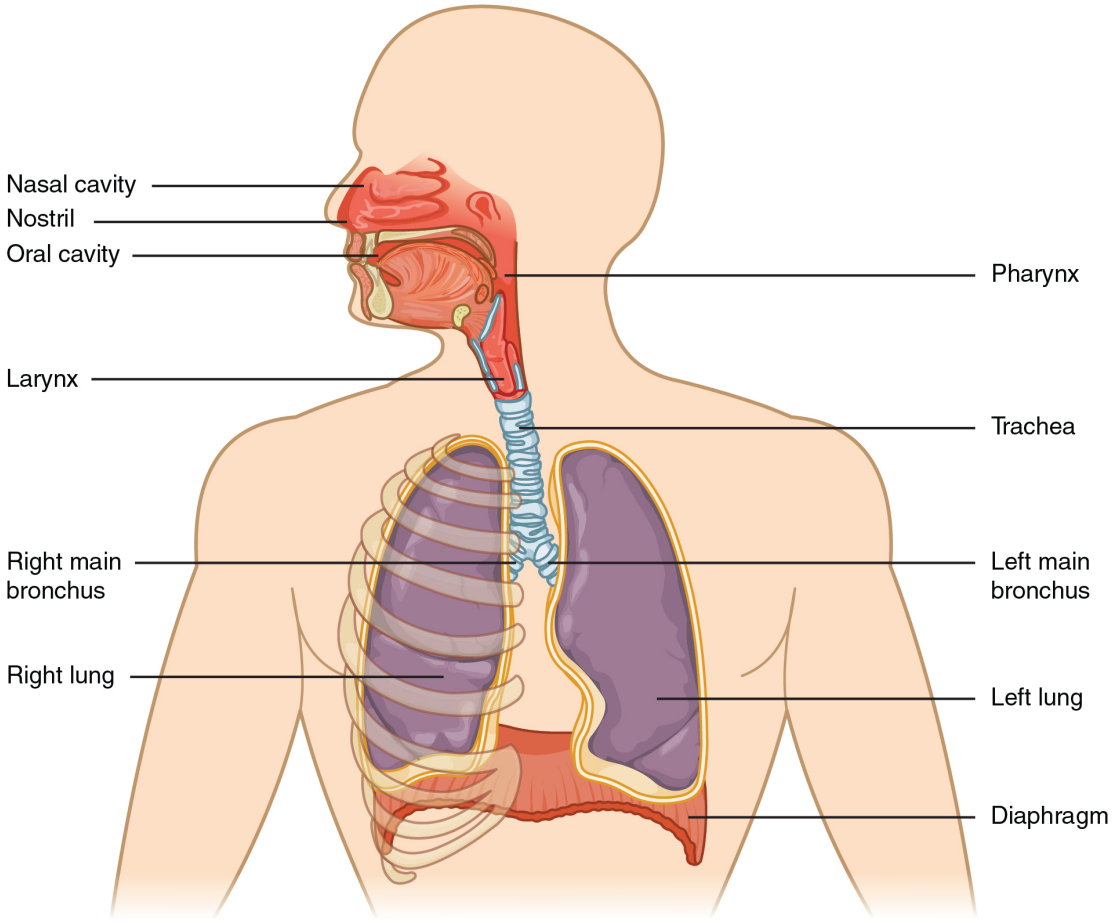

Figure 10.2: The major respiratory structures span the nasal cavity to the diaphragm.

10.2.1

10.2.1.1 The Nose and its Adjacent Structures

The major entrance and exit for the respiratory system is through the nose, via the nostrils. The inhaled air enters into the nasal cavity, which is separated into left and right sections by the nasal septum. The wall of the nasal cavity has three bony projections, called the superior, middle, and inferior nasal conchae. Conchae serve to increase the surface area of the nasal cavity and to disrupt the flow of air as it enters the nose, causing air to bounce along the epithelium, where it is filtered, warmed, and humidified. Air exits the nasal cavities and moves into the pharynx.

Several bones that help form the walls of the nasal cavity have air-containing spaces called the sinuses, which serve to warm and humidify incoming air. Sinuses are lined with a mucosa. Each **sinus** is named

for its associated bone: frontal sinus, maxillary sinus, sphenoidal sinus, and ethmoidal sinus. The sinuses produce mucus and lighten the weight of the skull.

Portions of the nasal cavities are lined with mucous membranes, containing sebaceous glands and hair follicles that serve to prevent the passage of large debris, such as dirt, through the nasal cavity.

The conchae and sinuses are lined by **respiratory epithelium** composed of pseudostratified ciliated columnar epithelium (Figure 10.3 (Pseudostratified Ciliated Columnar Epithelium)). The epithelium contains goblet cells, one of the specialized, columnar epithelial cells that produce mucus to trap debris. The cilia of the respiratory epithelium help remove the mucus and debris from the nasal cavity with a constant beating motion, sweeping materials towards the throat to be swallowed. Interestingly, cold air slows the movement of the cilia, resulting in accumulation of mucus that may in turn lead to a runny nose during cold weather. This moist epithelium functions to warm and humidify incoming air. Capillaries located just beneath the nasal epithelium warm the incoming air.

Pseudostratified Ciliated Columnar Epithelium

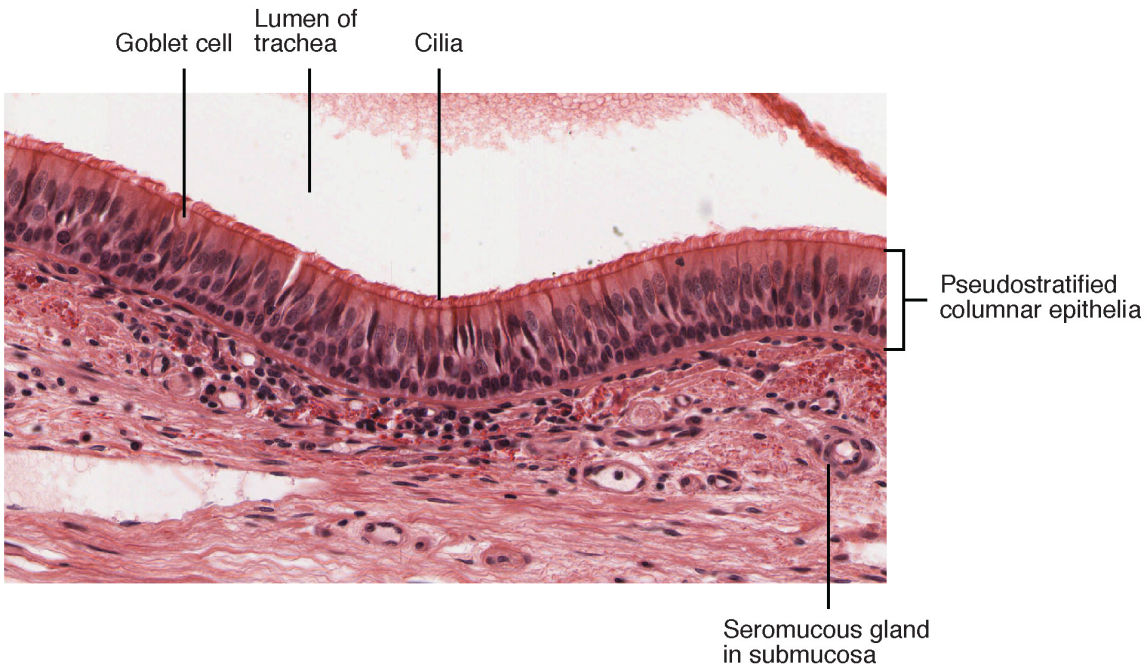

Figure 10.3: Respiratory epithelium is pseudostratified ciliated columnar epithelium. Seromucous glands provide lubricating mucus. LM × 680. (Micrograph provided by the Regents of University of Michigan Medical School ©2012)

10.2.1.2 Pharynx

The **pharynx** is a tube formed by skeletal muscle and lined by mucous membrane that is continuous with that of the nasal cavities. The pharynx is divided into three major regions: the nasopharynx, the oropharynx, and the laryngopharynx (Figure 10.4 (Divisions of the Pharynx)).

Divisions of the Pharynx

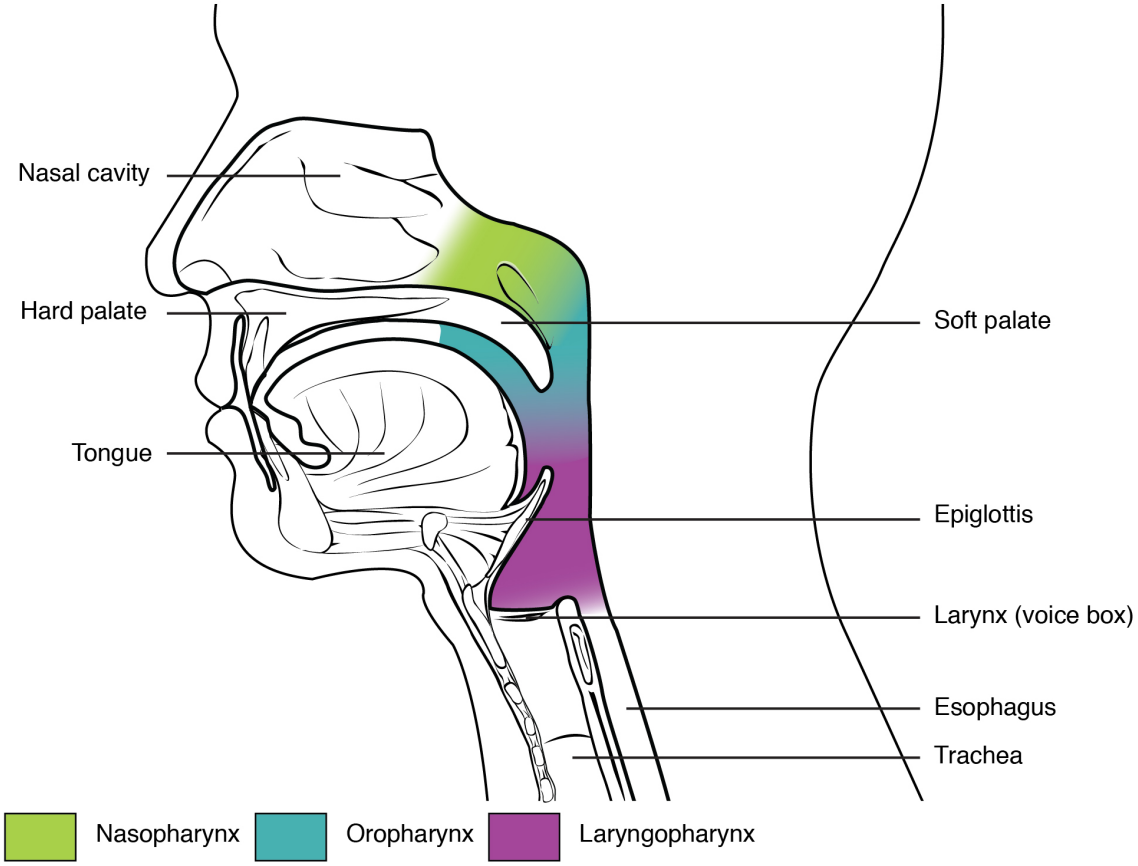

Figure 10.4: The pharynx is divided into three regions: the nasopharynx, the oropharynx, and the laryngopharynx.

The **nasopharynx** is flanked by the conchae of the nasal cavity, and it serves only as an airway. At the top of the nasopharynx are the pharyngeal tonsils. A **pharyngeal tonsil**, also called an adenoid, is a collection of tissue similar to a lymph node that lies at the top portion of the nasopharynx. The function of the pharyngeal tonsil is not well understood, but it contains a rich supply of lymphocytes (a type of WBC) and is covered with ciliated epithelium that traps and destroys invading pathogens that enter during inhalation. The pharyngeal tonsils are large in children, but interestingly, tend to regress with age and may even disappear. The uvula is a small bulbous, teardrop-shaped structure located at the apex of the soft palate. Both the uvula and soft palate move like a pendulum during swallowing, swinging upward to close off the nasopharynx to prevent ingested materials from entering the nasal cavity. In addition, auditory (Eustachian) tubes that connect to each middle ear cavity open into the nasopharynx. This connection is why colds often lead to ear infections.

The **oropharynx** is a passageway for both air and food. It contains two distinct sets of tonsils, the palatine and lingual tonsils. Similar to the pharyngeal tonsil, the palatine and lingual tonsils are composed of lymphoid tissue, and trap and destroy pathogens entering the body through the oral or nasal cavities.

The **laryngopharynx** continues the route for ingested material and air until its inferior end, where the digestive and respiratory systems split. To the front,the laryngopharynx opens into the larynx, whereas to the back, it enters the esophagus.

10.2.1.3 Larynx

The **larynx** is a structure below the laryngopharynx that connects the pharynx to the trachea and helps regulate the volume of air that enters and leaves the lungs (Figure 10.5 (Larynx)). The structure of the larynx is formed by several pieces of cartilage.

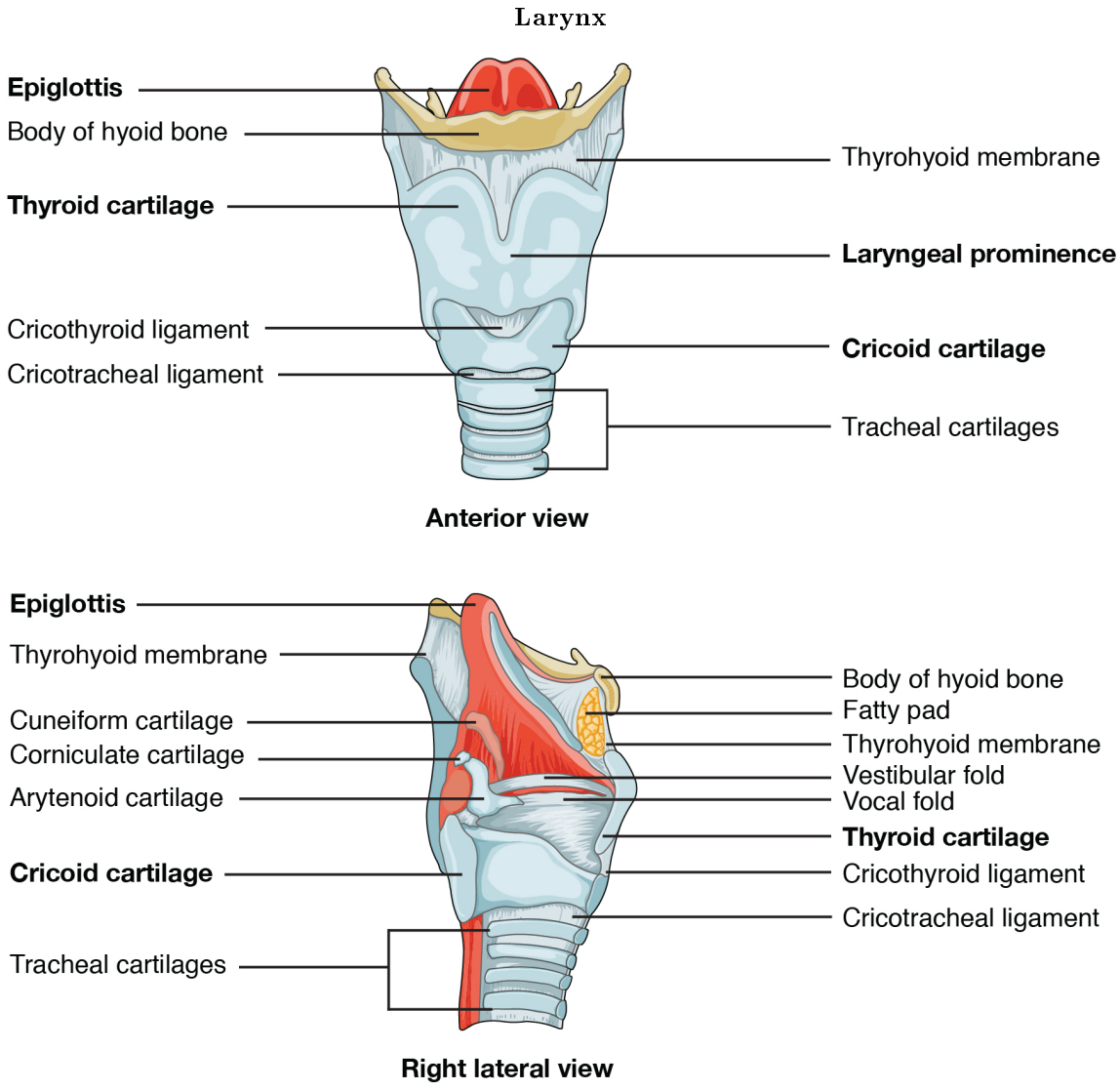

Figure 10.5: The larynx extends from the laryngopharynx and the hyoid bone to the trachea.

The **epiglottis**, attached to the thyroid cartilage, is a very flexible piece of elastic cartilage that covers the opening of the trachea (see). When in the "closed" position, the unattached end of the epiglottis rests on the glottis. The **glottis** is composed of the vestibular folds, the true vocal cords, and the space between these folds (Figure 10.6 (Vocal Cords)). The inner edges of the true vocal cords are free, allowing oscillation to produce sound. The size of the membranous folds of the true vocal cords differs between individuals, producing voices with different pitch ranges. Folds in males tend to be larger than those in females, which create a deeper voice. The act of swallowing causes the pharynx and larynx to lift upward, allowing the pharynx to expand and the epiglottis of the larynx to swing downward, closing the opening to the trachea. These movements produce a larger area for food to pass through, while preventing food and beverages from entering the trachea.

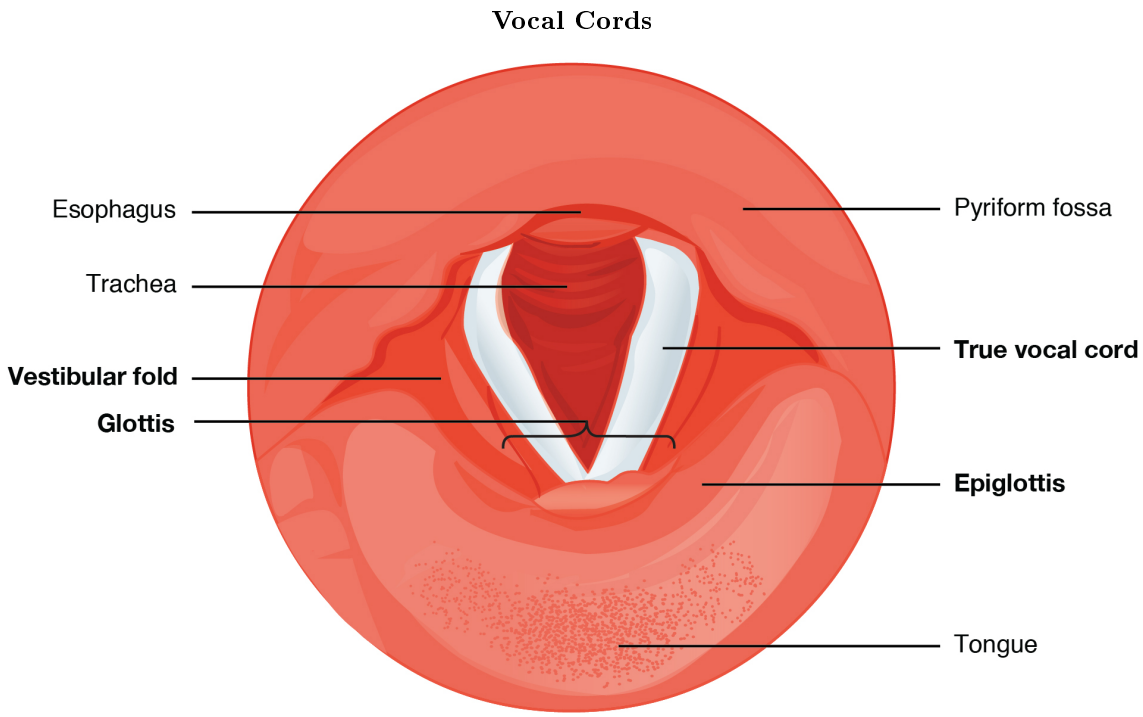

Figure 10.6: The true vocal cords and vestibular folds of the larynx are viewed looking down from the laryngopharynx.

10.2.1.4 Trachea

The trachea (windpipe) extends from the larynx toward the lungs (Figure 10.7 (Trachea)**a**). The **trachea** is formed by 16 to 20 stacked pieces of cartilage that are connected by connective tissue. The fibroelastic membrane of the trachea allows it to stretch and expand slightly during inhalation and exhalation, whereas the rings of cartilage provide structural support and prevent the trachea from collapsing.

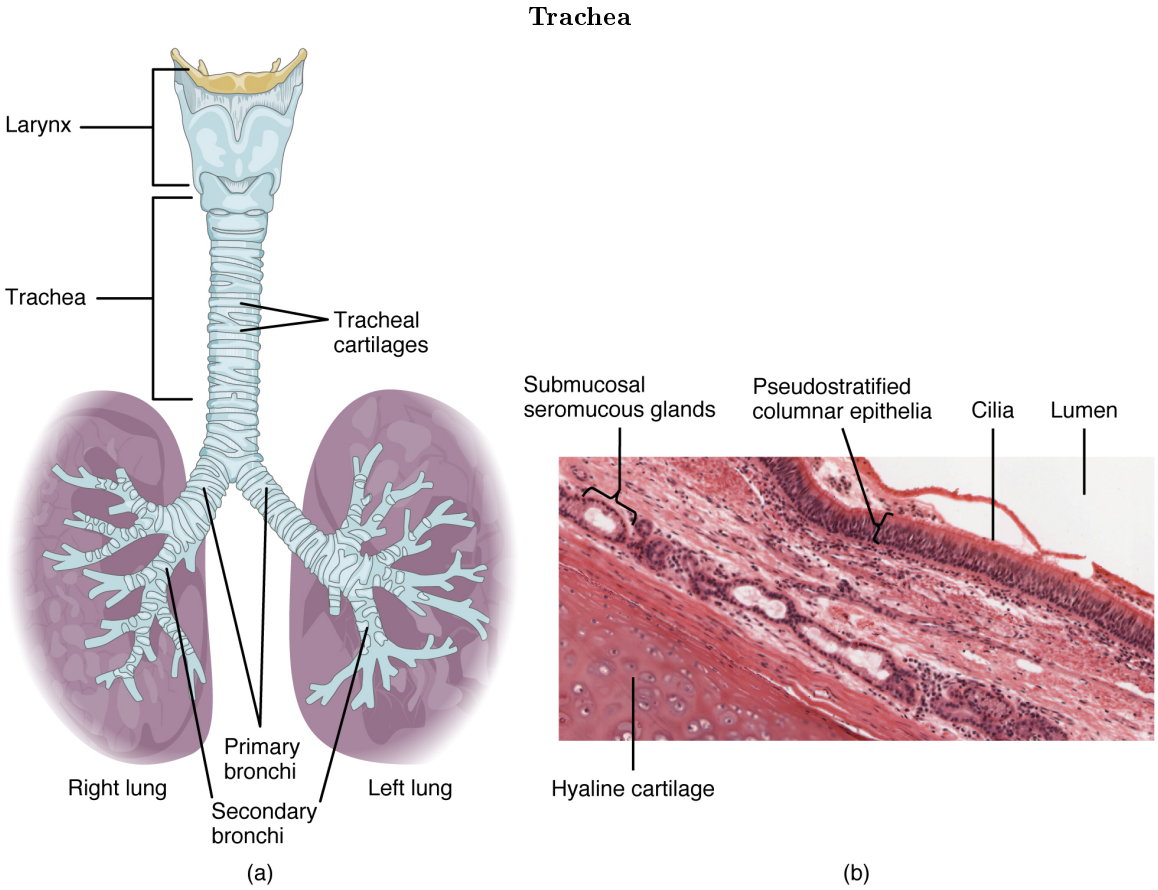

Figure 10.7: (a) The tracheal tube is formed by stacked, C-shaped pieces of hyaline cartilage. (b) The layer visible in this cross-section of tracheal wall tissue between the hyaline cartilage and the lumen of the trachea is the mucosa, which is composed of pseudostratified ciliated columnar epithelium that contains goblet cells. LM × 1220. (Micrograph provided by the Regents of University of Michigan Medical School ©2012)

10.2.1.5 Bronchi and Bronchioles

The right and left primary bronchi branch off the trachea towards the right and left lungs. The primary bronchi further branch into the secondary and tertiary bronchi. A **bronchiole** branches from the tertiary bronchi. Bronchioles, which are about 1 mm in diameter, further branch until they become the tiny terminal bronchioles, which lead to the structures of gas exchange. There are more than 1000 terminal bronchioles in each lung. The muscular walls of the bronchioles do not contain cartilage like those of the bronchi. However, smooth muscle can change the size of the tubing to increase or decrease airflow through it.

10.2.2 Respiratory Gas Exchange

The respiratory zone includes structures that are directly involved in gas exchange. The respiratory zone begins where the terminal bronchioles join a **respiratory bronchiole**, the smallest type of bronchiole (Figure 10.8 (Respiratory Zone)), which then leads to an alveolar duct, opening into a cluster of alveoli.

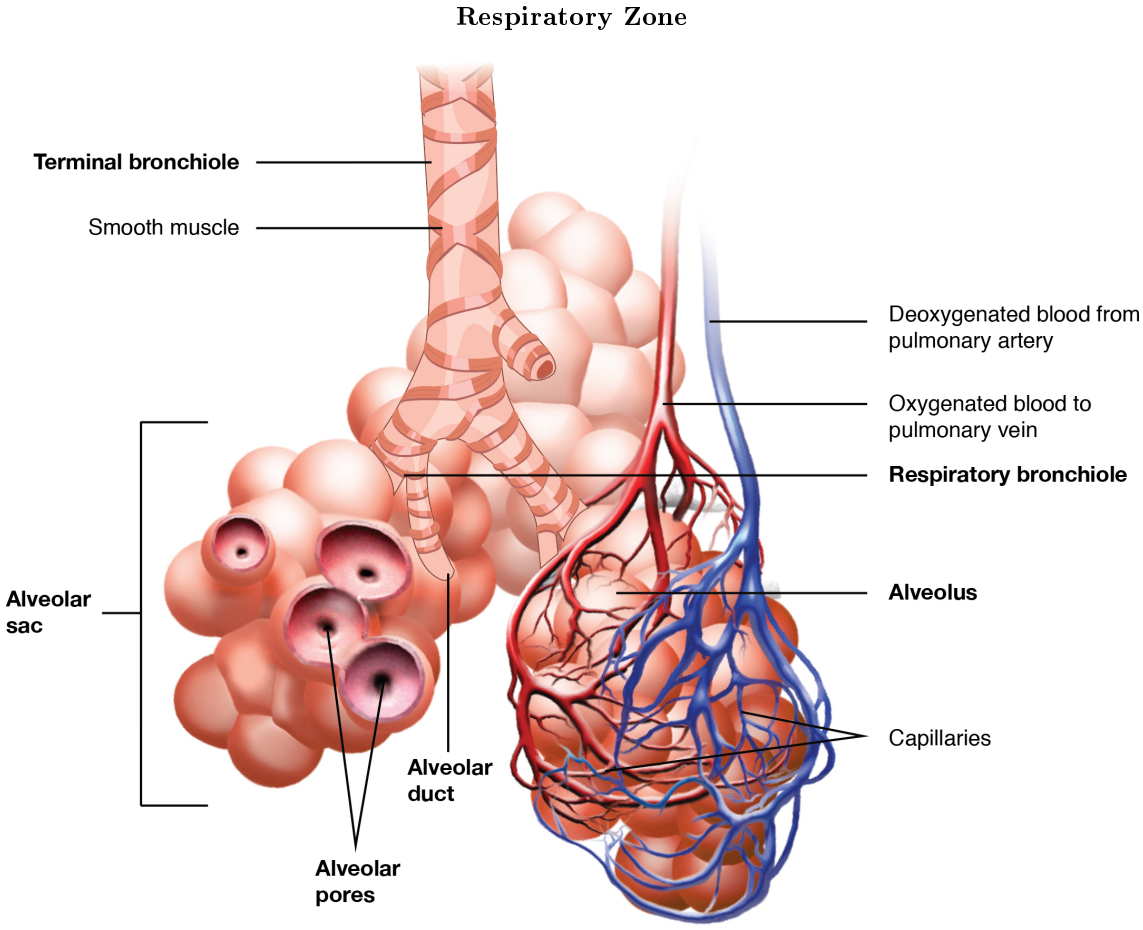

Figure 10.8: Bronchioles lead to alveolar sacs in the respiratory zone, where gas exchange occurs.

10.2.2.1 Alveoli

An **alveolar sac** is a cluster of many individual alveoli that are responsible for gas exchange. An alveolus is approximately 200 μm in diameter with elastic walls that allow the alveolus to stretch during air intake, which greatly increases the surface area available for gas exchange. Alveoli are connected to their neighbors by **alveolar pores**, which help maintain equal air pressure throughout the alveoli and lung (Figure 10.9 (Structures of the Respiratory Zone)).

Structures of the Respiratory Zone

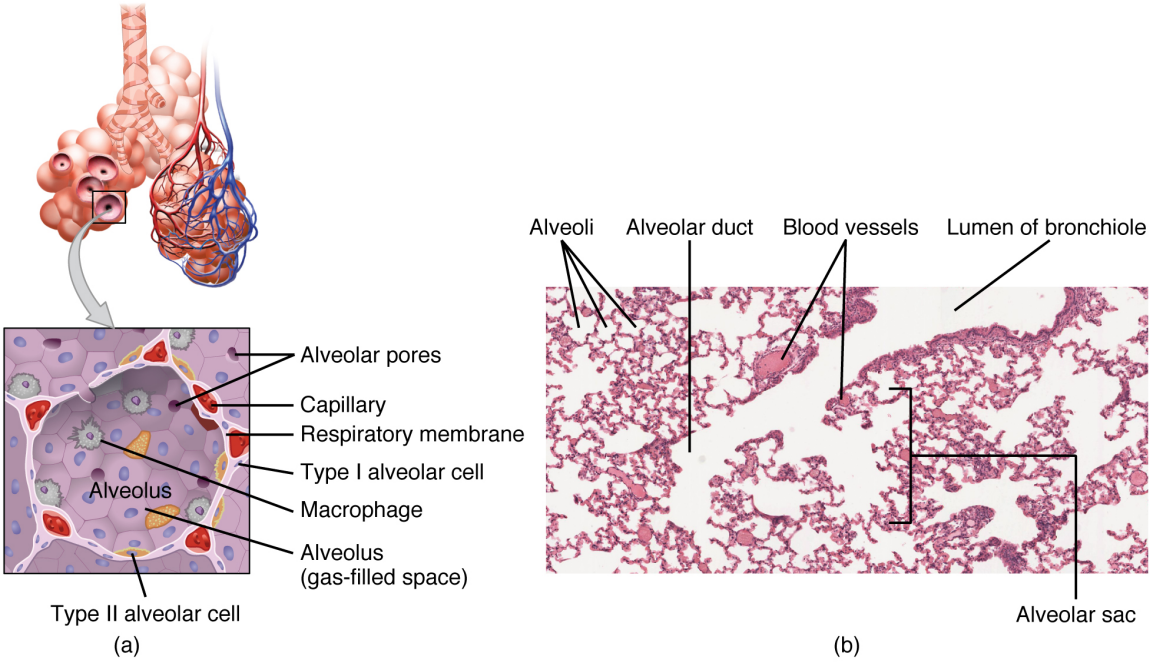

Figure 10.9: (a) The alveolus is responsible for gas exchange. (b) A micrograph shows the alveolar structures within lung tissue. LM × 178. (Micrograph provided by the Regents of University of Michigan Medical School ©2012)

: **Respiratory System Disorder: Asthma**

Asthma is common condition that affects the lungs in both adults and children. Approximately 8.2 percent of adults (18.7 million) and 9.4 percent of children (7 million) in the United States suffer from asthma. In addition, asthma is the most frequent cause of hospitalization in children.

Asthma is a chronic disease characterized by inflammation and fluid accumulation of the airway, and bronchospasms (that is, constriction of the bronchioles), which can inhibit air from entering the lungs. In addition, excessive mucus secretion can occur, which further contributes to blockage of the airway.

Bronchospasms occur periodically and lead to an "asthma attack." An attack may be triggered by environmental factors such as dust, pollen, pet hair, or dander, changes in the weather, mold, tobacco smoke, and respiratory infections, or by exercise and stress.

Symptoms of an asthma attack involve coughing, shortness of breath, wheezing, and tightness of the chest. Symptoms of a severe asthma attack that requires immediate medical attention would include difficulty breathing that results in blue (cyanotic) lips or face, confusion, drowsiness, a rapid pulse, sweating, and severe anxiety. The severity of the condition, frequency of attacks, and identified triggers influence the type of medication that an individual may require. Longer-term treatments are used for those with more severe asthma. Short-term, fast-acting drugs that are

used to treat an asthma attack are typically administered via an inhaler. For young children or individuals who have difficulty using an inhaler, asthma medications can be administered via a nebulizer.

10.2.3 Interactive Link Questions

Exercise 10.2.1 *(Solution on p. 251.)*

Visit this site[3] to learn more about what happens during an asthma attack. What are the three changes that occur inside the airways during an asthma attack?

10.2.4 Review Questions

Exercise 10.2.2 *(Solution on p. 251.)*

Which of the following anatomical structures is at the site of respiratory gas exchange?

a. pharynx
b. nasal cavity
c. alveoli
d. bronchi

Exercise 10.2.3 *(Solution on p. 251.)*

What is the function of the conchae in the nasal cavity?

a. increase surface area
b. exchange gases
c. maintain surface tension
d. maintain air pressure

Exercise 10.2.4 *(Solution on p. 251.)*

Which of the following are structural features of the trachea?

a. C-shaped cartilage
b. smooth muscle fibers
c. cilia
d. all of the above

10.2.5 Critical Thinking Questions

Exercise 10.2.5 *(Solution on p. 251.)*

If a person sustains an injury to the epiglottis, what would be the physiological result?

[3] http://openstaxcollege.org/l/asthma

10.2.6 References

Bizzintino J, Lee WM, Laing IA, Vang F, Pappas T, Zhang G, Martin AC, Khoo SK, Cox DW, Geelhoed GC, et al. Association between human rhinovirus C and severity of acute asthma in children. Eur Respir J [Internet]. 2010 [cited 2013 Mar 22]; 37(5):1037–1042. Available from: http://erj.ersjournals.com/gca?submit=Go&gca=erj%3B37%2F5%2F1037&allch=[4]

Kumar V, Ramzi S, Robbins SL. Robbins Basic Pathology. 7th ed. Philadelphia (PA): Elsevier Ltd; 2005.

Martin RJ, Kraft M, Chu HW, Berns, EA, Cassell GH. A link between chronic asthma and chronic infection. J Allergy Clin Immunol [Internet]. 2001 [cited 2013 Mar 22]; 107(4):595-601. Available from: http://erj.ersjournals.com/gca?submit=Go&gca=erj%3B37%2F5%2F1037&allch=[5]

10.3 Gas Pressure, Volume, and Breathing[6]

Breathing can be described as the movement of air into (inspiration/inhalation) and out of the lungs (expiration/exhalation). The major mechanism that drive breathing is differences between atmospheric pressure and the air pressure within the lungs.

10.3.1 Relationship Between Pressure and Volume

10.3.1.1

Inspiration (or inhalation) and expiration (or exhalation) are dependent on the differences in pressure between the atmosphere and the lungs. In a gas, pressure is a force created by the movement of gas molecules that are confined. For example, a certain number of gas molecules in a two-liter container has more room than the same number of gas molecules in a one-liter container (Figure 10.10 (Boyle's Law)). In this case, the force exerted by the movement of the gas molecules against the walls of the two-liter container is lower than the force exerted by the gas molecules in the one-liter container. Therefore, the pressure is lower in the two-liter container and higher in the one-liter container. At a constant temperature, changing the volume occupied by the gas changes the pressure, as does changing the number of gas molecules. **Boyle's law** describes the relationship between volume and pressure in a gas at a constant temperature. Boyle discovered that the pressure of a gas is inversely proportional to its volume: If volume increases, pressure decreases. Likewise, if volume decreases, pressure increases. Pressure and volume are inversely related ($P = \mathrm{k}/V$). Therefore, the pressure in the one-liter container (one-half the volume of the two-liter container) would be twice the pressure in the two-liter container. Boyle's law is expressed by the following formula:

$$P_1V_1 = P_2V_2 \tag{10.1}$$

In this formula, P_1 represents the initial pressure and V_1 represents the initial volume, whereas the final pressure and volume are represented by P_2 and V_2, respectively. If the two- and one-liter containers were connected by a tube and the volume of one of the containers were changed, then the gases would move from higher pressure (lower volume) to lower pressure (higher volume).

[4] http://erj.ersjournals.com/gca?submit=Go&gca=erj%3B37%2F5%2F1037&allch=
[5] http://www.jacionline.org/article/S0091-6749(01)31561-0/fulltext
[6] This content is available online at <http://cnx.org/content/m58000/1.3/>.

Boyle's Law

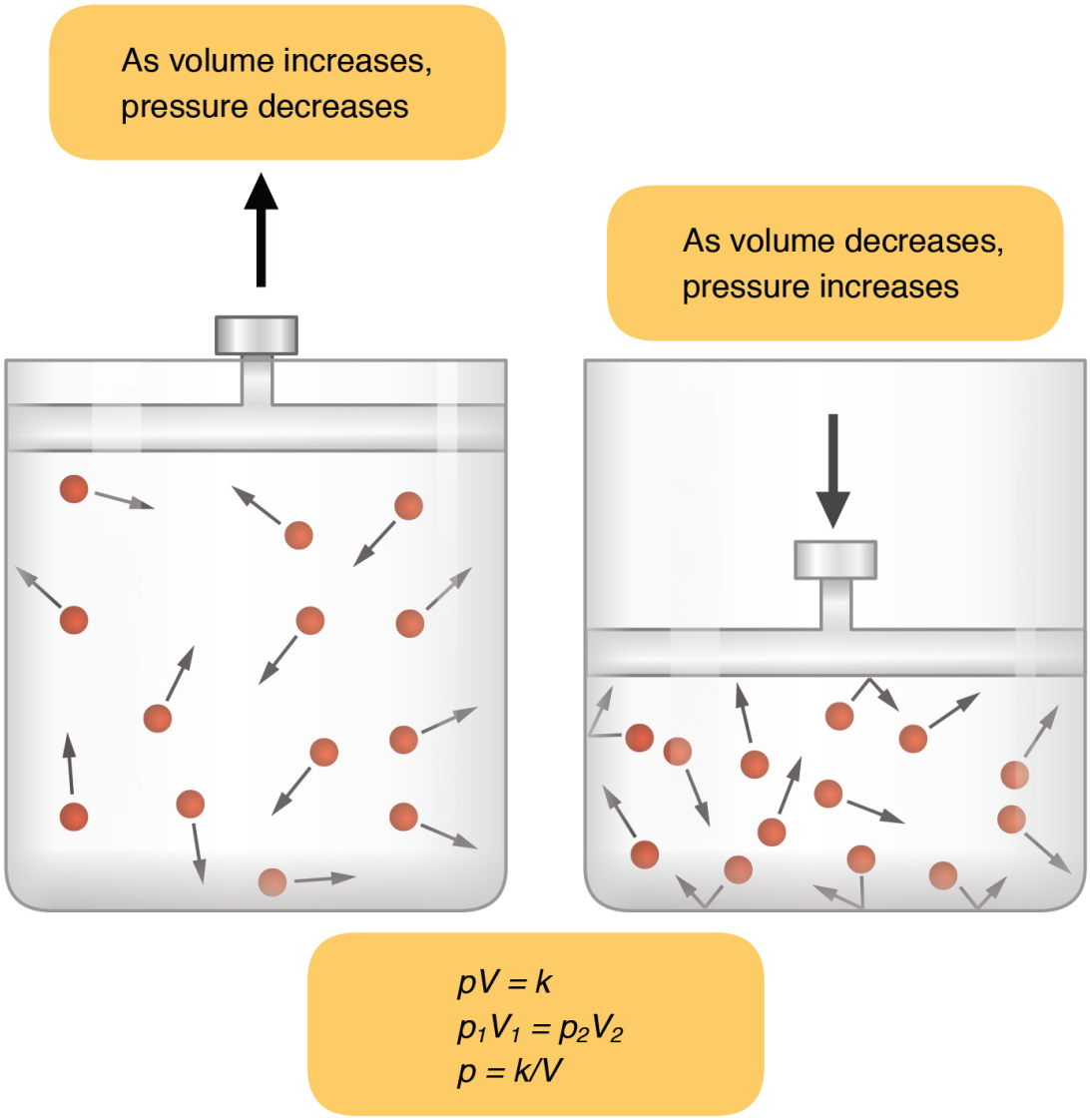

Figure 10.10: In a gas, pressure increases as volume decreases.

Atmospheric pressure is the amount of force that is exerted by gases in the air surrounding any given surface, such as the body. Atmospheric pressure can be expressed in millimeters of mercury (mm Hg), which is similar to the phrase "inches of mercury" used to describe atmospheric pressure on weather reports. 760 mm Hg is the atmospheric pressure at sea level under highly specific parameters of latitude and temperature.

10.3.1.2 How Changes in Volume and Pressure are Accomplished During Breathing

In addition to the differences in pressures, breathing is also dependent upon the contraction and relaxation of muscle fibers of both the diaphragm and thorax. The lungs themselves are passive during breathing, meaning they are not involved in creating the movement that helps inspiration and expiration. Contraction and relaxation of the diaphragm and intercostal muscles (found between the ribs) cause most of the pressure changes that result in inspiration and expiration. These muscle movements and subsequent pressure changes cause air to either rush in or be forced out of the lungs.

During inspiration, the diaphragm and external intercostal muscles contract, causing the rib cage to expand and move outward, and expanding the thoracic cavity and lung volume. This creates a lower pressure within the lung than that of the atmosphere, causing air to be drawn into the lungs. During expiration, the diaphragm and intercostals relax, causing the thorax and lungs to recoil. The air pressure within the lungs increases to above the pressure of the atmosphere, causing air to be forced out of the lungs.

10.3.2 Respiratory Rate

Breathing usually occurs without thought, although at times you can consciously control it, such as when you swim under water, sing a song, or blow bubbles. The **respiratory rate** is the total number of breaths, or respiratory cycles, that occur each minute. Respiratory rate can be an important indicator of disease, as the rate may increase or decrease during an illness or in a disease condition. The respiratory rate is controlled by the respiratory center located within the brain, which responds primarily to changes in carbon dioxide, oxygen, and pH levels in the blood.

The normal respiratory rate of a child decreases from birth to adolescence. A child under 1 year of age has a normal respiratory rate between 30 and 60 breaths per minute, but by the time a child is about 10 years old, the normal rate is closer to 18 to 30. By adolescence, the normal respiratory rate is similar to that of adults, 12 to 18 breaths per minute.

10.3.3 Chapter Review

The process of breathing is driven by pressure differences between the lungs and the atmosphere. Atmospheric pressure is the force exerted by gases present in the atmosphere. Pressure is determined by the volume of the space occupied by a gas. Air flows when a pressure gradient is created, from a space of higher pressure to a space of lower pressure. Boyle's law describes the relationship between volume and pressure. A gas is at lower pressure in a larger volume because the gas molecules have more space to in which to move. The same quantity of gas in a smaller volume results in gas molecules crowding together, producing increased pressure.

Pulmonary ventilation consists of the process of inspiration (or inhalation), where air enters the lungs, and expiration (or exhalation), where air leaves the lungs. During inspiration, the diaphragm and external intercostal muscles contract, causing the rib cage to expand and move outward, and expanding the thoracic cavity and lung volume. This creates a lower pressure within the lung than that of the atmosphere, causing air to be drawn into the lungs. During expiration, the diaphragm and intercostals relax, causing the thorax and lungs to recoil. The air pressure within the lungs increases to above the pressure of the atmosphere, causing air to be forced out of the lungs.

Both respiratory rate and depth are controlled by the respiratory centers of the brain, which are stimulated by factors such as chemical and pH changes in the blood. A rise in carbon dioxide or a decline in oxygen levels in the blood stimulates an increase in respiratory rate and depth.

10.3.4 Review Questions

Exercise 10.3.1 *(Solution on p. 251.)*

What are the units for measuring air pressure?

a. mm Hg

b. mm O2
c. Percent Hg
d. Percent O2

Exercise 10.3.2 *(Solution on p. 251.)*
A decrease in volume leads to a(n) _____ pressure.

a. decrease in
b. equalization of
c. increase in
d. zero

Exercise 10.3.3 *(Solution on p. 251.)*
Contraction of the external intercostal muscles causes which of the following to occur?

a. The diaphragm moves downward.
b. The rib cage is compressed.
c. The thoracic cavity volume decreases.
d. The ribs and sternum move upward.

10.3.5 Critical Thinking Questions

Exercise 10.3.4 *(Solution on p. 251.)*
Outline the steps involved in quiet breathing.

Exercise 10.3.5 *(Solution on p. 251.)*
What is respiratory rate and how is it controlled?

10.4 Gas Exchange[7]

The purpose of the respiratory system is to perform gas exchange. Inhaling provides air to the alveoli for this gas exchange process. At the respiratory membrane, where the alveolar and capillary walls meet, gases move across the membranes, with oxygen entering the bloodstream and carbon dioxide exiting. It is through this mechanism that blood is oxygenated and carbon dioxide, the waste product of cellular respiration, is removed from the body via exhaling.

10.4.1 Gas Exchange

In order to understand the mechanisms of gas exchange in the lung, it is important to understand the underlying principles of gases and their behavior. In addition to Boyle's law, several other gas laws help to describe the behavior of gases.

[7] This content is available online at <http://cnx.org/content/m58001/1.1/>.

10.4.1.1 Gas Laws and Air Composition

Gas molecules exert force on the surfaces with which they are in contact; this force is called pressure. In natural systems, gases are normally present as a mixture of different types of molecules. For example, the atmosphere consists of oxygen, nitrogen, carbon dioxide, and other gaseous molecules, and this gaseous mixture exerts a certain pressure referred to as atmospheric pressure (Table 10.1). **Partial pressure** (P_x) is the pressure of a single type of gas in a mixture of gases. For example, in the atmosphere, oxygen exerts a partial pressure, and nitrogen exerts another partial pressure, independent of the partial pressure of oxygen (Figure 10.11 (Partial and Total Pressures of a Gas)). **Total pressure** is the sum of all the partial pressures of a gaseous mixture.

Partial Pressures of Atmospheric Gases		
Gas	**Percent of total composition**	**Partial pressure (mm Hg)**
Nitrogen (N_2)	78.6	597.4
Oxygen (O_2)	20.9	158.8
Water (H_2O)	0.04	3.0
Carbon dioxide (CO_2)	0.004	0.3
Others	0.0006	0.5
Total composition/total atmospheric pressure	100%	760.0

Table 10.1: The partial pressure values are obtained by multiplying by the decimal form of the percentage (e.g. 0.784) and atmospheric pressure (760 mm Hg). For example, the partial pressure of oxygen is 0.209 x 760 = 158.8 mm Hg.

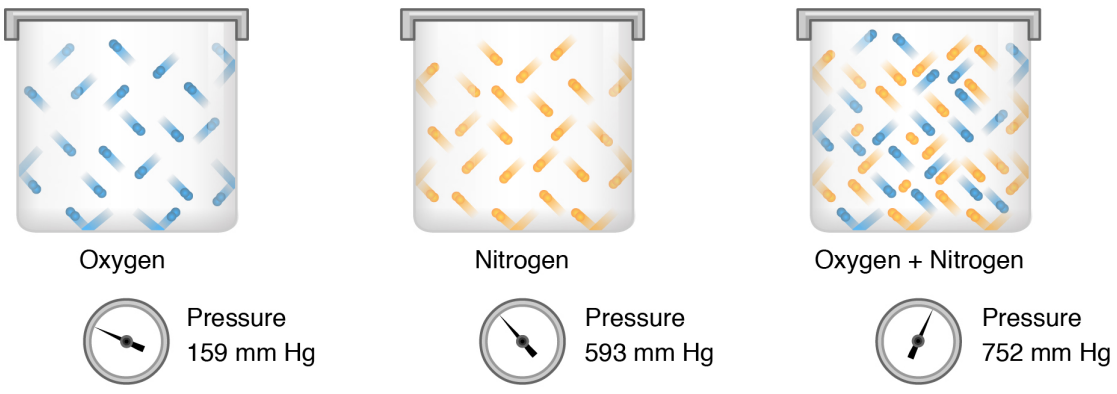

Figure 10.11: Partial pressure is the force exerted by a gas. The sum of the partial pressures of all the gases in a mixture equals the total pressure.

Partial pressure is extremely important in predicting the movement of gases. Recall that gases tend to equalize their pressure in two regions that are connected. A gas will move from an area where its partial pressure is higher to an area where its partial pressure is lower. In addition, the greater the partial pressure difference between the two areas, the more rapid is the movement of gases.

10.4.1.2 Solubility of Gases in Liquids

Henry's law describes the behavior of gases when they come into contact with a liquid, such as blood. Henry's law states that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas. The greater the partial pressure of the gas, the greater the number of gas molecules that will dissolve in the liquid. The concentration of the gas in a liquid is also dependent on the solubility of the gas in the liquid. For example, although nitrogen is present in the atmosphere, very little nitrogen dissolves into the blood, because the solubility of nitrogen in blood is very low. The exception to this occurs in scuba divers; the composition of the compressed air that divers breathe causes nitrogen to have a higher partial pressure than normal, causing it to dissolve in the blood in greater amounts than normal. Too much nitrogen in the bloodstream results in a serious condition that can be fatal if not corrected. Gas molecules establish an equilibrium between those molecules dissolved in liquid and those in air.

The composition of air in the atmosphere and in the alveoli differs. In both cases, the relative concentration of gases is nitrogen > oxygen > water vapor > carbon dioxide. The amount of water vapor present in alveolar air is greater than that in atmospheric air (Table 10.2). Recall that the respiratory system works to humidify incoming air, thereby causing the air present in the alveoli to have a greater amount of water vapor than atmospheric air. In addition, alveolar air contains a greater amount of carbon dioxide and less oxygen than atmospheric air. This is no surprise, as gas exchange removes oxygen from and adds carbon dioxide to alveolar air. Both deep and forced breathing cause the alveolar air composition to be changed more rapidly than during quiet breathing. As a result, the partial pressures of oxygen and carbon dioxide change, affecting the diffusion process that moves these materials across the membrane. This will cause oxygen to enter and carbon dioxide to leave the blood more quickly.

Composition and Partial Pressures of Alveolar Air		
Gas	**Percent of total composition**	**Partial pressure (mm Hg)**
Nitrogen (N_2)	74.9	569
Oxygen (O_2)	13.7	104
Water (H_2O)	6.2	40
Carbon dioxide (CO_2)	5.2	47
Total composition/total alveolar pressure	100%	760.0

Table 10.2

10.4.2 Gas Exchange

Gas exchange occurs at two sites in the body: in the lungs, where oxygen is picked up and carbon dioxide is released at the respiratory membrane, and at the tissues, where oxygen is released and carbon dioxide is picked up. External respiration is the exchange of gases with the external environment, and occurs in the alveoli of the lungs. Internal respiration is the exchange of gases with the internal environment, and occurs in the tissues. The actual exchange of gases occurs due to simple diffusion, because molecular oxygen and carbon dioxide are small and nonpolar. Energy is not required to move oxygen or carbon dioxide across

membranes. Instead, these gases follow pressure gradients that allow them to diffuse. The anatomy of the lung maximizes the diffusion of gases: The respiratory membrane is highly permeable to gases; the respiratory and blood capillary membranes are very thin; and there is a large surface area throughout the lungs.

10.4.2.1 External Respiration

The pulmonary artery carries deoxygenated blood into the lungs from the heart, where it branches and eventually becomes the capillary network composed of pulmonary capillaries. These pulmonary capillaries create the respiratory membrane with the alveoli (Figure 10.12 (External Respiration)). As the blood is pumped through this capillary network, gas exchange occurs. Although a small amount of the oxygen is able to dissolve directly into plasma from the alveoli, most of the oxygen is picked up by erythrocytes (red blood cells) and binds to a protein called hemoglobin, a process described later in this chapter. Oxygenated hemoglobin is red, causing the overall appearance of bright red oxygenated blood, which returns to the heart through the pulmonary veins. Carbon dioxide is released in the opposite direction of oxygen, from the blood to the alveoli. Some of the carbon dioxide is returned on hemoglobin, but can also be dissolved in plasma or is present as a converted form, also explained in greater detail later in this chapter.

External respiration occurs as a function of partial pressure differences in oxygen and carbon dioxide between the alveoli and the blood in the pulmonary capillaries.

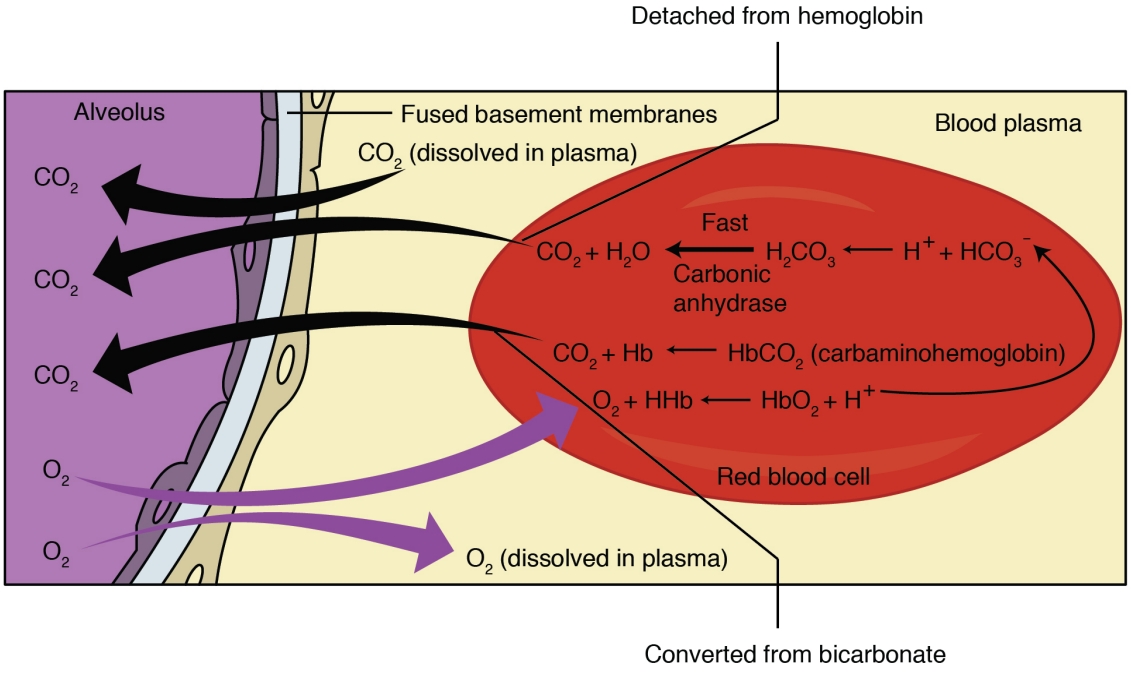

Figure 10.12: In external respiration, oxygen diffuses across the respiratory membrane from the alveolus to the capillary, whereas carbon dioxide diffuses out of the capillary into the alveolus.

The partial pressure of carbon dioxide is also different between the alveolar air and the blood of the capillary. However, the partial pressure difference is less than that of oxygen, about 5 mm Hg. The partial pressure of carbon dioxide in the blood of the capillary is about 45 mm Hg, whereas its partial pressure in the alveoli is about 40 mm Hg. However, the solubility of carbon dioxide is much greater than that of oxygen—by a factor of about 20—in both blood and alveolar fluids. As a result, the relative concentrations of oxygen and carbon dioxide that diffuse across the respiratory membrane are similar.

10.4.2.2 Internal Respiration

Internal respiration is gas exchange that occurs at the level of body tissues (Figure 10.13 (Internal Respiration)). Similar to external respiration, internal respiration also occurs as simple diffusion due to a partial pressure gradient. However, the partial pressure gradients are opposite of those present at the respiratory membrane. The partial pressure of oxygen in tissues is low because oxygen is continuously used for cellular respiration. In contrast, the partial pressure of oxygen in the blood is higher. This creates a pressure gradient that causes oxygen to dissociate from hemoglobin, diffuse out of the blood, cross the interstitial space, and enter the tissue. Hemoglobin that has little oxygen bound to it loses much of its brightness, so that blood returning to the heart is more burgundy (bluish-red) in color.

Considering that cellular respiration continuously produces carbon dioxide, the partial pressure of carbon dioxide is lower in the blood than it is in the tissue, causing carbon dioxide to diffuse out of the tissue, cross the interstitial fluid, and enter the blood. It is then carried back to the lungs either bound to hemoglobin, dissolved in plasma, or in a converted form. By the time blood returns to the heart, the partial pressure of oxygen has returned to about 40 mm Hg, and the partial pressure of carbon dioxide has returned to about 45 mm Hg. The blood is then pumped back to the lungs to be oxygenated once again during external respiration.

Internal Respiration

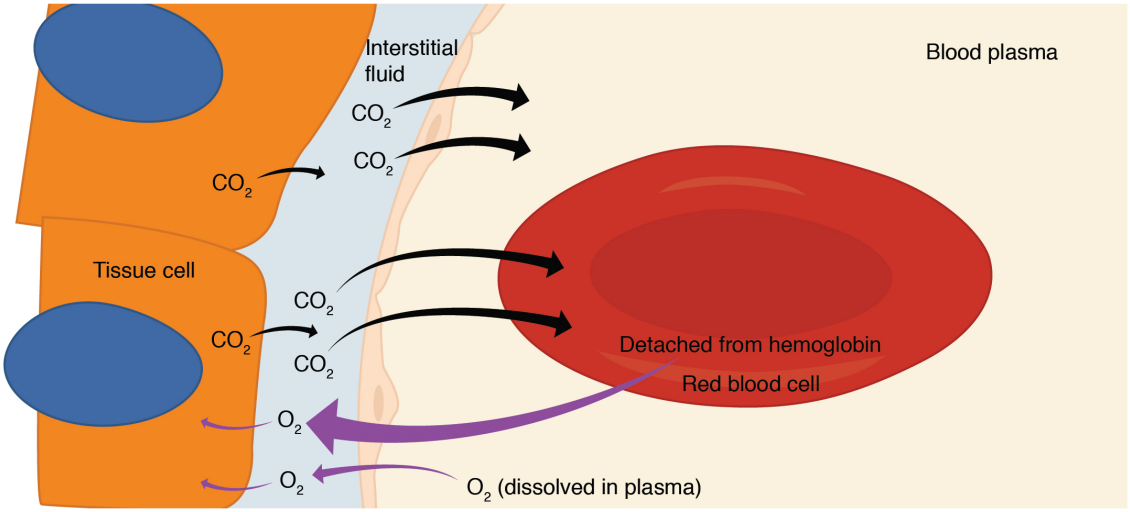

Figure 10.13: Oxygen diffuses out of the capillary and into cells, whereas carbon dioxide diffuses out of cells and into the capillary.

: **Hyperbaric Chamber Treatment**

A type of device used in some areas of medicine that exploits the behavior of gases is hyperbaric chamber treatment. A hyperbaric chamber is a unit that can be sealed and expose a patient to either 100 percent oxygen with increased pressure or a mixture of gases that includes a higher concentration of oxygen than normal atmospheric air, also at a higher partial pressure than the atmosphere. There are two major types of chambers: monoplace and multiplace. Monoplace chambers are typically for one patient, and the staff tending to the patient observes the patient from outside of the chamber (Figure 10.14 (Hyperbaric Chamber)). Some facilities have special monoplace hyperbaric chambers that allow multiple patients to be treated at once, usually in a sitting or reclining position, to help ease feelings of isolation or claustrophobia. Multiplace chambers are large enough for multiple patients to be treated at one time, and the staff attending these patients is present inside the chamber. In a multiplace chamber, patients are often treated with air via a mask or hood, and the chamber is pressurized.

Hyperbaric Chamber

Figure 10.14: (credit: "komunews"/flickr.com)

Hyperbaric chamber treatment is based on the behavior of gases. As you recall, gases move from a region of higher partial pressure to a region of lower partial pressure. In a hyperbaric chamber, the atmospheric pressure is increased, causing a greater amount of oxygen than normal to diffuse into the bloodstream of the patient. Hyperbaric chamber therapy is used to treat a variety of medical problems, such as wound and graft healing, anaerobic bacterial infections, and carbon monoxide poisoning. Exposure to and poisoning by carbon monoxide is difficult to reverse, because hemoglobin's affinity for carbon monoxide is much stronger than its affinity for oxygen, causing

carbon monoxide to replace oxygen in the blood. Hyperbaric chamber therapy can treat carbon monoxide poisoning, because the increased atmospheric pressure causes more oxygen to diffuse into the bloodstream. At this increased pressure and increased concentration of oxygen, carbon monoxide is displaced from hemoglobin. Another example is the treatment of anaerobic bacterial infections, which are created by bacteria that cannot or prefer not to live in the presence of oxygen. An increase in blood and tissue levels of oxygen helps to kill the anaerobic bacteria that are responsible for the infection, as oxygen is toxic to anaerobic bacteria. For wounds and grafts, the chamber stimulates the healing process by increasing energy production needed for repair. Increasing oxygen transport allows cells to ramp up cellular respiration and thus ATP production, the energy needed to build new structures.

10.4.3 Chapter Review

Each specific gas in a mixture of gases exerts force (its partial pressure) independently of the other gases in the mixture. Gas molecules move down a pressure gradient; in other words, gas moves from a region of high pressure to a region of low pressure. The partial pressure of oxygen is high in the alveoli and low in the blood of the pulmonary capillaries. As a result, oxygen diffuses across the respiratory membrane from the alveoli into the blood. In contrast, the partial pressure of carbon dioxide is high in the pulmonary capillaries and low in the alveoli. Therefore, carbon dioxide diffuses across the respiratory membrane from the blood into the alveoli. The amount of oxygen and carbon dioxide that diffuses across the respiratory membrane is similar.

External respiration refers to gas exchange that occurs in the alveoli, whereas internal respiration refers to gas exchange that occurs in the tissue. Both are driven by partial pressure differences.

10.4.4 Review Questions

Exercise 10.4.1 *(Solution on p. 251.)*

Gas moves from an area of _____ partial pressure to an area of _____ partial pressure.

a. low; high
b. low; low
c. high; high
d. high; low

Exercise 10.4.2 *(Solution on p. 251.)*

Gas exchange that occurs at the level of the tissues is called _____.

a. external respiration
b. interpulmonary respiration
c. internal respiration
d. pulmonary ventilation

Exercise 10.4.3 *(Solution on p. 251.)*

The partial pressure of carbon dioxide is 45 mm Hg in the blood and 40 mm Hg in the alveoli. What happens to the carbon dioxide?

a. It diffuses into the blood.
b. It diffuses into the alveoli.
c. The gradient is too small for carbon dioxide to diffuse.
d. It decomposes into carbon and oxygen.

10.4.5 Critical Thinking Questions

Exercise 10.4.4 *(Solution on p. 251.)*

A smoker develops damage to several alveoli that then can no longer function. How does this affect gas exchange?

10.5 Transport of Gases[8]

The other major activity in the lungs is the process of respiration, the process of gas exchange. The function of respiration is to provide oxygen for use by body cells during cellular respiration and to eliminate carbon dioxide, a waste product of cellular respiration, from the body. In order for the exchange of oxygen and carbon dioxide to occur, both gases must be transported between the external and internal respiration sites. Both gases require a specialized transport system for the majority of the gas molecules to be moved between the lungs and other tissues.

10.5.1 Oxygen Transport in the Blood

The majority of oxygen molecules are carried from the lungs to the body's tissues by a specialized transport system, which relies on the erythrocyte—the red blood cell. Erythrocytes contain hemoglobin, which serves to bind oxygen molecules to the erythrocyte (Figure 10.15 (Erythrocyte and Hemoglobin)). Heme is the portion of hemoglobin that contains iron, and it is heme that binds oxygen. One erythrocyte contains four iron ions, and because of this, each erythrocyte is capable of carrying up to four molecules of oxygen. As oxygen diffuses across the respiratory membrane from the alveolus to the capillary, it also diffuses into the red blood cell and is bound by hemoglobin. The following reversible chemical reaction describes the production of the final product, **oxyhemoglobin** (Hb–O_2), which is formed when oxygen binds to hemoglobin. Oxyhemoglobin is a bright red-colored molecule that contributes to the bright red color of oxygenated blood.

$$\mathrm{Hb} + \mathrm{O_2} \leftrightarrow \mathrm{Hb} - \mathrm{O_2} \tag{10.2}$$

[8] This content is available online at <http://cnx.org/content/m58002/1.2/>.

Erythrocyte and Hemoglobin

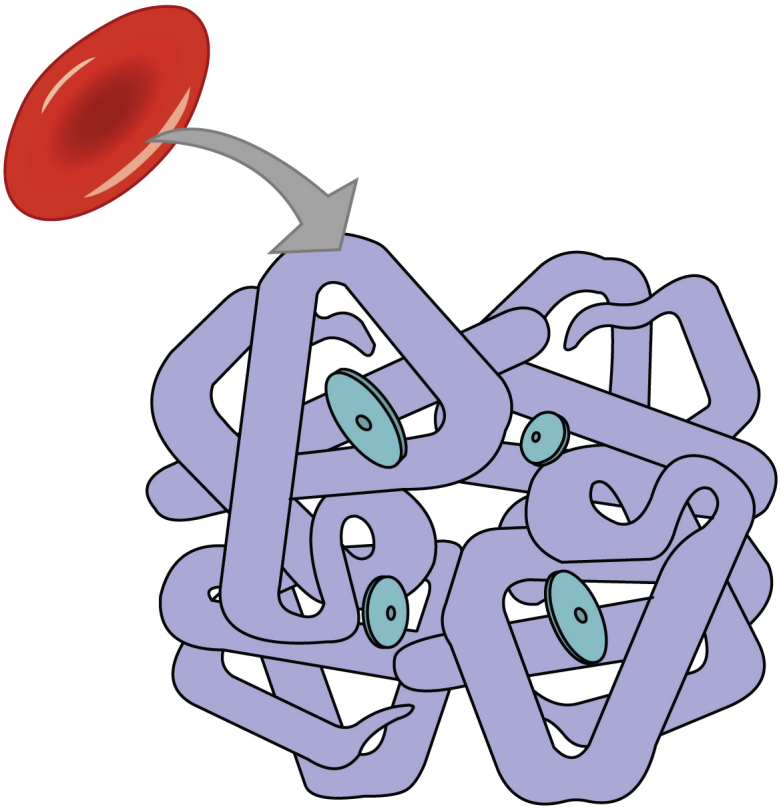

Figure 10.15: Hemoglobin consists of four subunits, each of which contains one molecule of iron.

10.5.1.1 Function of Hemoglobin

Hemoglobin is composed of subunits, a protein structure that is referred to as a quaternary structure. Each of the four subunits that make up hemoglobin is arranged in a ring-like fashion, with an iron atom covalently bound to the heme in the center of each subunit. When all four heme sites are occupied, the hemoglobin is said to be saturated. Hemoglobin saturation of 100 percent means that every heme unit in all of the erythrocytes of the body is bound to oxygen. In a healthy individual with normal hemoglobin levels, hemoglobin saturation generally ranges from 95 percent to 99 percent.

10.5.2 Carbon Dioxide Transport in the Blood

Carbon dioxide is transported by three major mechanisms. The first mechanism of carbon dioxide transport is by blood plasma, as some carbon dioxide molecules dissolve in the blood. The second mechanism is transport in the form of bicarbonate (HCO_3^-), which also dissolves in plasma. The third mechanism of carbon dioxide transport is similar to the transport of oxygen by erythrocytes (Figure 10.16 (Carbon Dioxide Transport)).

Carbon Dioxide Transport

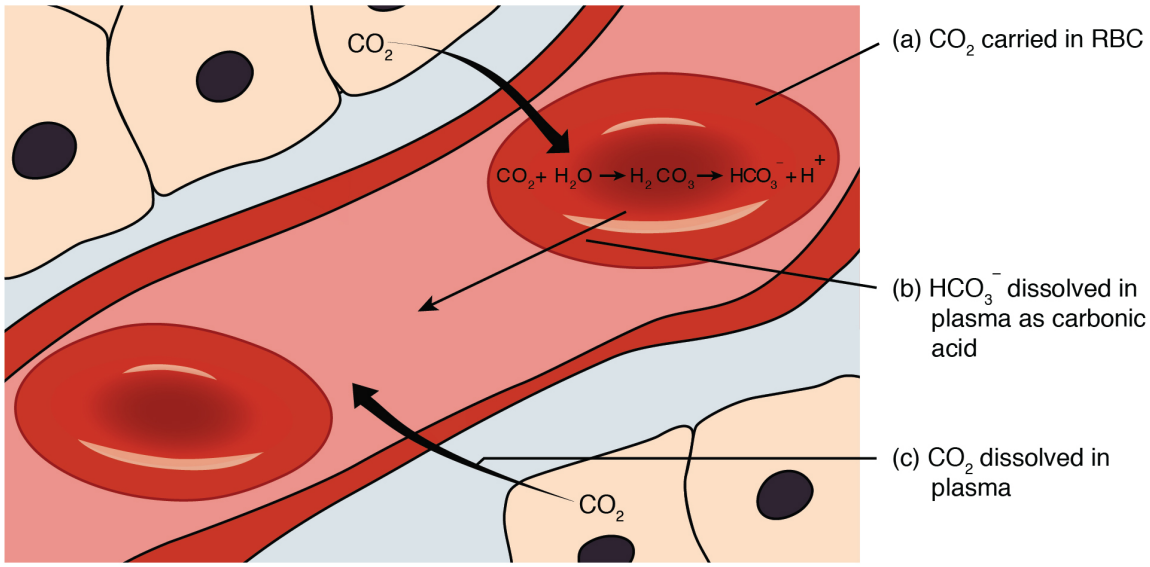

Figure 10.16: Carbon dioxide is transported by three different methods: (a) in erythrocytes; (b) after forming carbonic acid (H_2CO_3), which is dissolved in plasma; (c) and in plasma.

10.5.2.1 Dissolved Carbon Dioxide

Although carbon dioxide is not considered to be highly soluble in blood, a small fraction—about 7 to 10 percent—of the carbon dioxide that diffuses into the blood from the tissues dissolves in plasma. The dissolved carbon dioxide then travels in the bloodstream and when the blood reaches the pulmonary capillaries, the dissolved carbon dioxide diffuses across the respiratory membrane into the alveoli, where it is then exhaled during pulmonary ventilation.

10.5.2.2 Bicarbonate Buffer

A large fraction—about 70 percent—of the carbon dioxide molecules that diffuse into the blood is transported to the lungs as bicarbonate. Most bicarbonate is produced in erythrocytes after carbon dioxide diffuses into the capillaries, and subsequently into red blood cells. **Carbonic anhydrase (CA)** causes carbon dioxide and water to form carbonic acid (H_2CO_3), which dissociates into two ions: bicarbonate (HCO_3^-) and hydrogen (H^+). The following formula depicts this reaction:

$$CO_2 + H_2O \overset{CA}{\leftrightarrow} H_2CO_3 \leftrightarrow H^+ + HCO_{3-} \tag{10.3}$$

At the pulmonary capillaries, the chemical reaction that produced bicarbonate (shown above) is reversed, and carbon dioxide and water are the products. Hydrogen ions and bicarbonate ions join to form carbonic acid, which is converted into carbon dioxide and water by carbonic anhydrase. Carbon dioxide diffuses out of the erythrocytes and into the plasma, where it can further diffuse across the respiratory membrane into the alveoli to be exhaled during pulmonary ventilation.

10.5.2.3 Carbaminohemoglobin

About 20 percent of carbon dioxide is bound by hemoglobin and is transported to the lungs. Carbon dioxide does not bind to iron as oxygen does; instead, carbon dioxide binds amino acids on the globin portions of hemoglobin to form **carbaminohemoglobin**, which forms when hemoglobin and carbon dioxide bind. When hemoglobin is not transporting oxygen, it tends to have a bluish-purple tone to it, creating the darker maroon color typical of deoxygenated blood. The following formula depicts this reversible reaction:

$$CO_2 + Hb \leftrightarrow HbCO_2 \tag{10.4}$$

Similar to the transport of oxygen by heme, the binding and dissociation of carbon dioxide to and from hemoglobin is dependent on the partial pressure of carbon dioxide. Because carbon dioxide is released from the lungs, blood that leaves the lungs and reaches body tissues has a lower partial pressure of carbon dioxide than is found in the tissues. As a result, carbon dioxide leaves the tissues because of its higher partial pressure, enters the blood, and then moves into red blood cells, binding to hemoglobin. In contrast, in the pulmonary capillaries, the partial pressure of carbon dioxide is high compared to within the alveoli. As a result, carbon dioxide dissociates readily from hemoglobin and diffuses across the respiratory membrane into the air.

10.5.3 Chapter Review

Oxygen is primarily transported through the blood by erythrocytes. These cells contain a protein molecule called hemoglobin, which is composed of four subunits with a ring-like structure. Each subunit contains one atom of iron bound to a molecule of heme. Heme binds oxygen so that each hemoglobin molecule can bind up to four oxygen molecules. When all of the heme units in the blood are bound to oxygen, hemoglobin is considered to be saturated.

Carbon dioxide is transported in blood by three different mechanisms: as dissolved carbon dioxide, as bicarbonate, or as carbaminohemoglobin. A small portion of carbon dioxide remains. The largest amount of transported carbon dioxide is as bicarbonate, formed in erythrocytes. For this conversion, carbon dioxide is combined with water with the aid of an enzyme called carbonic anhydrase. This combination forms carbonic acid, which spontaneously dissociates into bicarbonate and hydrogen ions. As bicarbonate builds up in erythrocytes, it is moved across the membrane into the plasma. At the pulmonary capillaries, bicarbonate re-enters erythrocytes and the reaction with carbonic anhydrase is reversed, recreating carbon dioxide and water. Carbon dioxide then diffuses out of the erythrocyte and across the respiratory membrane into the air. An intermediate amount of carbon dioxide binds directly to hemoglobin to form carbaminohemoglobin.

10.5.4 Interactive Link Questions

Exercise 10.5.1 ***(Solution on p. 251.)***

Watch this video[9] to see the transport of oxygen from the lungs to the tissues. Why is oxygenated blood bright red, whereas deoxygenated blood tends to be more of a purple color?

10.5.5 Review Questions

Exercise 10.5.2 ***(Solution on p. 252.)***

Oxyhemoglobin forms by a chemical reaction between which of the following?

a. hemoglobin and carbon dioxide
b. carbonic anhydrase and carbon dioxide
c. hemoglobin and oxygen

[9] http://openstaxcollege.org/l/oxyblood

d. carbonic anhydrase and oxygen

Exercise 10.5.3 *(Solution on p. 252.)*
In what form is the majority of carbon dioxide transported in the blood?

a. Bicarbonate ion
b. Carbaminohemoglobin
c. Carbonic acid
d. Carbonic anhydrase

10.5.6 Critical Thinking Questions

Exercise 10.5.4 *(Solution on p. 252.)*
Describe the relationship between the partial pressure of oxygen and the binding of oxygen to hemoglobin.

Exercise 10.5.5 *(Solution on p. 252.)*
Describe three ways in which carbon dioxide can be transported.

Solutions to Exercises in Chapter 10

to Exercise 10.2.1 (p. 235)
Inflammation and the production of a thick mucus; constriction of the airway muscles, or bronchospasm; and an increased sensitivity to allergens.
to Exercise 10.2.2 (p. 235)
C
to Exercise 10.2.3 (p. 235)
A
to Exercise 10.2.4 (p. 235)
A
to Exercise 10.2.5 (p. 235)
The epiglottis is a region of the larynx that is important during the swallowing of food or drink. As a person swallows, the pharynx moves upward and the epiglottis closes over the trachea, preventing food or drink from entering the trachea. If a person's epiglottis were injured, this mechanism would be impaired. As a result, the person may have problems with food or drink entering the trachea, and possibly, the lungs. Over time, this may cause infections such as pneumonia to set in.
to Exercise 10.3.1 (p. 238)
A
to Exercise 10.3.2 (p. 239)
C
to Exercise 10.3.3 (p. 239)
D
to Exercise 10.3.4 (p. 239)
Quiet breathing occurs at rest and without active thought. During quiet breathing, the diaphragm and external intercostal muscles work at different extents, depending on the situation. For inspiration, the diaphragm contracts, causing the diaphragm to flatten and drop towards the abdominal cavity, helping to expand the thoracic cavity. The external intercostal muscles contract as well, causing the rib cage to expand, and the rib cage and sternum to move outward, also expanding the thoracic cavity. Expansion of the thoracic cavity also causes the lungs to expand. As a result, the pressure within the lungs drops below that of the atmosphere, causing air to rush into the lungs. In contrast, expiration is a passive process. As the diaphragm and intercostal muscles relax, the lungs and thoracic tissues recoil, and the volume of the lungs decreases. This causes the pressure within the lungs to increase above that of the atmosphere, causing air to leave the lungs.
to Exercise 10.3.5 (p. 239)
Respiratory rate is defined as the number of breaths taken per minute. Respiratory rate is controlled by the respiratory center, located in the brain. Conscious thought can alter the normal respiratory rate through control by skeletal muscle, although one cannot consciously stop the rate altogether. A typical resting respiratory rate is about 14 breaths per minute.
to Exercise 10.4.1 (p. 245)
D
to Exercise 10.4.2 (p. 245)
C
to Exercise 10.4.3 (p. 245)
B
to Exercise 10.4.4 (p. 246)
The damaged alveoli will have insufficient ventilation, causing the partial pressure of oxygen in the alveoli to decrease. As a result, the pulmonary capillaries serving these alveoli will constrict, redirecting blood flow to other alveoli that are receiving sufficient ventilation.
to Exercise 10.5.1 (p. 249)
When oxygen binds to the hemoglobin molecule, oxyhemoglobin is created, which has a red color to it. Hemoglobin that is not bound to oxygen tends to be more of a blue–purple color. Oxygenated blood

traveling through the systemic arteries has large amounts of oxyhemoglobin. As blood passes through the tissues, much of the oxygen is released into systemic capillaries. The deoxygenated blood returning through the systemic veins, therefore, contains much smaller amounts of oxyhemoglobin. The more oxyhemoglobin that is present in the blood, the redder the fluid will be. As a result, oxygenated blood will be much redder in color than deoxygenated blood.

to Exercise 10.5.2 (p. 249)

C

to Exercise 10.5.3 (p. 250)

A

to Exercise 10.5.4 (p. 250)

As the partial pressure of oxygen increases, the number of oxygen molecules bound by hemoglobin increases, thereby increasing the saturation of hemoglobin.

to Exercise 10.5.5 (p. 250)

Carbon dioxide can be transported by three mechanisms: dissolved in plasma, as bicarbonate, or as carbaminohemoglobin. Dissolved in plasma, carbon dioxide molecules simply diffuse into the blood from the tissues. Bicarbonate is created by a chemical reaction that occurs mostly in erythrocytes, joining carbon dioxide and water by carbonic anhydrase, producing carbonic acid, which breaks down into bicarbonate and hydrogen ions. Carbaminohemoglobin is the bound form of hemoglobin and carbon dioxide.

Chapter 11

Hormones

11.1 Endocrine System[1]

The endocrine system produces hormones that function to control and regulate many different body processes. The endocrine system coordinates with the nervous system to control the functions of the other organ systems. Cells of the endocrine system produce molecular signals called hormones. These cells may compose endocrine glands, may be tissues or may be located in organs or tissues that have functions in addition to hormone production. Hormones circulate throughout the body and stimulate a response in cells that have receptors able to bind with them. The changes brought about in the receiving cells affect the functioning of the organ targeted by the hormone. Many of the hormones are secreted in response to signals from the nervous system, thus the two systems act in concert to effect changes in the body.

11.1.1 Hormones

Maintaining homeostasis within the body requires the coordination of many different systems and organs. One mechanism of communication between neighboring cells, and between cells and tissues in distant parts of the body, occurs through the release of chemicals called hormones. **Hormones** are released into body fluids, usually blood, which carries them to their target cells where they elicit a response. The cells that secrete hormones are often located in specific organs, called **endocrine glands**, and the cells, tissues, and organs that secrete hormones make up the endocrine system. Examples of endocrine organs include the pancreas, which produces the hormones insulin and glucagon to regulate blood-glucose levels, the adrenal glands, which produce hormones such as epinephrine and norepinephrine that regulate responses to stress, and the thyroid gland, which produces thyroid hormones that regulate metabolic rates.

The endocrine glands differ from the exocrine glands. **Exocrine glands** secrete chemicals through ducts that lead outside the gland (not to the blood). For example, sweat produced by sweat glands is released into ducts that carry sweat to the surface of the skin. The pancreas has both endocrine and exocrine functions because besides releasing hormones into the blood. It also produces digestive juices, which are carried by ducts into the small intestine.

: **Endocrinologist**

An endocrinologist is a medical doctor who specializes in treating endocrine disorders. An endocrine surgeon specializes in the surgical treatment of endocrine diseases and glands. Some of the diseases that are managed by endocrinologists include disorders of the pancreas (diabetes mellitus), disorders of the pituitary (gigantism, acromegaly, and pituitary dwarfism), disorders of the thyroid gland (goiter and Graves' disease), and disorders of the adrenal glands (Cushing's disease and Addison's disease).

[1] This content is available online at <http://cnx.org/content/m58003/1.2/>.

Endocrinologists are required to assess patients and diagnose endocrine disorders through extensive use of laboratory tests. Many endocrine diseases are diagnosed using tests that stimulate or suppress endocrine organ functioning. Blood samples are then drawn to determine the effect of stimulating or suppressing an endocrine organ on the production of hormones. For example, to diagnose diabetes mellitus, patients are required to fast for 12 to 24 hours. They are then given a sugary drink, which stimulates the pancreas to produce insulin to decrease blood-glucose levels. A blood sample is taken one to two hours after the sugar drink is consumed. If the pancreas is functioning properly, the blood-glucose level will be within a normal range. Another example is the A1C test, which can be performed during blood screening. The A1C test measures average blood-glucose levels over the past two to three months. The A1C test is an indicator of how well blood glucose is being managed over a long time.

Once a disease such as diabetes has been diagnosed, endocrinologists can prescribe lifestyle changes and medications to treat the disease. Some cases of diabetes mellitus can be managed by exercise, weight loss, and a healthy diet; in other cases, medications may be required to enhance insulin's production or effect. If the disease cannot be controlled by these means, the endocrinologist may prescribe insulin injections.

In addition to clinical practice, endocrinologists may also be involved in primary research and development activities. For example, ongoing islet transplant research is investigating how healthy pancreas islet cells may be transplanted into diabetic patients. Successful islet transplants may allow patients to stop taking insulin injections.

11.1.2 How Hormones Work

Hormones cause changes in target cells by binding to specific cell-surface or **intracellular hormone receptors**, molecules embedded in the cell membrane or floating in the cytoplasm with a binding site that matches a binding site on the hormone molecule. In this way, even though hormones circulate throughout the body and come into contact with many different cell types, they only affect cells that possess the necessary receptors. Receptors for a specific hormone may be found on or in many different cells or may be limited to a small number of specialized cells. For example, thyroid hormones act on many different tissue types, stimulating metabolic activity throughout the body. Cells can have many receptors for the same hormone but often also possess receptors for different types of hormones. The number of receptors that respond to a hormone determines the cell's sensitivity to that hormone, and the resulting cellular response. Additionally, the number of receptors available to respond to a hormone can change over time, resulting in increased or decreased cell sensitivity.

11.1.3 Endocrine Glands

The endocrine glands secrete hormones into the surrounding interstitial fluid; those hormones then diffuse into blood and are carried to various organs and tissues within the body. The endocrine glands include the pituitary, thyroid, parathyroid, adrenal glands, gonads, pineal, and pancreas.

The **pituitary gland** is located at the base of the brain (Figure 11.1**a**). It is attached to the hypothalamus. The posterior lobe stores and releases oxytocin and antidiuretic hormone (ADH) produced by the hypothalamus. The anterior lobe responds to hormones produced by the hypothalamus by producing its own hormones, most of which regulate other hormone-producing glands.

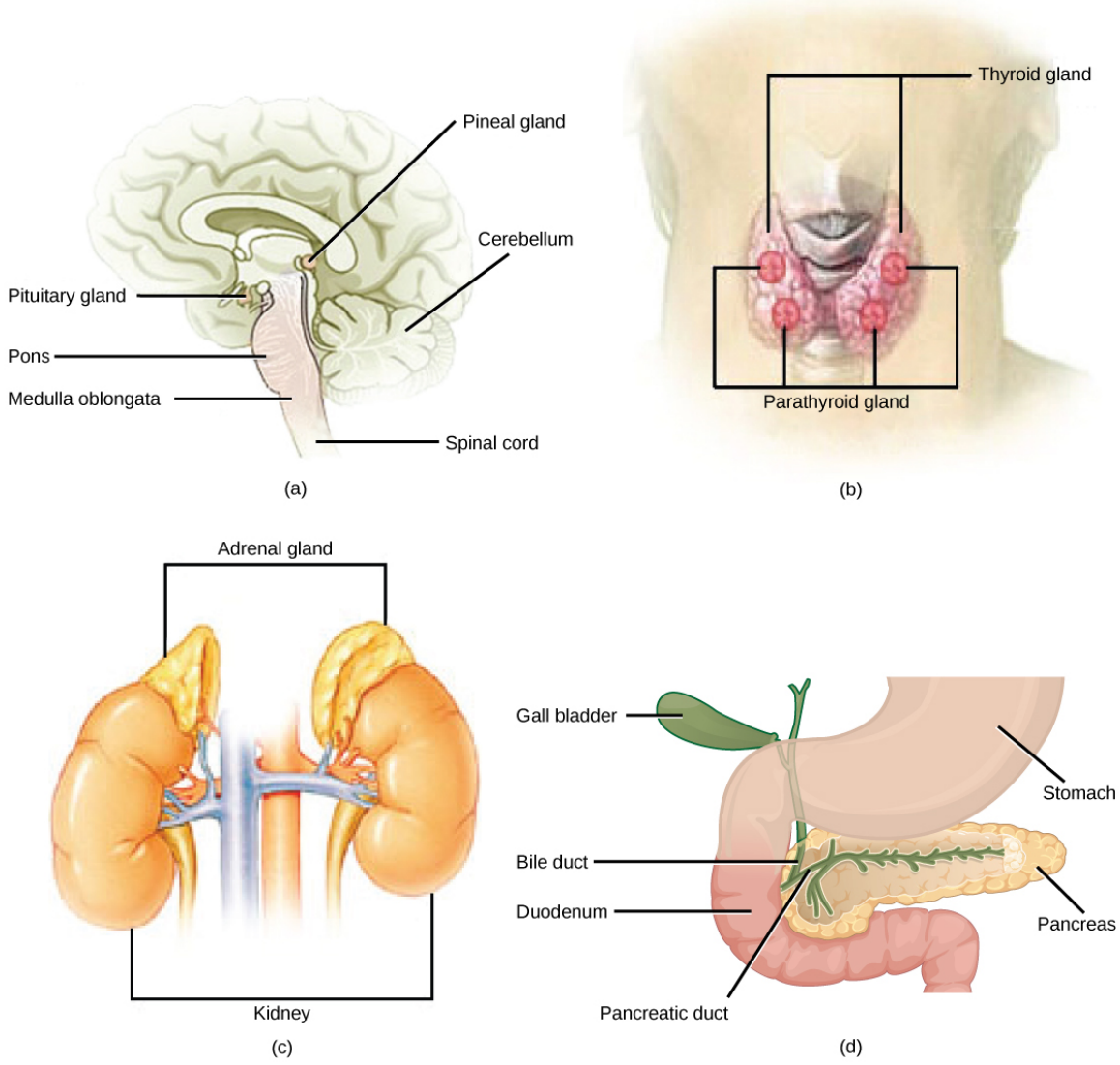

Figure 11.1: (a) The pituitary gland sits at the base of the brain, just above the brain stem. (b) The parathyroid glands are located on the posterior of the thyroid gland. (c) The adrenal glands are on top of the kidneys. d) The pancreas is found between the stomach and the small intestine. (credit: modification of work by NCI, NIH)

The anterior pituitary produces six hormones: growth hormone, prolactin, thyroid-stimulating hormone, adrenocorticotropic hormone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). Growth hormone stimulates cellular activities like protein synthesis that promote growth. Prolactin stimulates the production of milk by the mammary glands. The other hormones produced by the anterior pituitary regulate the production of hormones by other endocrine tissues (Table 11.1). The posterior pituitary is significantly different in structure from the anterior pituitary. It is a part of the brain, extending down from the hypotha-

lamus, and contains mostly nerve fibers that extend from the hypothalamus to the posterior pituitary.

The **thyroid gland** is located in the neck, just below the larynx and in front of the trachea (Figure 11.1**b**). It is a butterfly-shaped gland with two lobes that are connected. The thyroid follicle cells synthesize the hormone thyroxine, which is also known as T_4 because it contains four atoms of iodine, and triiodothyronine, also known as T_3 because it contains three atoms of iodine. T_3 and T_4 are released by the thyroid in response to thyroid-stimulating hormone produced by the anterior pituitary, and both T_3 and T_4 have the effect of stimulating metabolic activity in the body and increasing energy use. A third hormone, calcitonin, is also produced by the thyroid. Calcitonin is released in response to rising calcium ion concentrations in the blood and has the effect of reducing those levels.

Most people have four **parathyroid glands**; however, the number can vary from two to six. These glands are located on the posterior surface of the thyroid gland (Figure 11.1**b**).

The parathyroid glands produce parathyroid hormone. Parathyroid hormone increases blood calcium concentrations when calcium ion levels fall below normal.

The **adrenal glands** are located on top of each kidney (Figure 11.1**c**). The adrenal glands consist of an outer adrenal cortex and an inner adrenal medulla. These regions secrete different hormones.

The adrenal cortex produces mineralocorticoids, glucocorticoids, and gonadocorticoids (principally androgens). The main mineralocorticoid is aldosterone, which regulates the concentration of ions in urine, sweat, and saliva. Aldosterone release from the adrenal cortex is stimulated by a decrease in blood concentrations of sodium ions, blood volume, or blood pressure, or by an increase in blood potassium levels. The glucocorticoids maintain proper blood-glucose levels between meals. They also control a response to stress by increasing glucose synthesis from fats and proteins and interact with epinephrine to cause vasoconstriction. Androgens are sex hormones that are produced in small amounts by the adrenal cortex. They do not normally affect sexual characteristics and may supplement sex hormones released from the gonads. The adrenal medulla contains two types of secretory cells: one that produces epinephrine (adrenaline) and another that produces norepinephrine (noradrenaline). Epinephrine and norepinephrine cause immediate, short-term changes in response to stressors, inducing the so-called fight-or-flight response. The responses include increased heart rate, breathing rate, cardiac muscle contractions, and blood-glucose levels. They also accelerate the breakdown of glucose in skeletal muscles and stored fats in adipose tissue, and redirect blood flow toward skeletal muscles and away from skin and viscera. The release of epinephrine and norepinephrine is stimulated by neural impulses from the sympathetic nervous system that originate from the hypothalamus.

The **pancreas** is an elongate organ located between the stomach and the proximal portion of the small intestine (Figure 11.1**d**). It contains both exocrine cells that excrete digestive enzymes and endocrine cells that release hormones.

The endocrine cells of the pancreas form clusters called pancreatic islets or the islets of Langerhans. Among the cell types in each pancreatic islet are the alpha cells, which produce the hormone glucagon, and the beta cells, which produce the hormone insulin. These hormones regulate blood-glucose levels. Alpha cells release glucagon as blood-glucose levels decline. When blood-glucose levels rise, beta cells release insulin. Glucagon causes the release of glucose to the blood from the liver, and insulin facilitates the uptake of glucose by the body's cells.

The gonads(testes in the male and ovaries in the female)produce steroid hormones. The testes produce androgens, testosterone being the most prominent, which allow for the development of secondary sex characteristics and the production of sperm cells. The ovaries produce estrogen and progesterone, which cause secondary sex characteristics, regulate production of eggs, control pregnancy, and prepare the body for childbirth.

The kidneys also possess endocrine function. Erythropoietin (EPO) is released by kidneys in response to low blood oxygen levels. EPO triggers an increase in the rate of production of red blood cells in the red bone marrow. EPO has been used by athletes (e.g. cyclists) to improve performance because more RBCs mean more oxygen can be transported. However, EPO doping has its risks, because it thickens the blood and increases strain on the heart; it also increases the risk of blood clots and therefore heart attacks and stroke.

Endocrine Glands and Their Associated Hormones		
Endocrine Gland	**Associated Hormones**	**Effect**
Pituitary (anterior)	growth hormone	promotes growth of body tissues
	prolactin	promotes milk production
	thyroid-stimulating hormone	stimulates thyroid hormone release
	adrenocorticotropic hormone	stimulates hormone release by adrenal cortex
	follicle-stimulating hormone	stimulates gamete production
	luteinizing hormone	stimulates androgen production by gonads in males; stimulates ovulation and production of estrogen and progesterone in females
Pituitary (posterior)	antidiuretic hormone	stimulates water reabsorption by kidneys
	oxytocin	stimulates uterine contractions during childbirth
Thyroid	thyroxine, triiodothyronine	stimulate metabolism
	calcitonin	reduces blood Ca^{2+} levels
Parathyroid	parathyroid hormone	increases blood Ca^{2+} levels
Adrenal (cortex)	aldosterone	increases blood Na^{+} levels
	cortisol, corticosterone, cortisone	increase blood-glucose levels
Adrenal (medulla)	epinephrine, norepinephrine	stimulate fight-or-flight response
Pancreas	insulin	reduces blood-glucose levels
	glucagon	increases blood-glucose levels

Table 11.1

11.1.4 Regulation of Hormone Production

Hormone production and release are primarily controlled by negative feedback, as described in the discussion on homeostasis. In this way, the concentration of hormones in blood is maintained within a narrow range. For example, the anterior pituitary signals the thyroid to release thyroid hormones. Increasing levels of these hormones in the blood then give feedback to the hypothalamus and anterior pituitary to inhibit further signaling to the thyroid gland (Figure 11.2).

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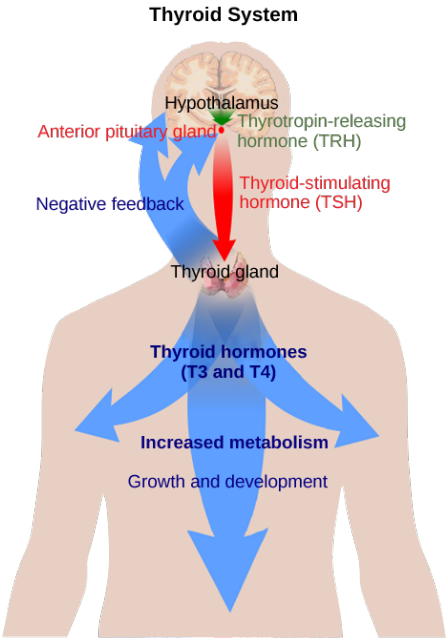

Figure 11.2: The anterior pituitary stimulates the thyroid gland to release thyroid hormones T_3 and T_4. Increasing levels of these hormones in the blood result in feedback to the hypothalamus and anterior pituitary to inhibit further signaling to the thyroid gland. (credit: modification of work by Mikael Häggström)

11.1.5 Section Summary

Hormones cause cellular changes by binding to receptors on or in target cells. The number of receptors on a target cell can increase or decrease in response to hormone activity.

Hormone levels are primarily controlled through negative feedback, in which rising levels of a hormone inhibit its further release.

The pituitary gland is located at the base of the brain. The anterior pituitary receives signals from the hypothalamus and produces six hormones. The posterior pituitary is an extension of the brain and releases hormones (antidiuretic hormone and oxytocin) produced by the hypothalamus. The thyroid gland is located in the neck and is composed of two lobes. The thyroid produces the hormones thyroxine and triiodothyronine. The thyroid also produces calcitonin. The parathyroid glands lie on the posterior surface of the thyroid gland and produce parathyroid hormone.

The adrenal glands are located on top of the kidneys and consist of the adrenal cortex and adrenal medulla. The adrenal cortex produces the glucocorticoids, mineralocorticoids, and gonadocorticoids. The adrenal medulla is the inner part of the adrenal gland and produces epinephrine and norepinephrine.

The pancreas lies in the abdomen between the stomach and the small intestine. Clusters of endocrine cells in the pancreas form the islets of Langerhans, which contain alpha cells that release glucagon and beta cells that release insulin. The kidneys produce erythropoietin. The gonads produce steroid hormones, including testosterone in males and estrogen and progesterone in females.

11.1.6 Art Connections

Exercise 11.1.1 *(Solution on p. 260.)*

Goiter, a disease caused by iodine deficiency, results in the inability of the thyroid gland to form T_3 and T_4. The body typically attempts to compensate by producing greater amounts of TSH. Which of the following symptoms would you expect goiter to cause?

a. Hypothyroidism, resulting in weight gain, cold sensitivity, and reduced mental activity.
b. Hyperthyroidism, resulting in weight loss, profuse sweating and increased heart rate.
c. Hyperthyroidism, resulting in weight gain, cold sensitivity, and reduced mental activity.
d. Hypothyroidism, resulting in weight loss, profuse sweating and increased heart rate.

11.1.7 Review Questions

Exercise 11.1.2 *(Solution on p. 260.)*

Most of the hormones produced by the anterior pituitary perform what function?

a. regulate growth
b. regulate the sleep cycle
c. regulate production of other hormones
d. regulate blood volume and blood pressure

Exercise 11.1.3 *(Solution on p. 260.)*

What is the function of the hormone erythropoietin?

a. stimulates production of red blood cells
b. stimulates muscle growth
c. causes the fight-or-flight response
d. causes testosterone production

Exercise 11.1.4 *(Solution on p. 260.)*

Which endocrine glands are associated with the kidneys?

a. thyroid glands
b. pituitary glands
c. adrenal glands
d. gonads

11.1.8 Free Response

Exercise 11.1.5 *(Solution on p. 260.)*

What is a similarity and a difference between an exocrine gland and an endocrine gland?

Exercise 11.1.6 *(Solution on p. 260.)*

Many hormone systems regulate body functions through opposing hormone actions. Describe how opposing hormone actions regulate blood-glucose levels?

Solutions to Exercises in Chapter 11

to Exercise 11.1.1 (p. 259)
Figure 11.2A
to Exercise 11.1.2 (p. 259)
C
to Exercise 11.1.3 (p. 259)
A
to Exercise 11.1.4 (p. 259)
C
to Exercise 11.1.5 (p. 259)
The cells of both exocrine and endocrine glands produce a product that will be secreted by the gland. An exocrine gland has a duct and secretes its product to the outside of the gland, not into the bloodstream. An endocrine gland secretes its product into the bloodstream and does not use a duct.
to Exercise 11.1.6 (p. 259)
Blood-glucose levels are regulated by hormones produced by the pancreas: insulin and glucagon. When blood-glucose levels are increasing, the pancreas releases insulin, which stimulates uptake of glucose by cells. When blood-glucose levels are decreasing, the pancreas releases glucagon, which stimulates the release of stored glucose by the liver to the bloodstream.

Chapter 12

Urinary System

12.1 Introduction to the Urinary System[1]

Sewage Treatment Plant

Figure 12.1: (credit: "eutrophication&hypoxia"/flickr.com)

[1] This content is available online at <http://cnx.org/content/m58004/1.1/>.

NOTE: After studying this chapter, you will be able to:

- Describe the composition of urine
- Label structures of the urinary system
- Characterize the roles of each of the parts of the urinary system
- Trace the flow of blood through the kidney
- Outline how blood is filtered in the kidney nephron
- List some of the solutes filtered, secreted, and reabsorbed in different parts of the nephron

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

If the kidneys fail, these functions are compromised or lost altogether, with devastating effects on homeostasis. The affected individual might experience weakness, lethargy, shortness of breath, anemia, widespread edema (swelling), metabolic acidosis, rising potassium levels, heart arrhythmias, and more. Each of these functions is vital to your well-being and survival. The urinary system, controlled by the nervous system, also stores urine until a convenient time for disposal and then provides the anatomical structures to transport this waste liquid to the outside of the body. Failure of nervous control or the anatomical structures leading to a loss of control of urination results in a condition called incontinence.

This chapter will help you to understand the anatomy of the urinary system and how it enables the physiologic functions critical to homeostasis. It is best to think of the kidney as a regulator of plasma makeup rather than simply a urine producer. As you read each section, ask yourself this question: "What happens if this does not work?" This question will help you to understand how the urinary system maintains homeostasis and affects all the other systems of the body and the quality of one's life.

: Watch this video[2] from the Howard Hughes Medical Institute for an introduction to the urinary system.

12.2 Urinary System Anatomy and Function[3]

12.2.1 Anatomy of the Urinary System

The **kidneys**, illustrated in Figure 12.2, are a pair of bean-shaped structures that are located just below and behind the liver in the abdominal cavity. The adrenal glands sit on top of each kidney and function as a component of the endocrine system. Kidneys filter blood and purify it. All the blood in the human body

[2] http://openstaxcollege.org/l/urineintro
[3] This content is available online at <http://cnx.org/content/m58008/1.2/>.

is filtered many times a day by the kidneys; these organs use up almost 25 percent of the oxygen absorbed through the lungs to perform this function. Oxygen allows the kidney cells to efficiently manufacture chemical energy in the form of ATP through aerobic respiration. The filtrate coming out of the kidneys is called **urine**. Urine is carried from the kidneys to the **urinary bladder** via the **ureters**, which are approximately 30 cm long. As urine passes through the ureters, it does not passively drain into the bladder but rather is propelled by waves of peristalsis (smooth muscle contractions). The bladder collects urine from both ureters . During late pregnancy, its capacity (typically several hundred milliliters) is reduced due to compression by the enlarging uterus, resulting in increased frequency of urination. The **urethra** transports urine from the bladder to the outside of the body for disposal. The urethra is the only urologic organ that shows any significant anatomic difference between males and females; all other urine transport structures are identical. In females, the urethra is relatively short length, about 4 cm, and is less of a barrier to fecal bacteria than the longer male urethra (approximately 20 cm). This length difference is the best explanation for the greater incidence of urinary tract infections (UTIs) in women. The urethra in males also has a reproductive function, as it transports semen (sperm and accessory fluids).

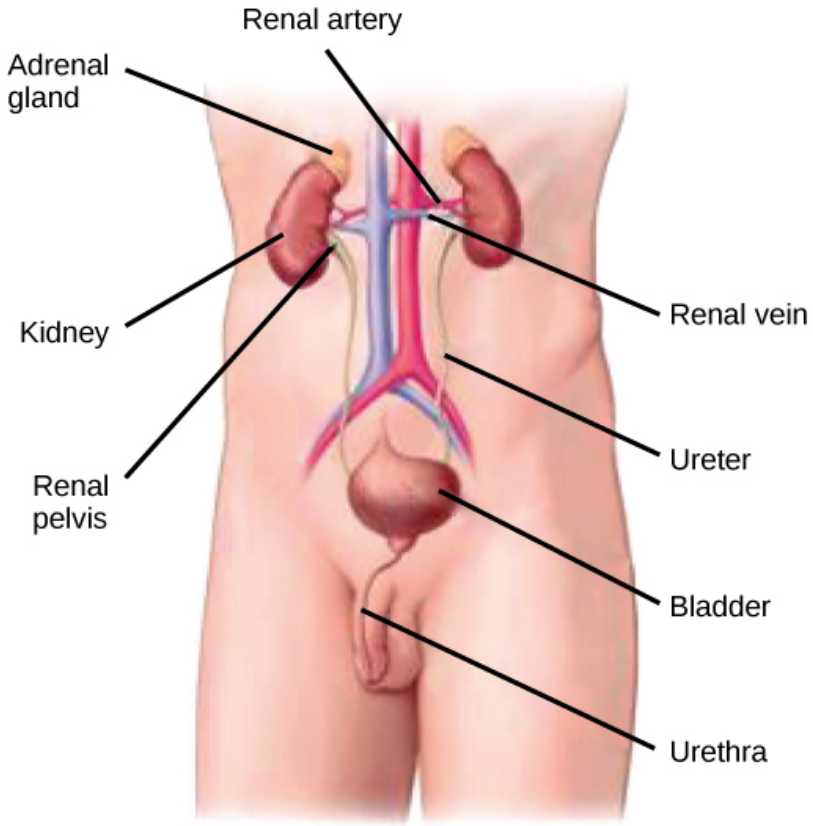

Figure 12.2: Kidneys filter the blood, producing urine that is stored in the bladder prior to elimination through the urethra. (credit: modification of work by NCI)

12.2.2 Kidney Structure

Internally, the kidney has three regions—an outer **cortex**, a **medulla** in the middle, and the **renal pelvis** in the region called the **hilum** of the kidney. The hilum is the concave part of the bean-shape where blood vessels and nerves enter and exit the kidney; it is also the point of exit for the ureters. The renal cortex is granular due to the presence of renal corpuscles; nephron tubules can be found throughout the renal cortex and **renal pyramids**, the multiple tissue masses that make up the majority of the renal medulla. There are, on average, eight renal pyramids in each kidney. Urine that is produced by the nephrons travels into the renal pelvis and then into the ureters, which carry the urine to the bladder.

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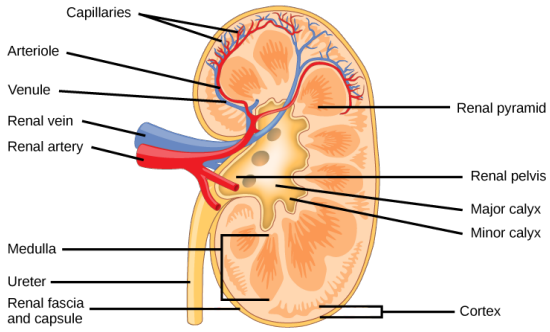

Figure 12.3: The internal structure of the kidney is shown. (credit: modification of work by NCI)

Because the kidney filters blood, its network of blood vessels is an important component of its structure and function. The arteries, veins, and nerves that supply the kidney enter and exit at the renal hilum. Renal blood supply starts with the branching of the aorta into the **renal arteries** and ends with the exiting of the **renal veins** to join the **inferior vena cava**, which transports blood back to the right atrium of the heart. The renal arteries split multiple times to form other blood vessels before branching into numerous afferent arterioles, and then enter the capillaries supplying the nephrons.

As mentioned previously, the functional unit of the kidney is the nephron, illustrated in Figure 12.4. Each kidney is made up of over one million nephrons that dot the renal cortex. A nephron consists of three parts—a **renal corpuscle**, a **renal tubule**, and the associated capillary network.

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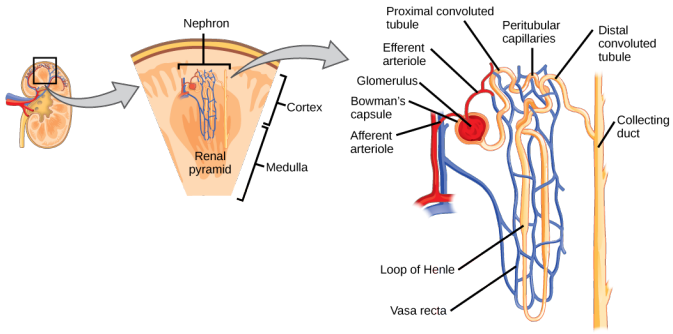

Figure 12.4: The nephron is the functional unit of the kidney. The glomerulus and convoluted tubules are located in the kidney cortex, while collecting ducts are located in the pyramids of the medulla. (credit: modification of work by NIDDK)

12.2.2.1 Renal Corpuscle

The renal corpuscle, located in the renal cortex, is made up of a network of capillaries known as the **glomerulus** and the capsule, a cup-shaped chamber that surrounds it, called the glomerular or **Bowman's capsule**.

12.2.2.2 Renal Tubule

The renal tubule is a long and convoluted structure that emerges from the glomerulus and can be divided into three parts based on function. The first part is called the **proximal convoluted tubule (PCT)** due to its proximity to the glomerulus. The second part is called the **loop of Henle**, because it forms a loop (with **descending** and **ascending limbs**). The third part of the renal tubule is called the **distal convoluted tubule (DCT)**. The DCT, which is the last part of the nephron, connects and empties its contents into collecting ducts. The urine will ultimately move into the renal pelvis and then into the ureters.

12.2.2.3 Capillary Network within the Nephron

The capillary network that originates from the renal arteries supplies the nephron with blood that needs to be filtered. The branch that enters the glomerulus is called the **afferent arteriole**. The branch that exits the glomerulus is called the **efferent arteriole**. Within the glomerulus, the network of capillaries is called the glomerular capillary bed. Once the efferent arteriole exits the glomerulus, it forms the **peritubular capillary network**, which surrounds and interacts with parts of the renal tubule.

: Go to this website[4] to see another section of the kidney and to explore an animation of the workings of nephrons.

[4] http://openstaxcollege.org/l/kidney_section

12.2.3 Kidney Function and Physiology

Kidneys filter blood in a three-step process. First, the nephrons filter blood that runs through the capillary network in the glomerulus. Almost all solutes, except for proteins, are filtered out into the glomerulus by a process called **glomerular filtration**. Second, the filtrate is collected in the renal tubules. Most of the solutes get reabsorbed in the PCT by a process called **tubular reabsorption**. In the loop of Henle, the filtrate continues to exchange solutes and water with the peritubular capillary network. Water is also reabsorbed during this step. Then, additional solutes and wastes are secreted into the kidney tubules during **tubular secretion**, which is, in essence, the opposite process to tubular reabsorption. The collecting ducts collect filtrate coming from the nephrons and this filtrate, called urine, will be transported into the renal pelvis and then to the ureters. This entire process is illustrated in Figure 12.5.

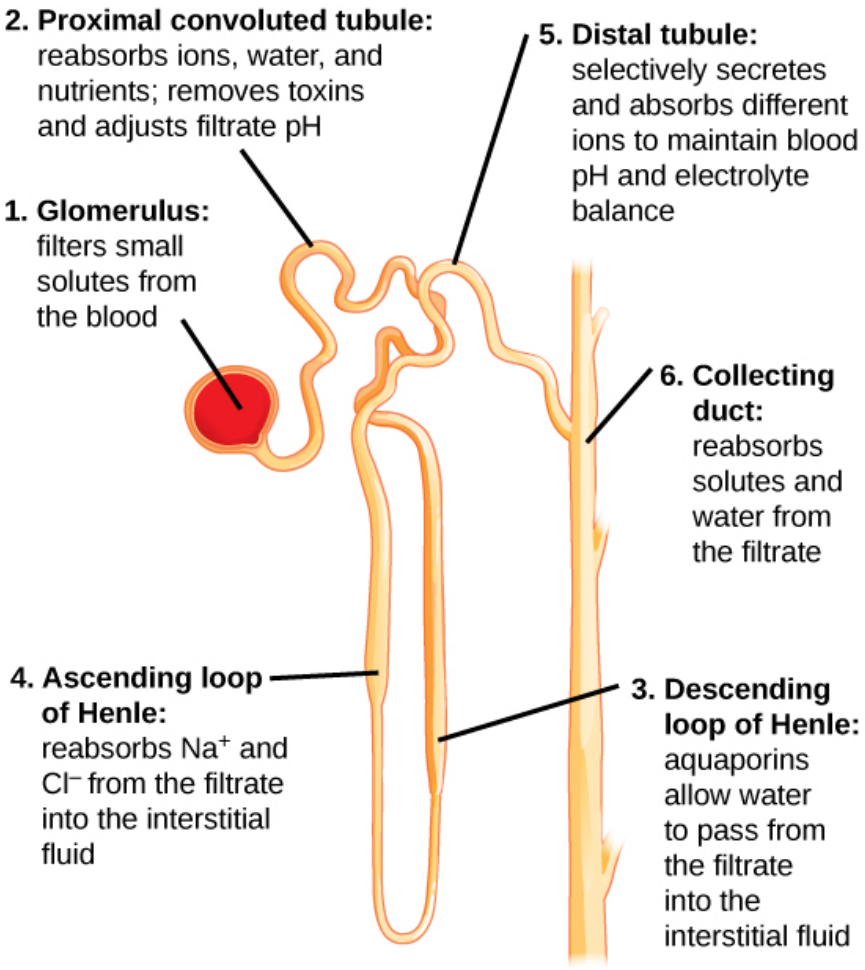

Figure 12.5: Each part of the nephron performs a different function in filtering waste and maintaining homeostatic balance. (1) The glomerulus forces small solutes out of the blood by pressure. (2) The proximal convoluted tubule reabsorbs ions, water, and nutrients from the filtrate into the interstitial fluid, and actively transports toxins and drugs from the interstitial fluid into the filtrate. The proximal convoluted tubule also adjusts blood pH by selectively secreting ammonia (NH_3) into the filtrate, where it reacts with H^+ to form NH_4^+. The more acidic the filtrate, the more ammonia is secreted. (3) The descending loop of Henle is lined with cells containing aquaporins that allow water to pass from the filtrate into the interstitial fluid. (4) In the thin part of the ascending loop of Henle, Na^+ and Cl^- ions diffuse into the interstitial fluid. In the thick part, these same ions are actively transported into the interstitial fluid. Because salt but not water is lost, the filtrate becomes more dilute as it travels up the limb. (5) In the distal convoluted tubule, K^+ and H^+ ions are selectively secreted into the filtrate, while Na^+, Cl^-, and HCO_3^- ions are reabsorbed to maintain pH and electrolyte balance in the blood. (6) The collecting duct reabsorbs solutes and water from the filtrate, forming dilute urine. (credit: modification of work by NIDDK)

12.2.3.1 Glomerular Filtration

Glomerular filtration filters out most of the solutes due to high blood pressure and specialized membranes in the afferent arteriole. The blood pressure in the glomerulus is maintained independent of factors that affect systemic blood pressure. The "leaky" connections between the endothelial cells of the glomerular capillary network allow solutes to pass through easily. All solutes in the glomerular capillaries, except for macromolecules like proteins, pass through by passive diffusion. There is no energy requirement at this stage of the filtration process. **Glomerular filtration rate (GFR)** is the volume of glomerular filtrate formed per minute by the kidneys. GFR is regulated by multiple mechanisms and is an important indicator of kidney function.

12.2.3.2 Tubular Reabsorption and Secretion

Tubular reabsorption occurs in the PCT part of the renal tubule. Almost all nutrients are reabsorbed, and this occurs either by passive or active transport. Reabsorption of water and some key electrolytes are regulated and can be influenced by hormones. Sodium (Na^+) is the most abundant ion and most of it is reabsorbed by active transport and then transported to the peritubular capillaries. Because Na^+ is actively transported out of the tubule, water follows it to even out the osmotic pressure. Water is also independently reabsorbed into the peritubular capillaries due to the presence of aquaporins, or water channels, in the PCT.

In the loop of Henle, the permeability of the membrane changes. The descending limb is permeable to water, not solutes; the opposite is true for the ascending limb.

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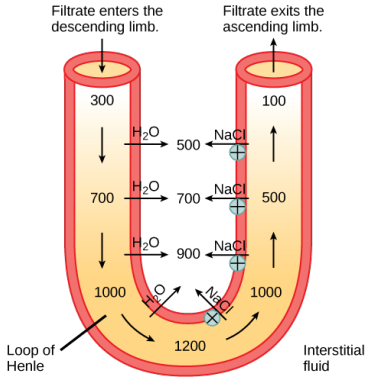

Figure 12.6: The loop of Henle acts as a countercurrent multiplier that uses energy to create concentration gradients. The descending limb is water permeable. Water flows from the filtrate to the interstitial fluid, so the concentration of solutes inside the limb increases as it descends into the renal medulla. At the bottom, the concentration of solutes is higher inside the loop than in the interstitial fluid. Thus, as filtrate enters the ascending limb, Na^+ and Cl^- ions exit through ion channels present in the cell membrane. Further up, Na^+ is actively transported out of the filtrate and Cl^- follows. The concentration of solutes is given in units of milliosmoles per liter.

By the time the filtrate reaches the DCT, most of the water and solutes have been reabsorbed. If the body requires additional water, more of it can be reabsorbed at this point. Further reabsorption is controlled by hormones, which will be discussed in a later section. Excretion of wastes occurs due to lack of reabsorption combined with tubular secretion. Undesirable products like metabolic wastes, urea, uric acid, and certain drugs, are excreted by tubular secretion. Most of the tubular secretion happens in the DCT, but some occurs in the early part of the collecting duct. Kidneys also maintain an acid-base balance by secreting excess H^+ ions.

: **Nephrologist**

A nephrologist studies and deals with diseases of the kidneys—both those that cause kidney failure (such as diabetes) and the conditions that are produced by kidney disease (such as hypertension). Blood pressure, blood volume, and changes in electrolyte balance come under the purview of a nephrologist.

Nephrologists usually work with other physicians who refer patients to them or consult with them about specific diagnoses and treatment plans. Patients are usually referred to a nephrologist for symptoms such as blood or protein in the urine, very high blood pressure, kidney stones, or renal failure.

Nephrology is a subspecialty of internal medicine. To become a nephrologist, medical school is followed by additional training to become certified in internal medicine. An additional two or more years is spent specifically studying kidney disorders and their accompanying effects on the body.

12.2.4 Section Summary

The kidneys are the main osmoregulatory organs in mammalian systems; they function to filter blood and maintain the correct concentration of solutes in body fluids. They are made up internally of three distinct regions—the cortex, medulla, and pelvis.

The blood vessels that transport blood into and out of the kidneys arise from and merge with the aorta and inferior vena cava, respectively. The renal arteries branch out from the aorta and enter the kidney where they further divide.

The nephron is the functional unit of the kidney, which actively filters blood and generates urine. The nephron is made up of the renal corpuscle and renal tubule. The nephron filters and exchanges water and solutes with two sets of blood vessels and the tissue fluid in the kidneys.

There are three steps in the formation of urine: glomerular filtration, which occurs in the glomerulus; tubular reabsorption, which occurs in the renal tubules; and tubular secretion, which also occurs in the renal tubules.

12.2.5 Art Connections

Exercise 12.2.1 ***(Solution on p. 273.)***

Figure 12.3 Which of the following statements about the kidney is false?

a. The renal pelvis drains into the ureter.
b. The renal pyramids are in the medulla.
c. The cortex covers the kidney.
d. Nephrons are in the renal cortex.

Exercise 12.2.2 ***(Solution on p. 273.)***

Figure 12.4 Which of the following statements about the nephron is false?

a. The collecting duct empties into the distal convoluted tubule.
b. The Bowman's capsule surrounds the glomerulus.
c. The loop of Henle is between the proximal and distal convoluted tubules.
d. The loop of Henle empties into the distal convoluted tubule.

Exercise 12.2.3 ***(Solution on p. 273.)***

Figure 12.6 Loop diuretics are drugs sometimes used to treat hypertension. These drugs inhibit the reabsorption of Na^+ and Cl^- ions by the ascending limb of the loop of Henle. A side effect is that they increase urination. Why do you think this is the case?

12.2.6 Review Questions

Exercise 12.2.4 *(Solution on p. 273.)*

The gland located at the top of the kidney is the _ _ _ _ _ _ _ _ gland.

a. adrenal
b. pituitary
c. thyroid
d. thymus

12.2.7 Free Response

Exercise 12.2.5 *(Solution on p. 273.)*

Describe the three major regions of the kidney's internal structure.

12.3 Hormonal Control of Urine Concentration[5]

While the kidneys operate to maintain osmotic balance and blood pressure in the body, they also act in concert with hormones. Hormones are small molecules that act as messengers within the body. Hormones are typically secreted from one cell and travel in the bloodstream to affect a target cell in another portion of the body. Different regions of the nephron bear specialized cells that have receptors to respond to chemical messengers and hormones. In this section, you will learn about two hormones, aldosterone and antidiuretic hormone, that control urine concentration.

12.3.1 Aldosterone

Aldosterone is a hormone synthesized by the adrenal cortex that affects urine concentration by regulating sodium levels in the blood. Almost all of the sodium in the blood is reclaimed by the renal tubules under the influence of aldosterone. Because sodium is always reabsorbed by active transport and water follows sodium to maintain osmotic balance, aldosterone manages not only sodium levels but also the water levels in urine. Aldosterone favors the production of a concentrated urine by the water following the reabsorbed sodium ions. A decrease in the secretion of aldosterone means that less sodium gets reabsorbed in the renal tubules; therefore, more of it gets excreted in the urine. Patients who have Addison's disease have a failing adrenal cortex and cannot produce aldosterone. They lose sodium in their urine constantly, and if the supply is not replenished, the consequences can be fatal.

12.3.2 Antidiurectic Hormone

Diuretics are drugs that can increase water loss by interfering with the recapture of solutes and water from the forming urine. They are often prescribed to lower blood pressure. Coffee, tea, and alcoholic beverages are familiar diuretics. Antidiuretic hormone or ADH, as the name suggests, helps the body conserve water when body fluid volume, especially that of blood, is low. It is formed by the hypothalamus and is stored and released from the posterior pituitary gland. It acts by inserting aquaporins, protein channels that allow water to leave, in the collecting ducts and promotes reabsorption of water. This action results in the formation of a concentrated urine. ADH also acts as a vasoconstrictor and increases blood pressure during hemorrhaging.

[5]This content is available online at <http://cnx.org/content/m58009/1.2/>.

12.3.3 Section Summary

Hormonal cues help the kidneys synchronize the osmotic needs of the body. Hormones like aldosterone and anti-diuretic hormone (ADH) help regulate the needs of the body as well as the communication between the different organ systems.

12.3.4 Review Questions

Exercise 12.3.1 *(Solution on p. 273.)*

Aldosterone is made by _ _ _ _ _ _ _ _.

a. the adrenal glands
b. the hypothalamus
c. the anterior pituitary gland
d. the posterior pituitary gland

Exercise 12.3.2 *(Solution on p. 273.)*

Patients with Addison's disease _ _ _ _ _ _ _ _.

a. retain water
b. retain salts
c. lose salts and water
d. have too much aldosterone

12.3.5 Free Response

Exercise 12.3.3 *(Solution on p. 273.)*

Describe how hormones regulate blood pressure, blood volume, and kidney function.

Solutions to Exercises in Chapter 12

to Exercise 12.2.1 (p. 270)
Figure 12.3 C
to Exercise 12.2.2 (p. 270)
Figure 12.4 A
to Exercise 12.2.3 (p. 270)
Figure 12.6 Loop diuretics decrease the excretion of salt into the renal medulla, thereby reducing its concentration of solutes. As a result, less water is excreted into the medulla by the descending limb, and more water is excreted as urine.
to Exercise 12.2.4 (p. 271)
A
to Exercise 12.2.5 (p. 271)
Internally, the kidney has three regions—an outer cortex, a medulla in the middle, and the renal pelvis in the region called the hilum of the kidney, which is the concave part of the "bean" shape.
to Exercise 12.3.1 (p. 272)
A
to Exercise 12.3.2 (p. 272)
C
to Exercise 12.3.3 (p. 272)
Hormones are small molecules that act as messengers within the body. Different regions of the nephron bear specialized cells, which have receptors to respond to chemical messengers and hormones. The hormones carry messages to the kidney. These hormonal cues help the kidneys synchronize the osmotic needs of the body. Both ADH and aldosterone promote water reabsorption from the filtrate, which increases blood volume and blood pressure while also producing a concentrated urine.

Chapter 13

Mitosis and Meiosis

13.1 Introduction to Cell Division[1]

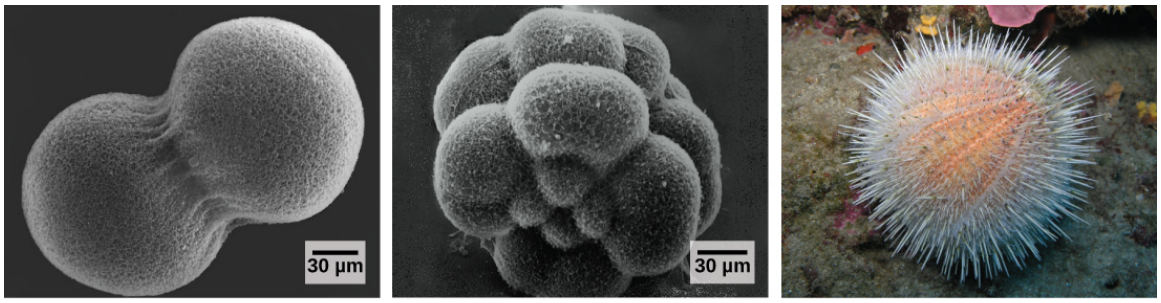

Figure 13.1: A sea urchin begins life as a single cell that (a) divides to form two cells, visible by scanning electron microscopy. After four rounds of cell division, (b) there are 16 cells, as seen in this SEM image. After many rounds of cell division, the individual develops into a complex, multicellular organism, as seen in this (c) mature sea urchin. (credit a: modification of work by Evelyn Spiegel, Louisa Howard; credit b: modification of work by Evelyn Spiegel, Louisa Howard; credit c: modification of work by Marco Busdraghi; scale-bar data from Matt Russell)

The individual sexually reproducing organism—including humans—begins life as a fertilized egg, or zygote. Trillions of cell divisions subsequently occur in a controlled manner to produce a complex, multicellular human. In other words, that original single cell was the ancestor of every other cell in the body. Once a human individual is fully grown, cell reproduction is still necessary to repair or regenerate tissues. For example, new blood and skin cells are constantly being produced. The type of cell division associated with these events is **mitosis**, which produces genetically-identical cells with two sets of chromosomes (i.e. diploid). However, Humans also have to be able to produce specialized cells for reproduction (i.e. gametes) that contain only one set of chromosomes (i.e. haploid). The type of cell division associated with gamete production is **meiosis**.

[1] This content is available online at <http://cnx.org/content/m58010/1.1/>.

13.2 Chromosomes and the Genome[2]

The continuity of life from one cell to another has its foundation in the reproduction of cells by way of the cell cycle. The cell cycle is an orderly sequence of events in the life of a cell from the division of a single parent cell to produce two new daughter cells, to the subsequent division of those daughter cells. The mechanisms involved in the cell cycle are highly conserved across eukaryotes.

13.2.1 Genomic DNA

Before discussing the steps a cell undertakes to replicate, a deeper understanding of the structure and function of a cell's genetic information is necessary. A complement of DNA in a gamete is referred to as the **genome**. A somatic cell (i.e. a cell with two sets of chromosomes) contains 2 copies of the genome - one from the mother's egg and one from the father's sperm. These two copies of the genome are found in the zygote.

In eukaryotes, the genome comprises several double-stranded, linear DNA molecules (Figure 13.2) bound with proteins to form complexes called chromosomes. Each species of eukaryote has a characteristic number of chromosomes in the nuclei of its cells. Human body cells (somatic cells) have 46 chromosomes. A somatic cell contains two matched sets of chromosomes, a configuration known as **diploid**. The letter n is used to represent a single set of chromosomes; therefore a diploid organism is designated $2n$. Human cells that contain one set of 23 chromosomes are called **gametes**, or sex cells; these eggs and sperm are designated n, or **haploid**.

[2]This content is available online at <http://cnx.org/content/m58011/1.1/>.

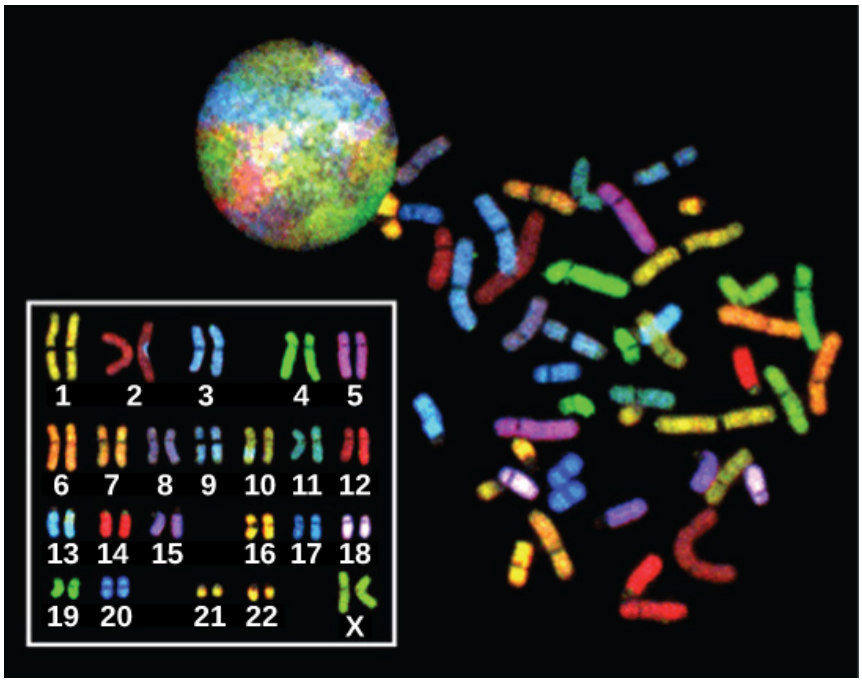

Figure 13.2: There are 23 pairs of homologous chromosomes in a female human somatic cell. These chromosomes are viewed within the nucleus (top), removed from a cell in mitosis (right), and arranged according to length (left) in an arrangement called a karyotype. In the karyotype, the first 22 pairs of chromosomes are called **autosomes**. The 23rd pair of chromosomes is called the **sex chromosomes**. A male has the sex chromosomes X and Y and the female has the sex chromosomes X and X. Therefore, the human karyotype shown is from a female. In this image, the chromosomes were exposed to fluorescent stains to distinguish them. (credit: "718 Bot"/Wikimedia Commons, National Human Genome Research)

The matched pairs of chromosomes in a diploid organism are called **homologous chromosomes**. Homologous chromosomes are the same length and have specific nucleotide segments called **genes** in exactly the same location, or **loci; singular: locus**. Genes, the functional units of chromosomes, determine specific characteristics by coding for specific proteins. Traits are the different forms of a characteristic. For example, the shape of earlobes is a characteristic with traits of free or attached.

Each copy of the homologous pair of chromosomes originates from a different parent; therefore, the copies of each of the genes themselves may not be identical. The variation of individuals within a species is caused by the specific combination of the genes inherited from both parents. For example, there are three possible gene sequences on the human chromosome that codes for blood type: sequence A, sequence B, and sequence O. Because all diploid human cells have two copies of the chromosome that determines blood type, the blood type (the trait) is determined by which two versions of the marker gene are inherited. It is possible to have two copies of the same gene sequence, one on each homologous chromosome (for example, AA, BB, or OO), or two different sequences, such as AB.

Minor variations in traits such as those for blood type, eye color, and height contribute to the natural variation found within a species. The sex chromosomes, X and Y, are the single exception to the rule of homologous chromosomes; other than a small amount of homology that is necessary to reliably produce gametes, the genes found on the X and Y chromosomes are not the same.

13.2.2 Section Summary

Eukaryotes have multiple, linear chromosomes surrounded by a nuclear membrane. Human somatic cells have 46 chromosomes consisting of two sets of 22 homologous chromosomes and a pair of nonhomologous sex chromosomes. This is the $2n$, or diploid, state. Human gametes have 23 chromosomes or one complete set of chromosomes. This is the n, or haploid, state. Genes are segments of DNA that code for a specific protein or RNA molecule. An organism's traits are determined in large part by the genes inherited from each parent, but also by the environment that they experience. Genes are expressed as characteristics of the organism and each characteristic may have different variants called traits that are caused by differences in the DNA sequence for a gene.

13.2.3 Multiple Choice

Exercise 13.2.1 *(Solution on p. 296.)*
A diploid cell has _ _ _ _ _ _ _ _ the number of chromosomes as a haploid cell.

a. one-fourth
b. one-half
c. twice
d. four times

Exercise 13.2.2 *(Solution on p. 296.)*
An organism's traits are determined by the specific combination of inherited _ _ _ _ _ _ _ _.

a. cells
b. genes
c. proteins
d. chromatids

13.2.4 Free Response

Exercise 13.2.3 *(Solution on p. 296.)*
Compare and contrast a human somatic cell to a human gamete.

13.3 The Cell Cycle[3]

The **cell cycle** is an ordered series of events involving cell growth and cell division (i.e. Mitosis) that produces two new daughter cells. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages of growth, DNA replication, and division that produce two genetically identical cells. The cell cycle has two major phases: interphase and the mitotic phase (Figure 13.3). During (**interphase**, the cell grows and DNA is replicated. During the **mitotic phase**, the replicated chromosomes separate (via mitosis), the cytoplasm divides (via cytokinesis, and the cell formally divides into two daughter cells. Watch this video about the cell cycle: https://www.youtube.com/watch?v=Wy3N5NCZBHQ[4]

[3] This content is available online at <http://cnx.org/content/m58012/1.1/>.
[4] https://www.youtube.com/watch?v=Wy3N5NCZBHQ

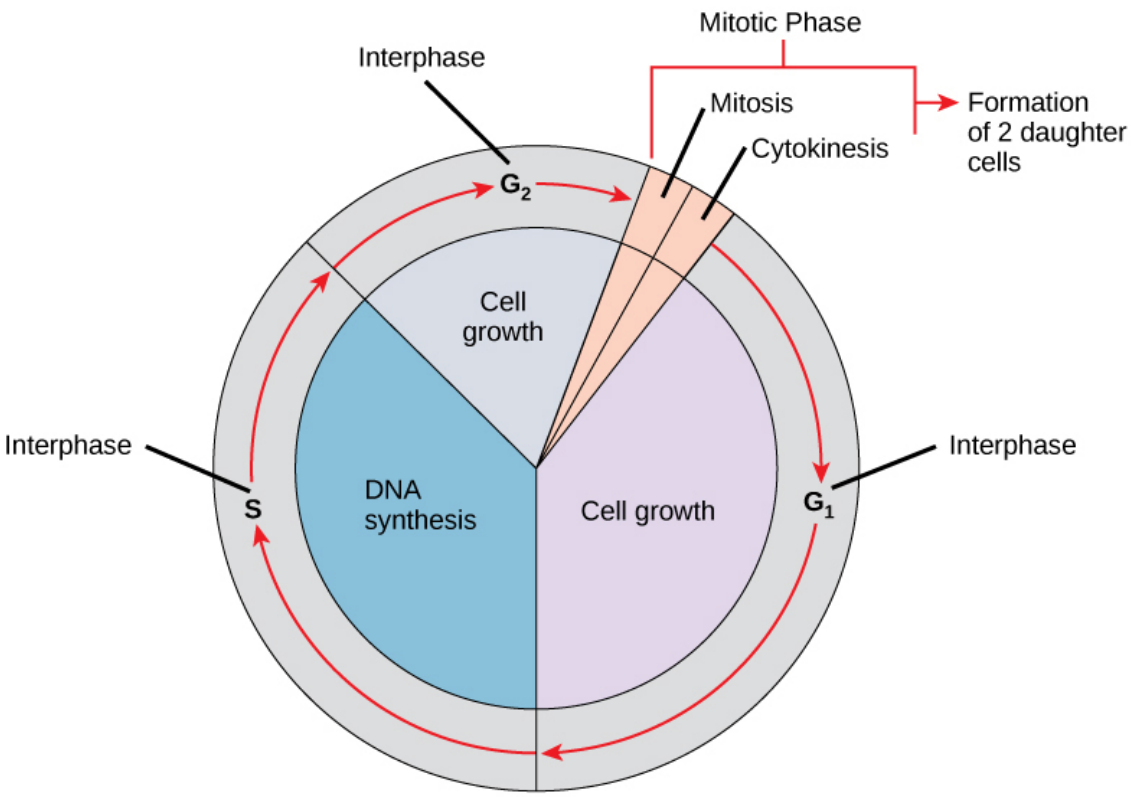

Figure 13.3: A cell moves through a series of phases in an orderly manner. During interphase, G_1 involves cell growth and protein synthesis, the S phase involves DNA replication and the replication of the centrosome, and G_2 involves further growth and protein synthesis. The mitotic phase follows interphase. Mitosis is nuclear division during which duplicated chromosomes are segregated and distributed into daughter nuclei. Usually the cell will divide after mitosis in a process called cytokinesis in which the cytoplasm is divided and two daughter cells are formed.

13.3.1 Interphase

During interphase, the cell undergoes normal processes while also preparing for cell division. For a cell to move from interphase to the mitotic phase, many internal and external conditions must be met. The three stages of interphase are called G_1, S, and G_2.

13.3.1.1 G_1 Phase

The first stage of interphase is called the **G_1 phase**, or first gap, because little change is visible. However, during the G_1 stage, the cell is quite active at the biochemical level. The cell is accumulating the building blocks of chromosomal DNA and the associated proteins, as well as accumulating enough energy reserves to complete the task of replicating each chromosome in the nucleus.

13.3.1.2 S Phase

Throughout interphase, nuclear DNA remains in a semi-condensed chromatin configuration. In the **S phase** (synthesis phase), DNA replication results in the formation of two identical copies of each chromosome—sister chromatids—that are firmly attached at the centromere region. At this stage, each chromosome is made of two sister chromatids and is a duplicated chromosome. The centrosome is duplicated during the S phase.

13.3.1.3 G_2 Phase

In the **G_2 phase**, or second gap, the cell replenishes its energy stores and synthesizes the proteins necessary for chromosome manipulation. Some cell organelles are duplicated, and the cytoskeleton is dismantled to provide resources for the mitotic spindle. There may be additional cell growth during G_2. The final preparations for the mitotic phase must be completed before the cell is able to enter the first stage of mitosis.

13.3.2 The Mitotic Phase

To make two daughter cells, the contents of the nucleus and the cytoplasm must be divided. The mitotic phase is a multistep process during which the duplicated chromosomes are aligned, separated, and moved to opposite poles of the cell, and then the cell is divided into two new identical daughter cells. The first portion of the mitotic phase, **mitosis**, is composed of five stages, which accomplish nuclear division. The second portion of the mitotic phase, called **cytokinesis**, is the physical separation of the cytoplasmic components into two daughter cells.

13.3.2.1 Mitosis

Mitosis is divided into a series of phases—prophase, prometaphase, metaphase, anaphase, and telophase—that result in the division of the cell nucleus (Figure 13.4).

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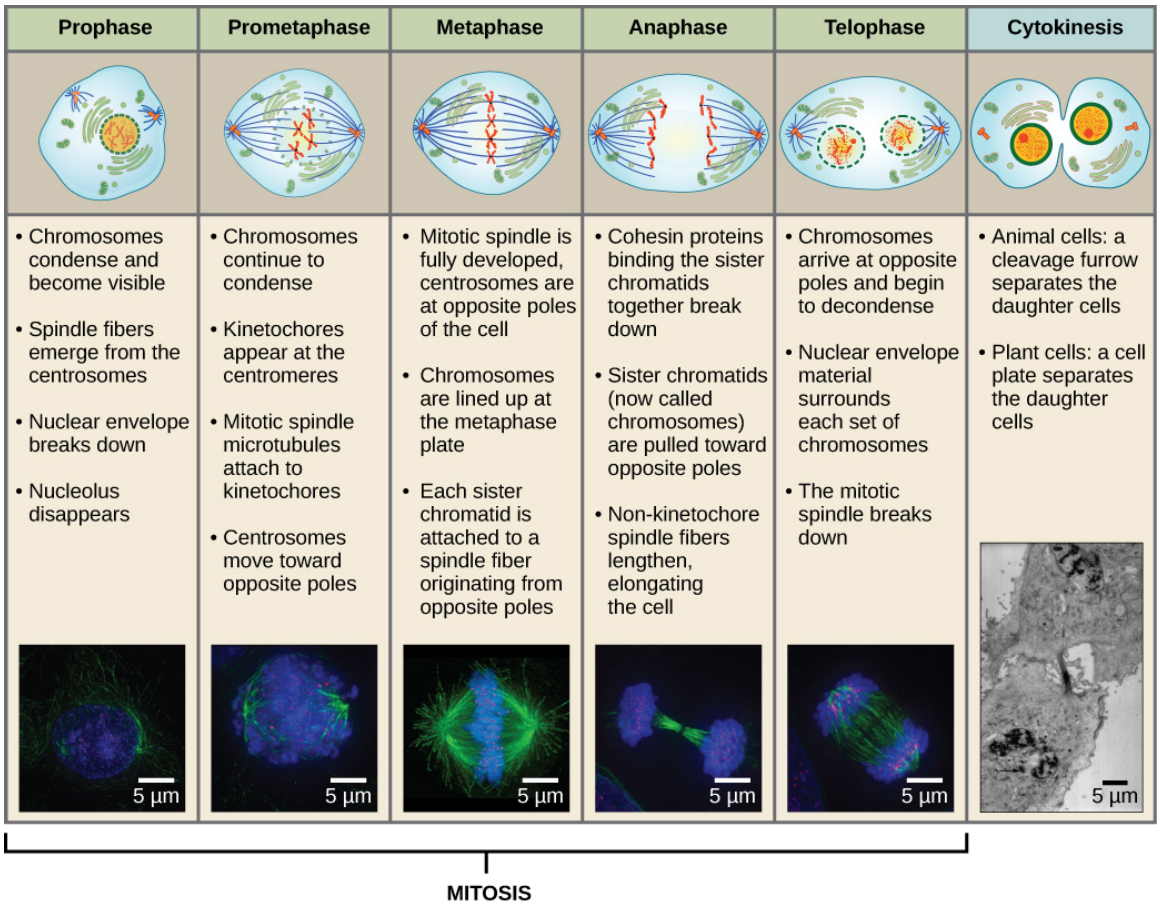


Figure 13.4: Animal cell mitosis is divided into five stages—prophase, prometaphase, metaphase, anaphase, and telophase—visualized here by light microscopy with fluorescence. Mitosis is usually accompanied by cytokinesis, shown here by a transmission electron microscope. (credit "diagrams": modification of work by Mariana Ruiz Villareal; credit "mitosis micrographs": modification of work by Roy van Heesbeen; credit "cytokinesis micrograph": modification of work by the Wadsworth Center, NY State Department of Health; donated to the Wikimedia foundation; scale-bar data from Matt Russell)

During **prophase**, the "first phase," several events must occur to provide access to the chromosomes in the nucleus. The nuclear envelope starts to break into small vesicles, and the Golgi apparatus and endoplasmic reticulum fragment and disperse to the periphery of the cell. The nucleolus disappears. The centrosomes begin to move to opposite poles of the cell. The microtubules that form the basis of the mitotic spindle extend between the centrosomes, pushing them farther apart as the microtubule fibers lengthen. The sister chromatids begin to coil more tightly and become visible under a light microscope.

During **prometaphase**, many processes that were begun in prophase continue to advance and culminate in the formation of a connection between the chromosomes and cytoskeleton. The remnants of the nuclear envelope disappear. The mitotic spindle continues to develop as more microtubules assemble and stretch across the length of the former nuclear area. Chromosomes become more condensed and visually discrete. Each sister chromatid attaches to spindle microtubules at the centromere via a protein complex called the **kinetochore**.

During **metaphase**, all of the chromosomes are aligned in a plane called the **metaphase plate**, or the equatorial plane, midway between the two poles of the cell. The sister chromatids are still tightly attached to each other. At this time, the chromosomes are maximally condensed.

During **anaphase**, the sister chromatids at the equatorial plane are split apart at the centromere. Each chromatid, now called a chromosome, is pulled rapidly toward the centrosome to which its microtubule was attached. The cell becomes visibly elongated as the non-kinetochore microtubules slide against each other at the metaphase plate where they overlap.

During **telophase**, all of the events that set up the duplicated chromosomes for mitosis during the first three phases are reversed. The chromosomes reach the opposite poles and begin to decondense (unravel). The mitotic spindles are broken down into monomers that will be used to assemble cytoskeleton components for each daughter cell. Nuclear envelopes form around chromosomes.

13.3.2.2 Cytokinesis

Cytokinesis is the second part of the mitotic phase during which cell division is completed by the physical separation of the cytoplasmic components into two daughter cells. Although the stages of mitosis are similar for most eukaryotes, the process of cytokinesis is quite different for eukaryotes that have cell walls, such as plant cells.

In cells such as animal cells that lack cell walls, cytokinesis begins following the onset of anaphase. A contractile ring composed of actin filaments forms just inside the plasma membrane at the former metaphase plate. The actin filaments pull the equator of the cell inward, forming a fissure. This fissure, or "crack," is called the **cleavage furrow**. The furrow deepens as the actin ring contracts, and eventually the membrane and cell are cleaved in two (Figure 13.5).

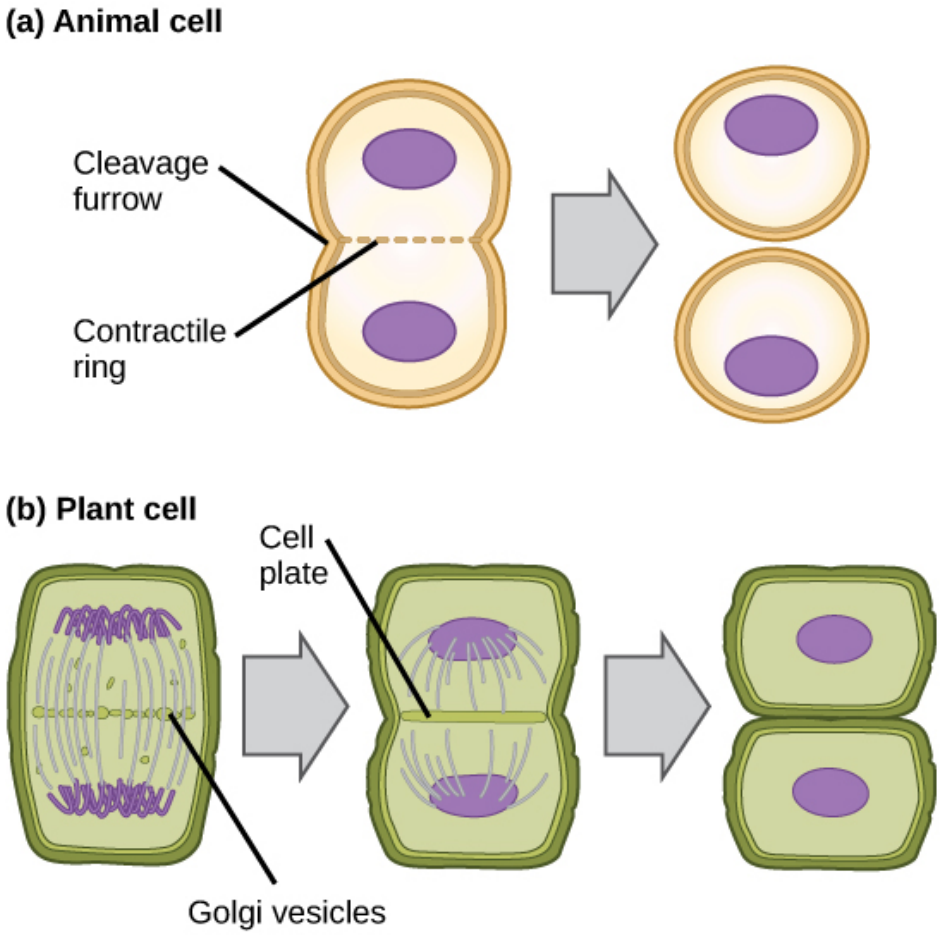


Figure 13.5: In part (a), a cleavage furrow forms at the former metaphase plate in the animal cell. The plasma membrane is drawn in by a ring of fibers contracting just inside the membrane. The cleavage furrow deepens until the cells are pinched in two.

13.3.3 Section Summary

The cell cycle is an orderly sequence of events. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages. In eukaryotes, the cell cycle consists of a long preparatory period, called interphase. Interphase is divided into G_1, S, and G_2 phases. Mitosis consists of five stages: prophase, prometaphase, metaphase, anaphase, and telophase. Mitosis is usually accompanied by cytokinesis, during which the cytoplasmic components of the daughter cells are separated either by an actin ring (animal cells) or by cell plate formation (plant cells).

13.3.4 Art Connections

Exercise 13.3.1 ***(Solution on p. 296.)***

Figure 13.4 Which of the following is the correct order of events in mitosis?

a. Sister chromatids line up at the metaphase plate. The kinetochore becomes attached to the mitotic spindle. The nucleus re-forms and the cell divides. The sister chromatids separate.
b. The kinetochore becomes attached to the mitotic spindle. The sister chromatids separate. Sister chromatids line up at the metaphase plate. The nucleus re-forms and the cell divides.
c. The kinetochore becomes attached to metaphase plate. Sister chromatids line up at the metaphase plate. The kinetochore breaks down and the sister chromatids separate. The nucleus re-forms and the cell divides.
d. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus re-forms and the cell divides.

13.3.5 Multiple Choice

Exercise 13.3.2 *(Solution on p. 296.)*

Chromosomes are duplicated during what portion of the cell cycle?

a. G_1 phase
b. S phase
c. prophase
d. prometaphase

Exercise 13.3.3 *(Solution on p. 296.)*

Separation of the sister chromatids is a characteristic of which stage of mitosis?

a. prometaphase
b. metaphase
c. anaphase
d. telophase

Exercise 13.3.4 *(Solution on p. 296.)*

The individual chromosomes become visible with a light microscope during which stage of mitosis?

a. prophase
b. prometaphase
c. metaphase
d. anaphase

13.4 Meiosis and Genetic Variation[5]

Sexual reproduction requires **fertilization**, a union of two haploid cells (i.e. gametes) from two individual organisms. If those two cells each contain one set of chromosomes, then the resulting cell contains two sets of chromosomes (i.e. is diploid). The number of sets of chromosomes in a cell is called its ploidy level. Haploid cells contain one set of chromosomes. Cells containing two sets of chromosomes are called diploid. If the reproductive cycle is to continue, the diploid cell must somehow reduce its number of chromosome sets before fertilization can occur again, or there will be a continual doubling in the number of chromosome sets in every generation. So, in addition to fertilization, sexual reproduction includes a nuclear division, known as

[5]This content is available online at <http://cnx.org/content/m58013/1.1/>.

meiosis, that reduces the number of chromosome sets. Meiosis consists of two division events, called Meiosis I and Meiosis II.

Most animals and plants are diploid, containing two sets of chromosomes; in each **somatic cell** (the nonreproductive cells of a multicellular organism), the nucleus contains two copies of each chromosome that are referred to as homologous chromosomes. Somatic cells are sometimes referred to as "body" cells. Homologous chromosomes are matched pairs containing genes for the same traits in identical locations along their length. Diploid organisms inherit one copy of each homologous chromosome from each parent; all together, they are considered a full set of chromosomes. In animals, haploid cells containing a single copy of each homologous chromosome are found only within gametes. Gametes fuse with another haploid gamete to produce a diploid cell.

The nuclear division that forms haploid cells, which is called meiosis, is related to mitosis. As you have learned, mitosis is part of a cell reproduction cycle that results in identical daughter nuclei that are also genetically identical to the original parent nucleus. In mitosis, both the parent and the daughter nuclei contain the same number of chromosome sets—diploid for most plants and animals. Meiosis employs many of the same mechanisms as mitosis. However, the starting nucleus is always diploid and the nuclei that result at the end of a meiotic cell division are haploid (n). To achieve the reduction in chromosome number, meiosis consists of one round of chromosome duplication and two rounds of nuclear division. Because the events that occur during each of the division stages are analogous to the events of mitosis, the same stage names are assigned. However, because there are two rounds of division, the stages are designated with a "I" or "II." Thus, **meiosis I** is the first round of meiotic division and consists of prophase I, prometaphase I, and so on. Meiosis I reduces the number of chromosome sets from two to one (i.e. reductional division). The genetic information is also mixed during this division to create unique recombinant chromosomes. **Meiosis II**, in which the second round of meiotic division takes place in a way that is similar to mitosis, includes prophase II, prometaphase II, and so on. Meiosis II produces daughter cells that are haploid in chromosome number (as in Meiosis I), but with the sister chromatids separated. In other words, there is no further reduction in chromosome number, thus it is also called equational division.

13.4.1 Interphase

Meiosis is preceded by an interphase consisting of the G_1, S, and G_2 phases, which are nearly identical to the phases preceding mitosis. The G_1 phase is the first phase of interphase and is focused on cell growth. In the S phase, the DNA of the chromosomes is replicated. Finally, in the G_2 phase, the cell undergoes the final preparations for meiosis.

During DNA duplication of the S phase, each chromosome becomes composed of two identical copies (called sister chromatids) that are held together at the centromere until they are pulled apart during meiosis II. Again, homologous chromosome pairs separate in meiosis I (i.e. reductional division) and sister chromatids separate during meiosis II (i.e. equational division).

13.4.2 Meiosis I

Early in prophase I, the chromosomes can be seen clearly microscopically. As the nuclear envelope begins to break down, the proteins associated with homologous chromosomes bring the pair close to each other. The tight pairing of the homologous chromosomes is called **synapsis**. In synapsis, the genes on the chromatids of the homologous chromosomes are precisely aligned with each other. An exchange of chromosome segments between non-sister homologous chromatids occurs and is called **crossing over**. This process is revealed visually after the exchange as **chiasmata** (singular = *chiasma*) (Figure 13.6). As will be discussed later, crossing over can result in genetic variability in the gametes.

As prophase I progresses, the close association between homologous chromosomes begins to break down, and the chromosomes continue to condense, although the homologous chromosomes remain attached to each other at chiasmata. The number of chiasmata varies with the species and the length of the chromosome. At the end of prophase I, the pairs are held together only at chiasmata (Figure 13.6) and are called **tetrads** because the four sister chromatids of each pair of homologous chromosomes are now visible.

The crossover events are the first source of genetic variation produced by meiosis. A single crossover event between homologous non-sister chromatids leads to a reciprocal exchange of equivalent DNA between a maternal chromosome and a paternal chromosome. Now, when that sister chromatid is moved into a gamete, it will carry some DNA from one parent of the individual and some DNA from the other parent. The **recombinant** sister chromatid has a combination of maternal and paternal genes that did not exist before the crossover. It is important to note that crossing over will only produce genetic diversity if there was diversity between the maternal and paternal chromosomes.

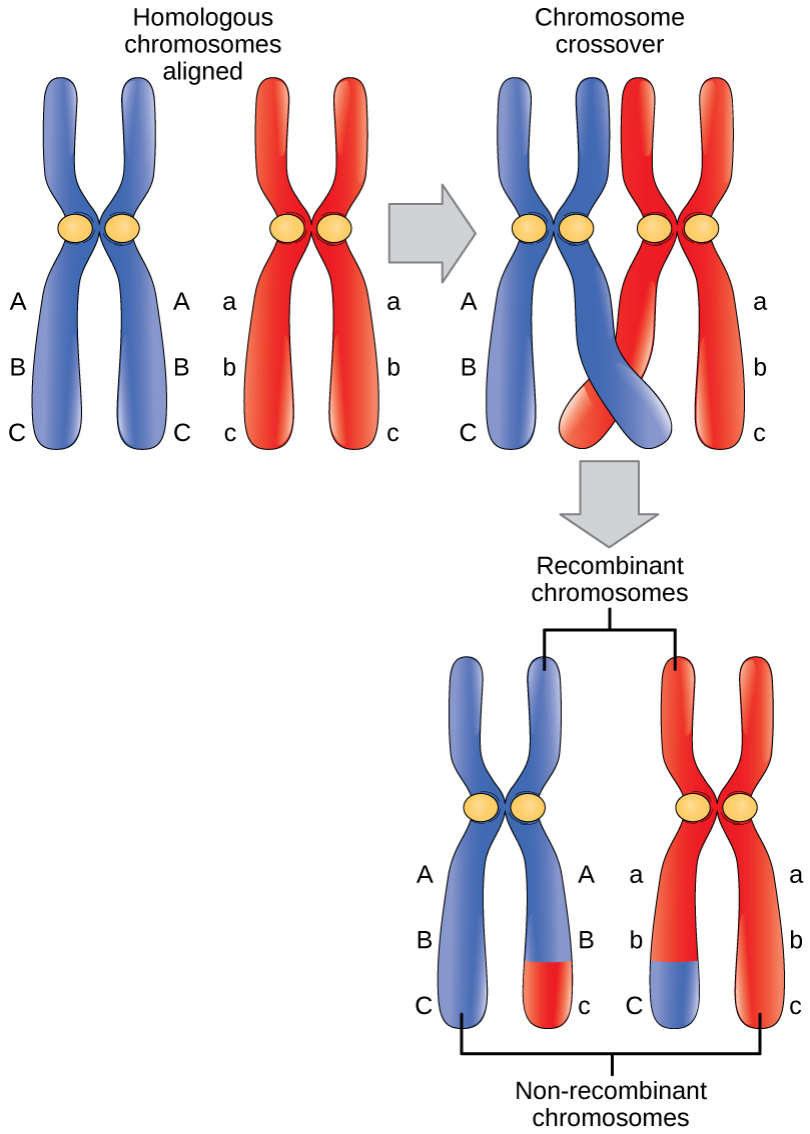


Figure 13.6: In this illustration of the effects of crossing over, the blue chromosome came from the individual's father and the red chromosome came from the individual's mother. Crossover occurs between non-sister chromatids of homologous chromosomes. The result is an exchange of genetic material between homologous chromosomes. The chromosomes that have a mixture of maternal and paternal sequence that differ genetically are called recombinant and the chromosomes that are completely paternal or maternal are called non-recombinant. Note: Crossing over can occur several times between the same pair of homologous chromosomes.

During metaphase I, the homologous chromosomes are arranged in the center of the cell with the kinetochores facing opposite poles. The orientation of each pair of homologous chromosomes at the center of the cell is random. As is discussed later, this too can contribute to genetic variation in the gametes.

This randomness, called independent assortment, is the physical basis for the generation of the second

form of genetic variation in offspring. Consider that the homologous chromosomes of a sexually reproducing organism are originally inherited as two separate sets, one from each parent. Using humans as an example, one set of 23 chromosomes is present in the egg donated by the mother. The father provides the other set of 23 chromosomes in the sperm that fertilizes the egg. In metaphase I, these pairs line up at the midway point between the two poles of the cell. Because there is an equal chance that a microtubule fiber will encounter a maternally or paternally inherited chromosome, the arrangement of the tetrads at the metaphase plate is random. Any maternally inherited chromosome may face either pole. Any paternally inherited chromosome may also face either pole. The orientation of each tetrad is independent of the orientation of the other 22 tetrads.

In each cell that undergoes meiosis, the arrangement of the tetrads is different. The number of variations depends on the number of chromosomes making up a set. There are two possibilities for orientation (for each tetrad); thus, the possible number of alignments equals 2^n where n is the number of chromosomes per set. Humans have 23 chromosome pairs, which results in over eight million (2^{23}) possibilities. This number does not include the variability previously created in the sister chromatids by crossover. Given these two mechanisms, it is highly unlikely that any two haploid cells resulting from meiosis will have the same genetic composition (Figure 13.7).

To summarize the genetic consequences of meiosis I: the maternal and paternal genes are recombined by crossover events occurring on each homologous pair during prophase I; in addition, the random assortment of tetrads at metaphase produces a unique combination of maternal and paternal chromosomes that will make their way into the gametes.

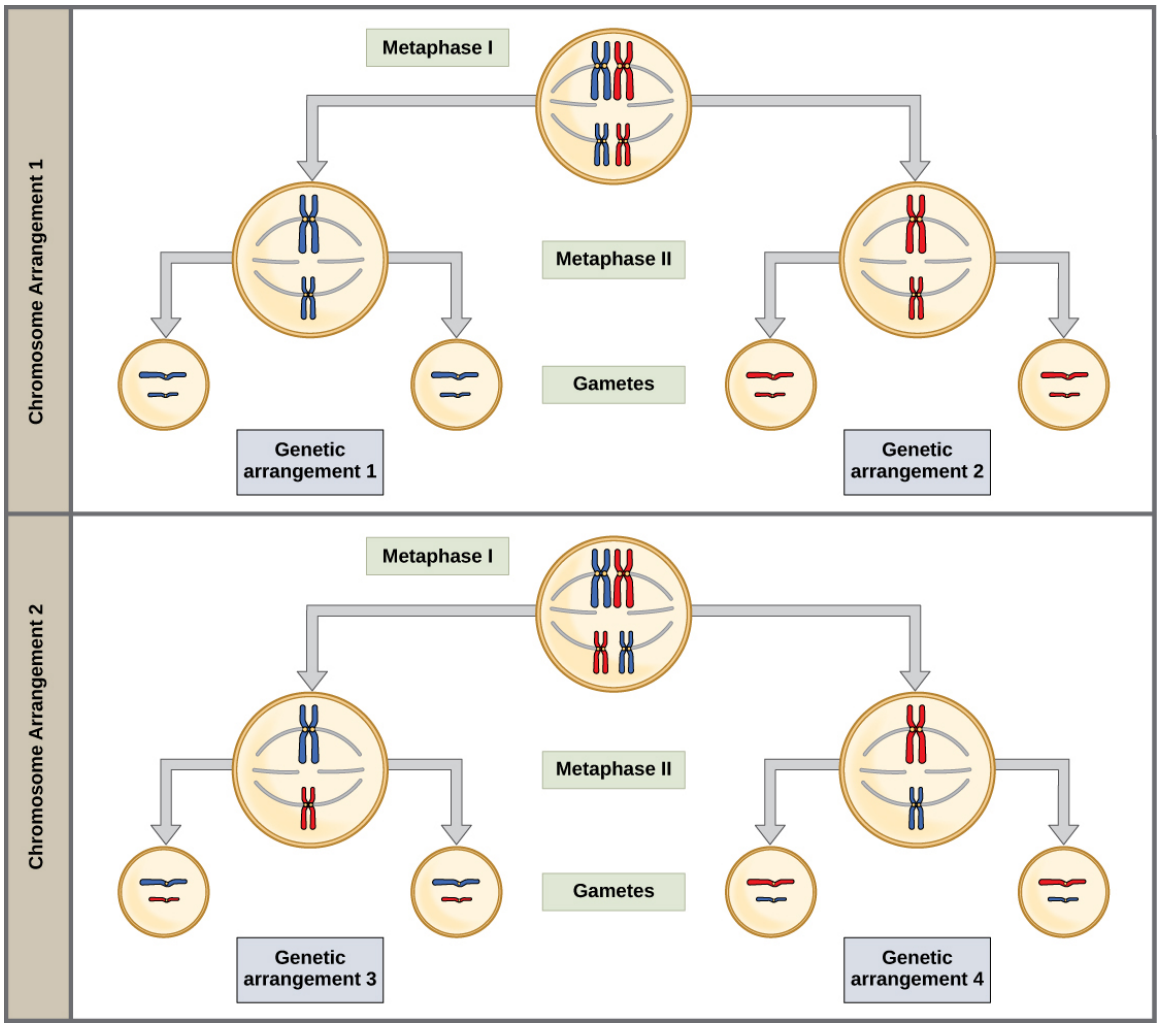


Figure 13.7: To demonstrate random, independent assortment at metaphase I, consider a cell with $n = 2$. In this case, there are two possible arrangements at the equatorial plane in metaphase I, as shown in the upper cell of each panel. These two possible orientations lead to the production of genetically different gametes. With more chromosomes, the number of possible arrangements increases dramatically.

In anaphase I, the spindle fibers pull the linked chromosomes apart. The sister chromatids remain tightly bound together at the centromere. It is the chiasma connections that are broken in anaphase I as the fibers attached to the fused kinetochores pull the homologous chromosomes apart (Figure 13.8).

In telophase I, the separated chromosomes arrive at opposite poles. The remainder of the typical telophase events may or may not occur depending on the species. In some organisms, the chromosomes decondense and nuclear envelopes form around the chromatids in telophase I.

Cytokinesis, the physical separation of the cytoplasmic components into two daughter cells, occurs without reformation of the nuclei in other organisms. In nearly all animals, cytokinesis separates the cell contents by a cleavage furrow. At each pole, there is just one member of each pair of the homologous chromosomes, so only one full set of the chromosomes is present. This is why the cells are considered haploid—there is only

one chromosome set, even though there are duplicate copies of the set because each homolog still consists of two sister chromatids that are still attached to each other. However, although the sister chromatids were once duplicates of the same chromosome, they are no longer identical at this stage because of crossovers.

: Review the process of meiosis, observing how chromosomes align and migrate, at this site[6] .

13.4.3 Meiosis II

In meiosis II, the connected sister chromatids remaining in the haploid cells from meiosis I will be split to form four haploid cells. In some species, cells enter a brief interphase, or **interkinesis**, that lacks an S phase, before entering meiosis II. Chromosomes are not duplicated during interkinesis. The two cells produced in meiosis I go through the events of meiosis II in synchrony. Overall, meiosis II resembles the mitotic division of a haploid cell.

In prophase II, if the chromosomes decondensed in telophase I, they condense again. If nuclear envelopes were formed, they fragment into vesicles. The centrosomes duplicated during interkinesis move away from each other toward opposite poles, and new spindles are formed. In prometaphase II, the nuclear envelopes are completely broken down, and the spindle is fully formed. Each sister chromatid forms an individual kinetochore that attaches to microtubules from opposite poles. In metaphase II, the sister chromatids are maximally condensed and aligned at the center of the cell. In anaphase II, the sister chromatids are pulled apart by the spindle fibers and move toward opposite poles.

[6] http://openstaxcollege.org/l/animal_meiosis2

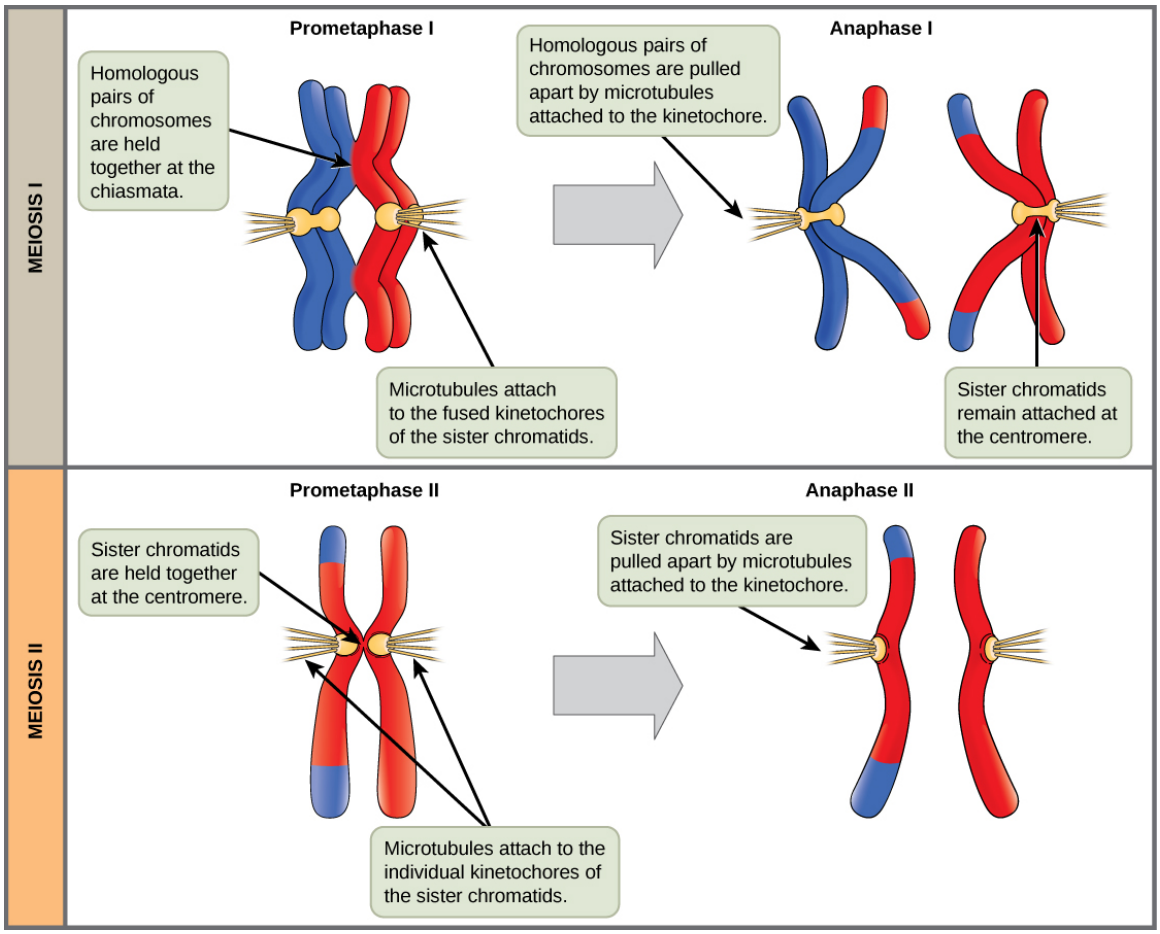


Figure 13.8: In prometaphase I, microtubules attach to the fused kinetochores of homologous chromosomes. In anaphase I, the homologous chromosomes are separated. In prometaphase II, microtubules attach to individual kinetochores of sister chromatids. In anaphase II, the sister chromatids are separated.

In telophase II, the chromosomes arrive at opposite poles and begin to decondense. Nuclear envelopes form around the chromosomes. Cytokinesis separates the two cells into four genetically unique haploid cells. At this point, the nuclei in the newly produced cells are both haploid and have only one copy of the single set of chromosomes. The cells produced are genetically unique because (assuming there was parental genetic variation) of the random assortment of paternal and maternal homologs and because of the recombination of maternal and paternal segments of chromosomes—with their sets of genes—that occurs during crossover.

13.4.4 Comparing Meiosis and Mitosis

Mitosis and meiosis, which are both forms of division of the nucleus in eukaryotic cells, share some similarities, but also exhibit distinct differences that lead to their very different outcomes. Mitosis is a single nuclear division that results in two nuclei, usually partitioned into two new cells. The nuclei resulting from a mitotic division are genetically identical to the original. They have the same number of sets of chromosomes: one in the case of haploid cells, and two in the case of diploid cells. On the other hand, meiosis is two nuclear

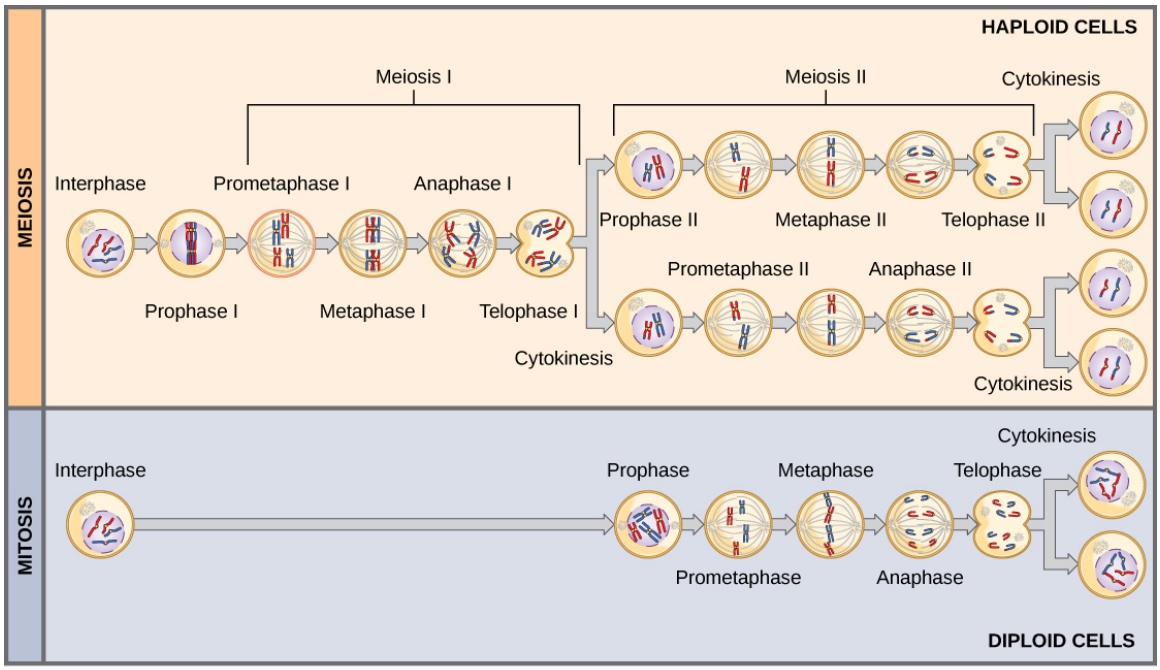
divisions that result in four nuclei, usually partitioned into four new cells. The nuclei resulting from meiosis are never genetically identical, and they contain one chromosome set only—this is half the number of the original cell, which was diploid (Figure 13.9).

The differences in the outcomes of meiosis and mitosis occur because of differences in the behavior of the chromosomes during each process. Most of these differences in the processes occur in meiosis I, which is a very different nuclear division than mitosis. In meiosis I, the homologous chromosome pairs become associated with each other, are bound together, experience chiasmata and crossover between sister chromatids, and line up along the metaphase plate in tetrads with spindle fibers from opposite spindle poles attached to each kinetochore of a homolog in a tetrad. All of these events occur only in meiosis I, never in mitosis.

Homologous chromosomes move to opposite poles during meiosis I so the number of sets of chromosomes in each nucleus-to-be is reduced from two to one. For this reason, meiosis I is referred to as a **reduction division**. There is no such reduction in ploidy level in mitosis.

Meiosis II is much more analogous to a mitotic division. In this case, duplicated chromosomes (only one set of them) line up at the center of the cell with divided kinetochores attached to spindle fibers from opposite poles. During anaphase II, as in mitotic anaphase, the kinetochores divide and one sister chromatid is pulled to one pole and the other sister chromatid is pulled to the other pole. If it were not for the fact that there had been crossovers, the two products of each meiosis II division would be identical as in mitosis; instead, they are different because there has always been at least one crossover per chromosome. Meiosis II is not a reduction division because, although there are fewer copies of the genome in the resulting cells, there is still one set of chromosomes, as there was at the end of meiosis I.

Cells produced by mitosis will function in different parts of the body as a part of growth or replacing dead or damaged cells. Cells produced by meiosis in animals will only participate in sexual reproduction.



	OUTCOME					
PROCESS	DNA synthesis	Synapsis of homologous chromosomes	Crossover	Homologous chromosomes line up at metaphase plate	Sister chromatids line up at metaphase plate	Number and genetic composition of daughter cells
MEIOSIS	Occurs in S phase of interphase	During prophase I	During prophase I	During metaphase I	During metaphase II	Four haploid cells at the end of meiosis II
MITOSIS	Occurs in S phase of interphase	Does not occur in mitosis	Does not occur in mitosis	Does not occur in mitosis	During metaphase	Two diploid cells at the end of mitosis

Figure 13.9: Meiosis and mitosis are both preceded by one round of DNA replication; however, meiosis includes two nuclear divisions. The four daughter cells resulting from meiosis are haploid and genetically distinct. The daughter cells resulting from mitosis are diploid and identical to the parent cell.

: For an animation comparing mitosis and meiosis, go to this website[7] .

13.4.5 Section Summary

Sexual reproduction requires that diploid organisms produce haploid cells that can fuse during fertilization to form diploid offspring. The process that results in haploid cells is called meiosis. Meiosis is a series of events that arrange and separate chromosomes into daughter cells. During the interphase of meiosis, each chromosome is duplicated. In meiosis, there are two rounds of nuclear division resulting in four nuclei and usually four haploid daughter cells, each with half the number of chromosomes as the parent cell. During meiosis, variation in the daughter nuclei is introduced because of crossover in prophase I and random alignment at metaphase I. The cells that are produced by meiosis are genetically unique.

Meiosis and mitosis share similarities, but have distinct outcomes. Mitotic divisions are single nuclear divisions that produce daughter nuclei that are genetically identical and have the same number of chromosome sets as the original cell. Meiotic divisions are two nuclear divisions that produce four daughter nuclei that are genetically different and have one chromosome set rather than the two sets the parent cell had. The main differences between the processes occur in the first division of meiosis. The homologous chromosomes separate into different nuclei during meiosis I causing a reduction of ploidy level. The second division of meiosis is much more similar to a mitotic division.

13.4.6 Multiple Choice

Exercise 13.4.1 *(Solution on p. 296.)*

Meiosis produces _____ daughter cells.

a. two haploid
b. two diploid
c. four haploid
d. four diploid

Exercise 13.4.2 *(Solution on p. 296.)*

At which stage of meiosis are sister chromatids separated from each other?

a. prophase I
b. prophase II
c. anaphase I
d. anaphase II

Exercise 13.4.3 *(Solution on p. 296.)*

The part of meiosis that is similar to mitosis is _____.

[7] http://openstaxcollege.org/l/how_cells_dvid2

a. meiosis I
b. anaphase I
c. meiosis II
d. interkinesis

Exercise 13.4.4 *(Solution on p. 296.)*
If a muscle cell of a typical organism has 32 chromosomes, how many chromosomes will be in a gamete of that same organism?

a. 8
b. 16
c. 32
d. 64

13.4.7 Free Response

Exercise 13.4.5 *(Solution on p. 296.)*
Explain how the random alignment of homologous chromosomes during metaphase I contributes to variation in gametes produced by meiosis.

Exercise 13.4.6 *(Solution on p. 296.)*
In what ways is meiosis II similar to and different from mitosis of a diploid cell?

Solutions to Exercises in Chapter 13

to Exercise 13.2.1 (p. 278)
C
to Exercise 13.2.2 (p. 278)
B
to Exercise 13.2.3 (p. 278)
Human somatic cells have 46 chromosomes, including 22 homologous pairs and one pair of nonhomologous sex chromosomes. This is the $2n$, or diploid, condition. Human gametes have 23 chromosomes, one each of 23 unique chromosomes. This is the n, or haploid, condition.
to Exercise 13.3.1 (p. 283)
Figure 13.4 D. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. The kinetochore breaks apart and the sister chromatids separate. The nucleus reforms and the cell divides.
to Exercise 13.3.2 (p. 284)
B
to Exercise 13.3.3 (p. 284)
C
to Exercise 13.3.4 (p. 284)
A
to Exercise 13.4.1 (p. 294)
C
to Exercise 13.4.2 (p. 294)
D
to Exercise 13.4.3 (p. 294)
C
to Exercise 13.4.4 (p. 295)
B
to Exercise 13.4.5 (p. 295)
Random alignment leads to new combinations of traits. The chromosomes that were originally inherited by the gamete-producing individual came equally from the egg and the sperm. In metaphase I, the duplicated copies of these maternal and paternal homologous chromosomes line up across the center of the cell to form a tetrad. The orientation of each tetrad is random. There is an equal chance that the maternally derived chromosomes will be facing either pole. The same is true of the paternally derived chromosomes. The alignment should occur differently in almost every meiosis. As the homologous chromosomes are pulled apart in anaphase I, any combination of maternal and paternal chromosomes will move toward each pole. The gametes formed from these two groups of chromosomes will have a mixture of traits from the individual's parents. Each gamete is unique.
to Exercise 13.4.6 (p. 295)
The two divisions are similar in that the chromosomes line up along the metaphase plate individually, meaning unpaired with other chromosomes (as in meiosis I). In addition, each chromosome consists of two sister chromatids that will be pulled apart. The two divisions are different because in meiosis II there are half the number of chromosomes that are present in a diploid cell of the same species undergoing mitosis. This is because meiosis I reduced the number of chromosomes to a haploid state.

Chapter 14

Reproductive Systems

14.1 Introduction to the Reproductive Systems[1]

Ovulation

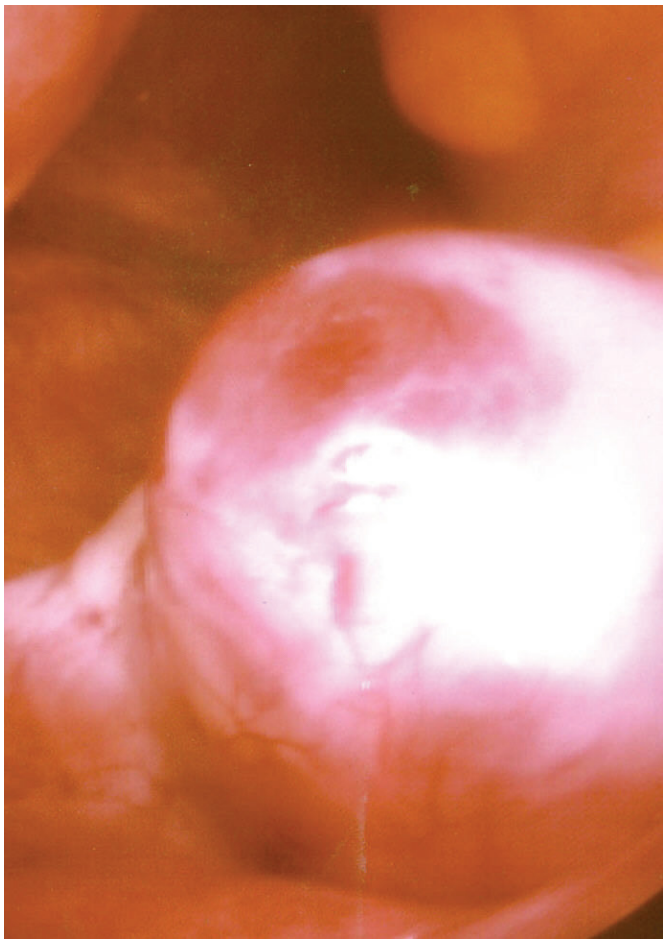


Figure 14.1: Following a surge of luteinizing hormone (LH), an oocyte (immature egg cell) will be released into the uterine tube, where it will then be available to be fertilized by a male's sperm. Ovulation marks the end of the follicular phase of the ovarian cycle and the start of the luteal phase.

Available for free at Connexions <http://cnx.org/content/col11496/1.3>

NOTE: After studying this chapter, you will be able to:

- Describe the anatomy of the male and female reproductive systems, including their accessory structures
- Explain the role of hypothalamic and pituitary hormones in male and female reproductive function
- Trace the path of a sperm cell from its initial production through fertilization of an oocyte
- Explain the events in the ovary prior to ovulation

Small, uncoordinated, and slick with amniotic fluid, a newborn encounters the world outside of her mother's womb. We do not often consider that a child's birth is proof of the healthy functioning of both her mother's and father's reproductive systems. Moreover, her parents' endocrine systems had to secrete the appropriate regulating hormones to induce the production and release of unique male and female gametes, reproductive cells containing the parents' genetic material (one set of 23 chromosomes). Her parent's reproductive behavior had to facilitate the transfer of male gametes—the sperm—to the female reproductive tract at just the right time to encounter the female gamete, an oocyte (egg). Finally, combination of the gametes (fertilization) had to occur, followed by implantation and development. In this chapter, you will explore the male and female reproductive systems, whose healthy functioning can culminate in the powerful sound of a newborn's first cry.

14.2 Male Reproductive Anatomy and Physiology[2]

14.2.1 Human Reproductive Anatomy

The reproductive tissues of male and female humans develop similarly *in utero* until about the seventh week of gestation when a low level of the hormone testosterone is released from the gonads of the developing male. Testosterone causes the primitive gonads to differentiate into male sexual organs. When testosterone is absent, the primitive gonads develop into ovaries. Tissues that produce a penis in males produce a clitoris in females. The tissue that will become the scrotum in a male becomes the labia in a female. Thus the male and female anatomies arise from a divergence in the development of what were once common embryonic structures.

14.2.1.1 Male Reproductive Anatomy

Proper development of sperm cells requires a temperature slightly lower than the normal body temperature; therefore, the pair of testes must be suspended outside the pelvic cavity (in the scrotum) so the environment of the sperm is about 2 °C lower than body temperature. If the testes do not descend through the abdominal cavity during fetal development, the individual has reduced fertility.

The **scrotum** houses the testicles or **testes** (singular: testis), and provides passage for blood vessels, nerves, and muscles related to testicular function. The testes are a pair of male gonads that produce sperm and reproductive hormones. Coiled in each testis are seminiferous tubules, where sperm production begins.

The **penis** drains urine from the urinary bladder and is a copulatory organ during intercourse (Figure 14.3; Table 14.1). The penis contains three tubes of erectile tissue that become engorged with blood, making the penis erect, in preparation for intercourse. The organ is inserted into the vagina culminating with an ejaculation. During orgasm, the accessory organs and glands connected to the testes contract and empty the semen (containing sperm) into the urethra and the fluid is expelled from the body by muscular contractions causing ejaculation. After intercourse, the blood drains from the erectile tissue and the penis becomes flaccid.

Semen is a mixture of sperm (about five percent of the total) and fluids from accessory glands (prostate, bulbourethral glands, and seminal vesicles) that contribute most of the semen's volume. Sperm are haploid cells, consisting of a flagellum for movement, a neck that contains the cell's energy-producing mitochondria,

[2]This content is available online at <http://cnx.org/content/m58078/1.3/>.

and a head that contains the genetic material (Figure 14.2). An acrosome (acrosomal vesicle) is found at the top of the head of the sperm. This structure contains enzymes that can digest the protective coverings that surround the egg and allow the sperm to fuse with the egg. An ejaculate will contain from two to five milliliters of fluid and from 50–120 million sperm per milliliter.

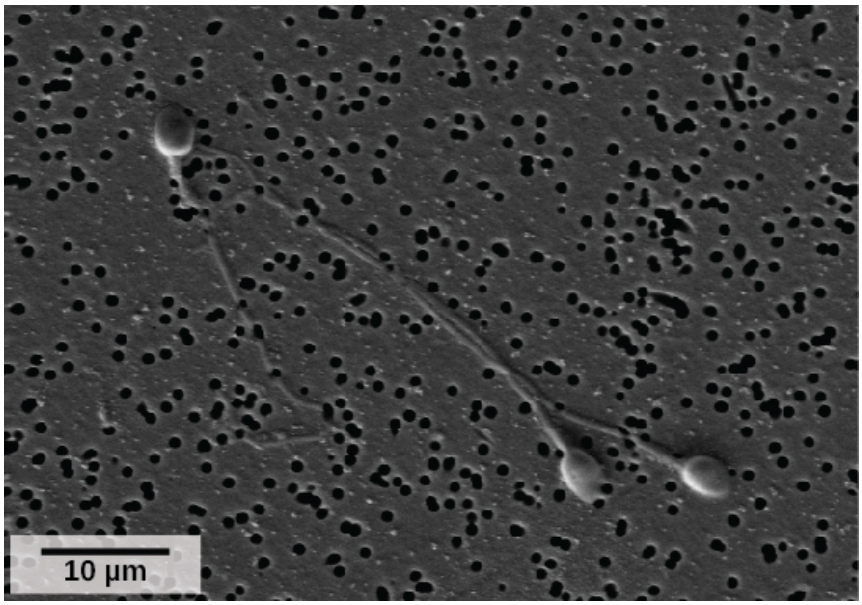


Figure 14.2: As seen in this scanning electron micrograph, human sperm has a flagellum, neck, and head. (credit: scale-bar data from Matt Russell)

Sperm cell formation begins in the walls of **seminiferous tubules** that are coiled inside the testes (Figure 14.3; Table 14.1). The walls of the seminiferous tubules are made up of the developing sperm cells, with the least developed sperm at the periphery of the tubule; the cells get pushed closer to the lumen as maturation continues. The sperm cells are associated with **Sertoli cells** that nourish and promote the development of the sperm. Other cells present between the walls of the tubules are the **Leydig/interstitial cells**, which produce testosterone once the male reaches puberty.

When the sperm have developed flagella they leave the seminiferous tubules and enter the epididymis (Figure 14.3; Table 14.1). This structure lies along the top and back side of the testes and is the site of sperm maturation. The sperm leave the epididymis and enter the vas deferens, which carries the sperm behind the bladder, and forms the ejaculatory duct with the duct from the seminal vesicles. During a vasectomy, a section of the vas deferens is removed, preventing sperm (but not the secretions of the accessory glands) from being passed out of the body during ejaculation and preventing fertilization. Although a vasectomy is in many cases reversible via surgery, it is still considered to be a permanent procedure.

The bulk of the semen comes from the accessory glands associated with the male reproductive system. These are the **seminal vesicles**, the **prostate gland**, and the **bulbourethral gland** (Figure 14.3; Table 14.1). The secretions from the accessory glands provide important compounds for the sperm including nutrients, electrolytes, and pH buffering.

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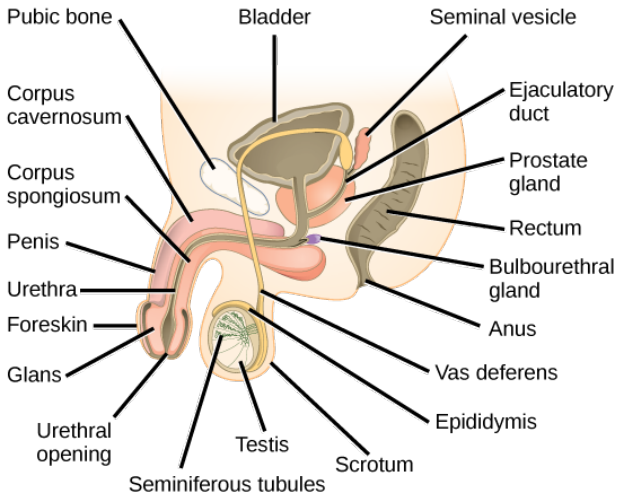

Figure 14.3: The reproductive structures of the human male are shown.

Male Reproductive Anatomy		
Organ	**Location**	**Function**
Scrotum	External	Supports testes and regulates their temperature
Penis	External	Delivers urine, copulating organ
Testes	Internal	Produce sperm and male hormones
Seminal Vesicles	Internal	Contribute to semen production
Prostate Gland	Internal	Contributes to semen production
Bulbourethtral Glands	Internal	Neutralize urine in urethra

Table 14.1

14.2.2 Gametogenesis: Spermatogenesis

Gametogenesis, the production of sperm and eggs, involves the process of meiosis. During meiosis, two nuclear divisions separate the paired chromosomes in the nucleus and then separate the chromatids that were made during an earlier stage of the cell's life cycle. Meiosis and its associated cell divisions produces haploid (n) cells with half of each pair of chromosomes normally found in diploid (2n)cells. The production of sperm is called **spermatogenesis**.

14.2.2.1 Spermatogenesis

Spermatogenesis occurs in the wall of the seminiferous tubules, with the most primitive cells at the periphery of the tube and the most mature sperm at the lumen of the tube (Figure 14.4). Immediately under the capsule of the tubule are diploid, undifferentiated cells. These stem cells, each called a spermatogonium (pl. spermatogonia), go through mitosis to produce one cell that remains as a stem cell and a second cell called a primary spermatocyte that will undergo meiosis to produce sperm.

The diploid primary spermatocyte goes through meiosis I to produce two haploid cells called secondary spermatocytes. Each secondary spermatocyte divides after meiosis II to produce two cells called spermatids. The spermatids eventually reach the lumen of the tubule and grow a flagellum, becoming sperm cells. Four sperm result from each primary spermatocyte that goes through meiosis.

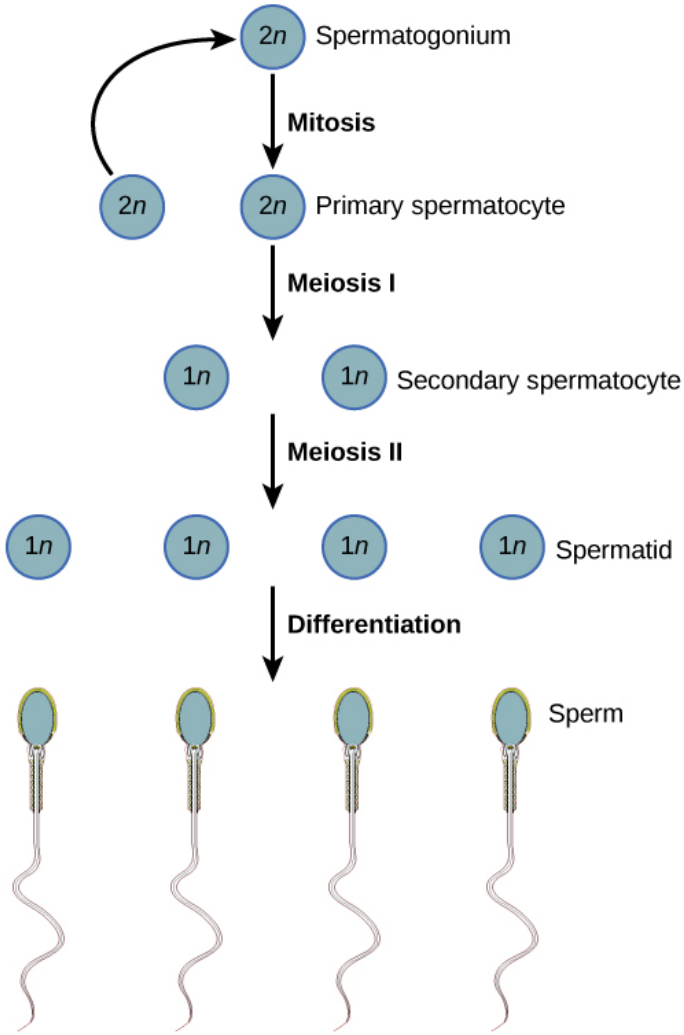

Figure 14.4: During spermatogenesis, four sperm result from each primary spermatocyte. The process also maps onto the physical structure of the wall of the seminiferous tubule, with the spermatogonia on the outer side of the tubule, and the sperm with their developing tails extended into the lumen of the tubule. The process takes approximately 70 days.

: Visit this site[3] to see the process of spermatogenesis.

14.2.3 Hormonal Control of Reproduction

The human male and female reproductive cycles are controlled by the interaction of hormones from the hypothalamus and anterior pituitary with hormones from reproductive tissues and organs. In both sexes, the hypothalamus monitors and causes the release of hormones from the anterior pituitary gland. When the reproductive hormone is required, the hypothalamus sends a **gonadotropin-releasing hormone (GnRH)** to the anterior pituitary. This causes the release of **follicle stimulating hormone (FSH)** and **luteinizing hormone (LH)** from the anterior pituitary into the blood. Although these hormones are named after their functions in female reproduction, they are produced in both sexes and play important roles in controlling reproduction. Other hormones have specific functions in the male and female reproductive systems.

14.2.3.1 Male Hormones

At the onset of puberty, the hypothalamus causes the release of FSH and LH into the male system for the first time. FSH enters the testes and stimulates the Sertoli cells located in the walls of the seminiferous tubules to begin promoting spermatogenesis (Figure 14.5). LH also enters the testes and stimulates the interstitial cells of Leydig, located in between the walls of the seminiferous tubules, to make and release testosterone into the testes and the blood.

Testosterone stimulates spermatogenesis. This hormone is also responsible for the secondary sexual characteristics that develop in the male during adolescence. The secondary sex characteristics in males include a deepening of the voice, the growth of facial, axillary, and pubic hair, an increase in muscle bulk, and the beginnings of the sex drive.

[3] http://openstaxcollege.org/l/spermatogenes2

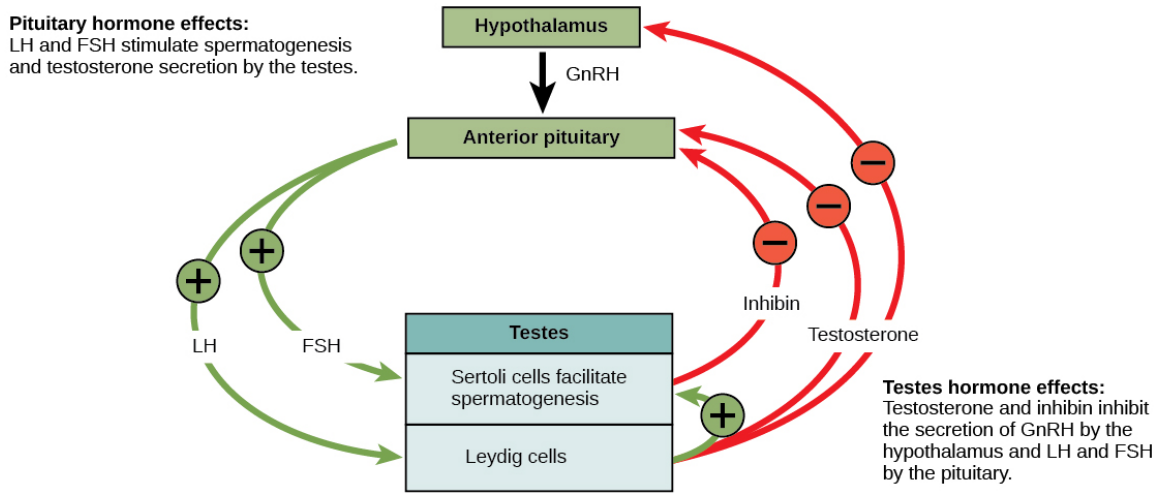

Figure 14.5: Hormones control sperm production in a negative feedback system.

A negative feedback system occurs in the male with rising levels of testosterone acting on the hypothalamus and anterior pituitary to inhibit the release of GnRH, FSH, and LH. In addition, the Sertoli cells produce the hormone **inhibin**, which is released into the blood when the sperm count is too high. This inhibits the release of GnRH and FSH, which will cause spermatogenesis to slow down. If the sperm count reaches a low of 20 million/mL, the Sertoli cells cease the release of inhibin, and the sperm count increases.

14.2.4 Section Summary

The reproductive structures that evolved in land animals allow males and females to mate, fertilize internally, and support the growth and development of offspring. Gametogenesis, the production of sperm in the male (spermatogenesis), takes place through the process of meiosis.

The male and female reproductive cycles are controlled by hormones released from the hypothalamus and anterior pituitary and hormones from reproductive tissues and organs. The hypothalamus monitors the need for FSH and LH production and release from the anterior pituitary. FSH and LH affect reproductive structures to cause the formation of sperm and the preparation of eggs for release and possible fertilization. In the male, FSH and LH stimulate Sertoli cells and interstitial cells of Leydig in the testes to facilitate sperm production. The Leydig cells produce testosterone, which also is responsible for the secondary sexual characteristics of males. In females, FSH and LH cause estrogen and progesterone to be produced. They regulate the female reproductive cycle, which is divided into the ovarian cycle and the menstrual cycle.

14.2.5 Art Connections

Exercise 14.2.1 ***(Solution on p. 315.)***

Figure 14.3 Which of the following statements about the male reproductive system is false?

a. The vas deferens carries sperm from the testes to the seminal vesicles.
b. The ejaculatory duct joins the urethra.
c. Both the prostate and the bulbourethral glands produce components of the semen.
d. The prostate gland is located in the testes.

14.2.6 Review Questions

Exercise 14.2.2 *(Solution on p. 315.)*

Sperm are produced in the _____.

a. scrotum
b. seminal vesicles
c. seminiferous tubules
d. prostate gland

Exercise 14.2.3 *(Solution on p. 315.)*

Which hormone causes FSH and LH to be released?

a. testosterone
b. estrogen
c. GnRH
d. progesterone

14.2.7 Free Response

Exercise 14.2.4 *(Solution on p. 315.)*

Discuss spermatogenesis with respect to the timing of the process, and the number and types of cells finally produced.

14.3 Female Reproductive Anatomy and Physiology; Gestation and Labor[4]

14.3.1 Human Reproductive Anatomy

14.3.1.1 Female Reproductive Anatomy

A number of female reproductive structures are exterior to the body. These include the breasts and the vulva, which consists of the mons pubis, **clitoris**, and **labia**. (Figure 14.6; Table 14.2).

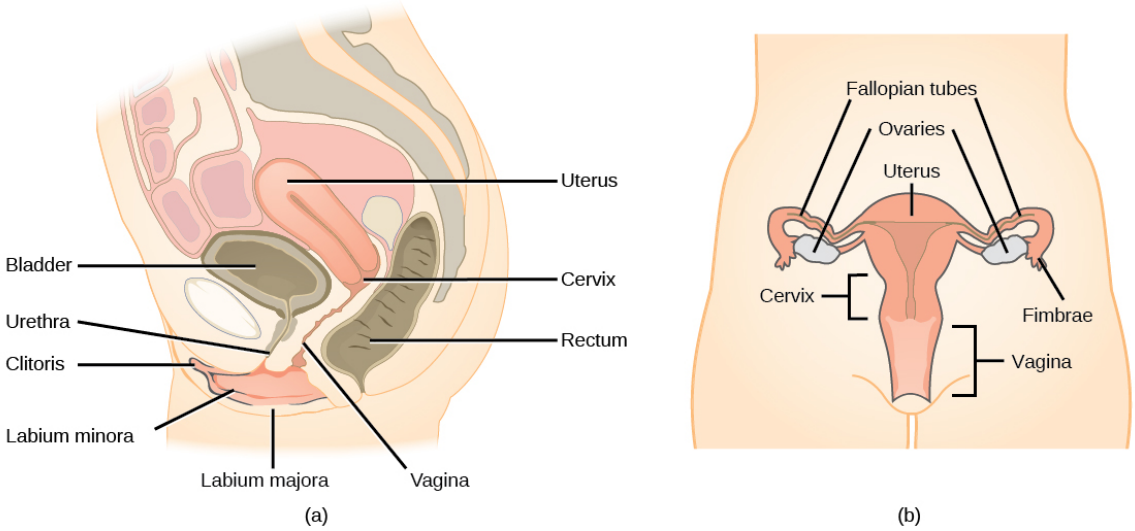

Figure 14.6: The reproductive structures of the human female are shown. (credit a: modification of work by Gray's Anatomy; credit b: modification of work by CDC)

The breasts consist of mammary glands and fat. Each gland consists of 15 to 25 lobes that have ducts that empty at the nipple and that supply the nursing child with nutrient- and antibody-rich milk to aid development and protect the child.

Internal female reproductive structures include ovaries, oviducts, the uterus, and the vagina (Figure 14.6; Table 14.2). The pair of ovaries is held in place in the abdominal cavity by a system of ligaments. The outermost layer of the ovary is made up of follicles that surround, nourish, and protect a single egg. During the menstrual period, a batch of follicles develops and prepares their eggs for release. At ovulation, one follicle ruptures and one egg is released. Following ovulation, the follicular tissue that surrounded the ovulated egg stays within the ovary and grows to form a solid mass called the **corpus luteum**. The corpus luteum secretes additional estrogen and the hormone progesterone that helps maintain the uterine lining during pregnancy. The ovaries also produce hormones, such as estrogen.

The **oviducts**, or fallopian tubes, extend from the uterus in the lower abdominal cavity to the ovaries, but they are not in contact with the ovaries. The lateral ends of the oviducts flare out into a trumpet-like structure and have a fringe of finger-like projections called fimbrae. When an egg is released at ovulation, the fimbrae help the nonmotile egg enter into the tube. The walls of the oviducts have a ciliated epithelium

[4]This content is available online at <http://cnx.org/content/m58079/1.3/>.

over smooth muscle. The cilia beat, and the smooth muscle contracts, moving the egg toward the uterus. Fertilization usually takes place within the oviduct and the developing embryo is moved toward the uterus. It usually takes the egg or embryo a week to travel through the oviduct.

Sterilization in women is called a tubal ligation; it is analogous to a vasectomy in males in that the oviducts are severed and sealed, preventing sperm from reaching the egg.

The **uterus** is a structure about the size of a woman's fist. The uterus has a thick muscular wall and is lined with an endometrium rich in blood vessels and mucus glands that develop and thicken during the female cycle. Thickening of the endometrium prepares the uterus to receive the fertilized egg or zygote, which will then implant itself in the endometrium. The uterus supports the developing embryo and fetus during gestation. Contractions of the smooth muscle in the uterus aid in forcing the baby through the vagina during labor. If fertilization does not occur, a portion of the lining of the uterus sloughs off during each menstrual period. The endometrium builds up again in preparation for implantation. Part of the uterus, called the cervix, protrudes into the top of the vagina.

The **vagina** is a muscular tube that serves several purposes. It allows menstrual flow to leave the body. It is the receptacle for the penis during intercourse and the pathway for the delivery of offspring.

Female Reproductive Anatomy		
Organ	**Location**	**Function**
Clitoris	External	Sensory organ
Mons pubis	External	Fatty area overlying pubic bone
Breast	External	Produces and delivers milk
Ovaries	Internal	Produce and develop eggs
Oviducts	Internal	Transport egg to uterus; site of fertilization
Uterus	Internal	Supports developing embryo
Vagina	Internal	Common tube for intercourse, birth canal, passing menstrual flow

Table 14.2

14.3.2 Gametogenesis (Oogenesis)

Gametogenesis, the production of sperm and eggs, involves the process of meiosis. During meiosis, two nuclear divisions separate the paired chromosomes in the nucleus and then separate the chromatids that were made during an earlier stage of the cell's life cycle. Meiosis and its associated cell divisions produces haploid (n) cells with half of each pair of chromosomes normally found in diploid (2n) cells. The production of sperm is called **spermatogenesis** and the production of eggs is called **oogenesis**.

14.3.2.1 Oogenesis

Oogenesis occurs in the outermost layers of the ovaries. As with sperm production, oogenesis starts with a germ cell. In oogenesis, this germ cell is called an oogonium and forms during the embryological development of the individual. The oogonium undergoes mitosis to produce about one to two million oocytes by the time of birth.

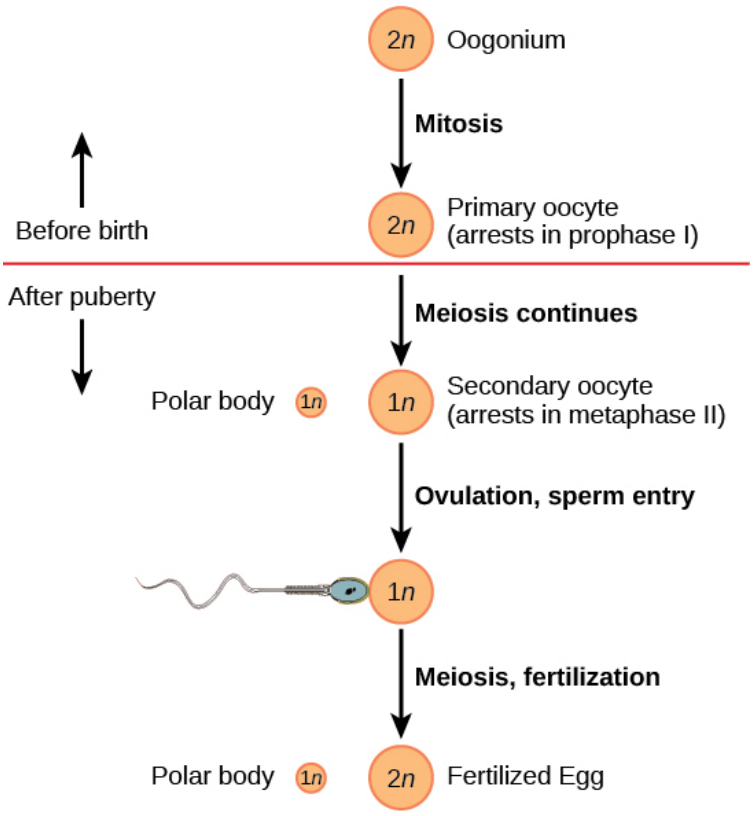

Figure 14.7: The process of oogenesis occurs in the ovary's outermost layer.

The primary oocytes begin meiosis before birth (Figure 14.7). However, the meiotic division is arrested in its progress in the first prophase stage. At the time of birth, all future eggs are in prophase I. This situation is in contrast with the male reproductive system in which sperm are produced continuously throughout the life of the individual. Starting at adolescence, anterior pituitary hormones cause the development of a few follicles in an ovary each month. This results in a primary oocyte finishing the first meiotic division. The cell divides unequally, with most of the cytoplasm and organelles going to one cell, called a secondary oocyte, and only one set of chromosomes and a small amount of cytoplasm going to the other cell. This second cell is called a polar body and usually dies. Cell division is again arrested, this time at metaphase II. At ovulation, this secondary oocyte is released and travels toward the uterus through the oviduct. If the secondary oocyte is fertilized, the cell continues through meiosis II, producing a second polar body and haploid egg, which fuses with the haploid sperm to form a fertilized egg (zygote) containing all 46 chromosomes.

14.3.3 Hormonal Control of Reproduction

The human male and female reproductive cycles are controlled by the interaction of hormones from the hypothalamus and anterior pituitary with hormones from reproductive tissues and organs. In both sexes, the hypothalamus monitors and causes the release of hormones from the anterior pituitary gland. When the reproductive hormone is required, the hypothalamus sends a **gonadotropin-releasing hormone (GnRH)** to the anterior pituitary. This causes the release of **follicle stimulating hormone (FSH)** and **luteinizing**

hormone (LH) from the anterior pituitary into the blood. Although these hormones are named after their functions in female reproduction, they are produced in both sexes and play important roles in controlling reproduction. Other hormones have specific functions in the male and female reproductive systems.

14.3.4 Female Hormones

The control of reproduction in females is more complex that in males. The female reproductive cycle is divided into the ovarian cycle and the menstrual cycle. The **ovarian cycle** governs the preparation of endocrine tissues and release of eggs, while the **menstrual cycle** governs the preparation and maintenance of the uterine lining (Figure 14.8). These cycles are coordinated over a 22–32 day cycle, with an average length of 28 days.

As with the male, the GnRH from the hypothalamus causes the release of the hormones FSH and LH from the anterior pituitary. In addition, **estrogen** and relatively small amounts of **progesterone** are released from the developing follicles. As with testosterone in males, estrogen is responsible for the secondary sexual characteristics of females. These include breast development, flaring of the hips, and a shorter period for bone growth.

14.3.4.1 The Ovarian Cycle and the Menstrual Cycle

The ovarian and menstrual cycles are regulated by hormones of the hypothalamus, pituitary, and ovaries (Figure 14.8). The ebb and flow of the hormones causes the ovarian and menstrual cycles to advance. The ovarian and menstrual cycles occur concurrently. The first half of the ovarian cycle is the follicular phase. Slowly rising levels of FSH cause the growth of follicles on the surface of the ovary. This process prepares the egg for ovulation. As the follicles grow, they begin releasing estrogen. The first few days of this cycle coincide with menstruation or the sloughing off of the functional layer of the endometrium in the uterus. After about five days, estrogen levels rise and the menstrual cycle enters the proliferative phase. The endometrium begins to regrow, replacing the blood vessels and glands that deteriorated during the end of the last cycle.

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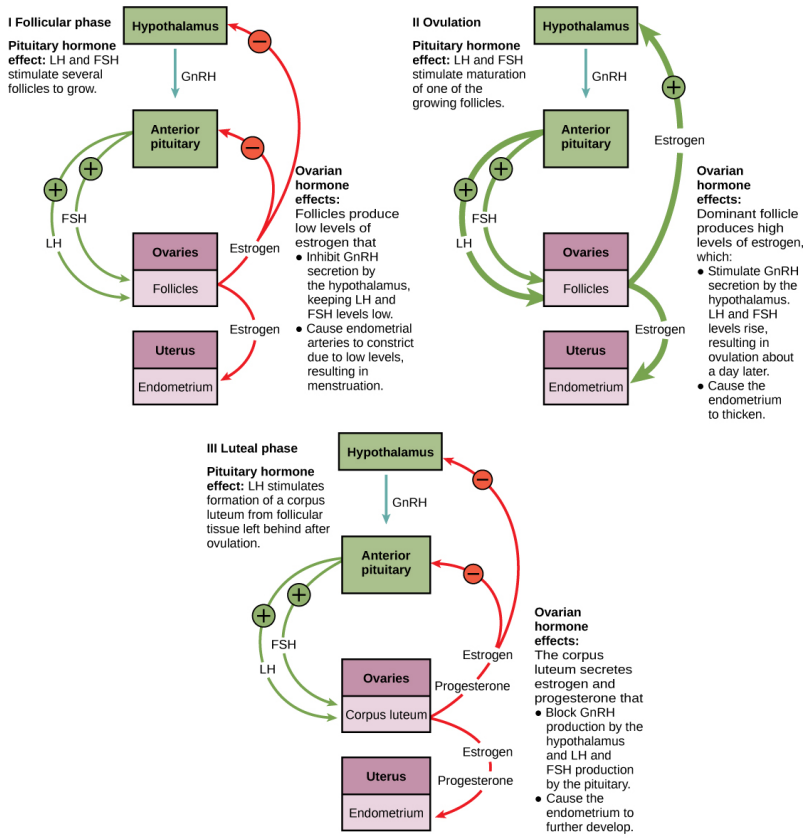

Figure 14.8: The ovarian and menstrual cycles of female reproduction are regulated by hormones produced by the hypothalamus, pituitary, and ovaries.

Just prior to the middle of the cycle (approximately day 14), the high level of estrogen causes FSH and especially LH to rise rapidly then fall. The spike in LH causes the most mature follicle to rupture and release its egg. This is **ovulation**. The follicles that did not rupture degenerate and their eggs are lost. The level of estrogen decreases when the extra follicles degenerate.

Following ovulation, the ovarian cycle enters its luteal phase and the menstrual cycle enters its secretory phase, both of which run from about day 15 to 28. The luteal and secretory phases refer to changes in the ruptured follicle. The cells in the follicle undergo physical changes and produce a structure called a corpus luteum. The corpus luteum produces estrogen and larger amounts of progesterone. The progesterone facilitates the regrowth of the uterine lining and inhibits the release of further FSH and LH. The uterus is being prepared to accept a fertilized egg, should it occur during this cycle. The inhibition of FSH and LH prevents any further eggs and follicles from developing, while the progesterone is elevated. The level of estrogen produced by the corpus luteum increases to a steady level for the next few days.

If no fertilized egg is implanted into the uterus, the corpus luteum degenerates and the levels of estrogen and progesterone decrease. The endometrium begins to degenerate as the progesterone levels drop, initiating the next menstrual cycle. The decrease in progesterone also allows the hypothalamus to send GnRH to the anterior pituitary, releasing FSH and LH and starting the cycles again.

: **Reproductive Endocrinologist**

A reproductive endocrinologist is a physician who treats a variety of hormonal disorders related to

reproduction and infertility in both men and women. The disorders include menstrual problems, infertility, pregnancy loss, sexual dysfunction, and menopause. Doctors may use fertility drugs, surgery, or assisted reproductive techniques (ART) in their therapy. ART involves the use of procedures to manipulate the egg or sperm to facilitate reproduction, such as *in vitro* fertilization.

Reproductive endocrinologists undergo extensive medical training, first in a four-year residency in obstetrics and gynecology, then in a three-year fellowship in reproductive endocrinology. To be board certified in this area, the physician must pass written and oral exams in both areas.

14.3.5 Gestation

Pregnancy begins with the fertilization of an egg and continues through to the birth of the individual. The length of time of **gestation**, or the **gestation period**, in humans is approximately 266 days.

Within 24 hours of fertilization, the egg nucleus has finished meiosis and the egg and sperm nuclei fuse. With fusion, the cell is known as a zygote. The zygote initiates cleavage and the developing embryo travels through the oviduct to the uterus. The developing embryo must implant into the wall of the uterus within seven days, or it will deteriorate and die. The outer layers of the developing embryo or blastocyst grow into the endometrium by digesting the endometrial cells, and healing of the endometrium closes up the blastocyst into the tissue. Another layer of the blastocyst, the chorion, begins releasing a hormone called **human beta chorionic gonadotropin (β-HCG)**, which makes its way to the corpus luteum and keeps that structure active. This ensures adequate levels of progesterone that will maintain the endometrium of the uterus for the support of the developing embryo. Pregnancy tests determine the level of β-HCG in urine or serum. If the hormone is present, the test is positive.

The gestation period is divided into three equal periods or trimesters. During the first two-to-four weeks of the first trimester, nutrition and waste are handled by the endometrial lining through diffusion. As the trimester progresses, the outer layer of the embryo begins to merge with the endometrium, and the placenta forms. The **placenta** takes over the nutrient and waste requirements of the embryo and fetus, with the mother's blood passing nutrients to the placenta and removing waste from it. Chemicals from the fetus, such as bilirubin, are processed by the mother's liver for elimination. Some of the mother's immunoglobulins will pass through the placenta, providing passive immunity against some potential infections.

Internal organs and body structures begin to develop during the first trimester. By five weeks, limb buds, eyes, the heart, and liver have been basically formed. By eight weeks, the term fetus applies, and the body is essentially formed (Figure 14.9**a**). The individual is about five centimeters (two inches) in length and many of the organs, such as the lungs and liver, are not yet functioning. Exposure to any toxins is especially dangerous during the first trimester, as all of the body's organs and structures are going through initial development. Anything that interferes with chemical signaling during that development can have a severe effect on the fetus' survival.

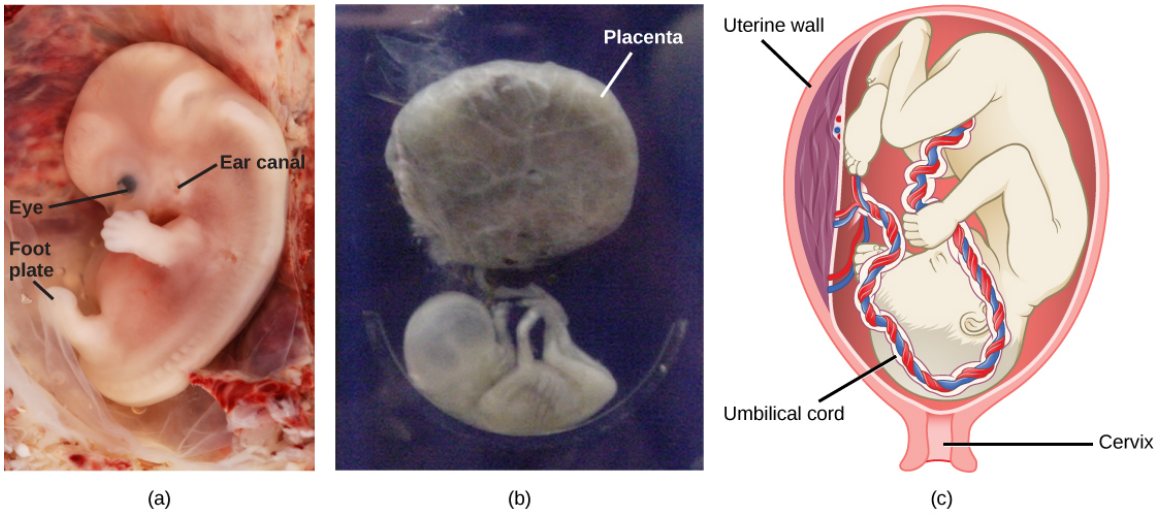

Figure 14.9: (a) Fetal development is shown at nine weeks gestation. (b) This fetus is just entering the second trimester, when the placenta takes over more of the functions performed as the baby develops. (c) There is rapid fetal growth during the third trimester. (credit a: modification of work by Ed Uthman; credit b: modification of work by National Museum of Health and Medicine; credit c: modification of work by Gray's Anatomy)

During the second trimester, the fetus grows to about 30 cm (about 12 inches) (Figure 14.9**b**). It becomes active and the mother usually feels the first movements. All organs and structures continue to develop. The placenta has taken over the functions of nutrition and waste elimination and the production of estrogen and progesterone from the corpus luteum, which has degenerated. The placenta will continue functioning up through the delivery of the baby. During the third trimester, the fetus grows to 3 to 4 kg (6.5–8.5 lbs.) and about 50 cm (19–20 inches) long (Figure 14.9**c**). This is the period of the most rapid growth during the pregnancy as all organ systems continue to grow and develop.

Labor is the muscular contractions to expel the fetus and placenta from the uterus. Toward the end of the third trimester, estrogen causes receptors on the uterine wall to develop and bind the hormone oxytocin. At this time, the baby reorients, facing forward and down with the back or crown of the head engaging the cervix (uterine opening). This causes the cervix to stretch and nerve impulses are sent to the hypothalamus, which signals the release of oxytocin from the posterior pituitary. Oxytocin causes smooth muscle in the uterine wall to contract. At the same time, the placenta releases prostaglandins into the uterus, increasing the contractions. A positive feedback relay occurs between the uterus, hypothalamus, and the posterior pituitary to assure an adequate supply of oxytocin. As more smooth muscle cells are recruited, the contractions increase in intensity and force.

There are three stages to labor. During stage one, the cervix thins and dilates. This is necessary for the baby and placenta to be expelled during birth. The cervix will eventually dilate to about 10 cm. During stage two, the baby is expelled from the uterus. The uterus contracts and the mother pushes as she compresses her abdominal muscles to aid the delivery. The last stage is the passage of the placenta after the baby has been born and the organ has completely disengaged from the uterine wall. If labor should stop before stage two is reached, synthetic oxytocin, known as Pitocin, can be administered to restart and maintain labor.

14.3.6 Section Summary

The female reproductive cycle is controlled by hormones released from the hypothalamus and anterior pituitary and hormones from reproductive tissues and organs. The hypothalamus monitors the need for FSH and LH production and release from the anterior pituitary. FSH and LH affect reproductive structures to cause the preparation of eggs for release and possible fertilization. In females, FSH and LH cause estrogen and progesterone to be produced. They regulate the female reproductive cycle, which is divided into the ovarian cycle and the menstrual cycle.

Human pregnancy begins with fertilization of an egg and proceeds through the three trimesters of gestation. The first trimester lays down the basic structures of the body, including the limb buds, heart, eyes, and the liver. The second trimester continues the development of all of the organs and systems. The third trimester exhibits the greatest growth of the fetus and culminates in labor and delivery. The labor process has three stages (contractions, delivery of the fetus, and expulsion of the placenta), each propelled by hormones.

14.3.7 Art Connections

Exercise 14.3.1 ***(Solution on p. 315.)***

Figure 14.8 Which of the following statements about hormone regulation of the female reproductive cycle is false?

a. LH and FSH are produced in the pituitary, and estrogen and progesterone are produced in the ovaries.
b. Estrogen and progesterone secreted from the corpus luteum (CL) cause the endometrium to thicken.
c. Follicles produce high levels of progesterone.
d. Secretion of GnRH by the hypothalamus is inhibited by high levels of estrogen.

14.3.8 Review Questions

Exercise 14.3.2 ***(Solution on p. 315.)***

Which female organ has an endometrial lining that will support a developing baby?

a. labia minora
b. breast
c. ovaries
d. uterus

Exercise 14.3.3 ***(Solution on p. 315.)***

Which hormone causes FSH and LH to be released?

a. testosterone
b. estrogen
c. GnRH
d. progesterone

Exercise 14.3.4 ***(Solution on p. 315.)***

Nutrient and waste requirements for the developing fetus are handled during the first few weeks by _ _ _ _ _ _ _ _.

a. the placenta

b. diffusion through the endometrium
c. the chorion
d. the blastocyst

Exercise 14.3.5 *(Solution on p. 315.)*
Which hormone is primarily responsible for the contractions during labor?

a. oxytocin
b. estrogen
c. β-HCG
d. progesterone

14.3.9 Free Response

Exercise 14.3.6 *(Solution on p. 315.)*
Describe oogenesis with respect to the timing of the processes and the number and type of cells finally produced.

Exercise 14.3.7 *(Solution on p. 315.)*
Describe the events in the ovarian cycle leading up to ovulation.

Exercise 14.3.8 *(Solution on p. 315.)*
Describe the stages of labor.

Solutions to Exercises in Chapter 14

to Exercise 14.2.1 (p. 304)
Figure 14.3 D
to Exercise 14.2.2 (p. 305)
C
to Exercise 14.2.3 (p. 305)
C
to Exercise 14.2.4 (p. 305)
Stem cells are laid down in the male during gestation and lie dormant until adolescence/puberty. At this time, spermatogenesis begins and continues until death, producing the maximum number of sperm (i.e. four per cell that started meiosis) with each meiotic division. The process takes approximately 70 days and the sperm are released into the lumen of the seminiferous tubules.

Solutions to Female Reproductive Anatomy and Physiology; Gestation and Labor

to Exercise 14.3.1 (p. 313)
Figure 14.8 C
to Exercise 14.3.2 (p. 313)
D
to Exercise 14.3.3 (p. 313)
C
to Exercise 14.3.4 (p. 313)
B
to Exercise 14.3.5 (p. 314)
A
to Exercise 14.3.6 (p. 314)
Stem cells in the female increase to one to two million and enter the first meiotic division and are arrested in prophase. Oogenesis continues again at adolescence in batches of eggs with each menstrual cycle. These primary oocytes finish the first meiotic division, producing a viable egg with most of the cytoplasm and its contents, and a second cell called a polar body containing 23 chromosomes. The second meiotic division is initiated and arrested in metaphase. At ovulation, one egg is released. If this egg is fertilized, it finishes the second meiotic division. This is a diploid, fertilized egg.
to Exercise 14.3.7 (p. 314)
Low levels of progesterone allow the hypothalamus to send GnRH to the anterior pituitary and cause the release of FSH and LH. FSH stimulates follicles on the ovary to grow and prepare the eggs for ovulation. As the follicles increase in size, they begin to release estrogen and a low level of progesterone into the blood. The level of estrogen rises to a peak, causing a spike in the concentration of LH. This causes the most mature follicle to rupture and ovulation occurs.
to Exercise 14.3.8 (p. 314)
Stage one of labor results in uterine contractions, which thin the cervix and dilate the cervical opening. Stage two delivers the baby, and stage three delivers the placenta.

Chapter 15

Skeletal System

15.1 Introduction to Bone Tissue[1]

Child Looking at Bones

Figure 15.1: Bone is a living tissue. Unlike the bones of a fossil made inert by a process of mineralization, a child's bones will continue to grow and develop while contributing to the support and function of other body systems. (credit: James Emery)

[1] This content is available online at <http://cnx.org/content/m58080/1.1/>.

NOTE: After studying this chapter, you will be able to:

- List and describe the functions of bones
- Describe the classes of bones
- Discuss the process of bone formation and development
- Explain how bone repairs itself after a fracture
- Discuss the effect of exercise, nutrition, and hormones on bone tissue

Bones make good fossils. While the soft tissue of a once living organism will decay and fall away over time, bone tissue will, under the right conditions, undergo a process of mineralization, effectively turning the bone to stone. A well-preserved fossil skeleton can give us a good sense of the size and shape of an organism, just as your skeleton helps to define your size and shape. Unlike a fossil skeleton, however, your skeleton is a structure of living tissue that grows, repairs, and renews itself. The bones within it are dynamic and complex organs that serve a number of important functions, including some necessary to maintain homeostasis.

15.2 Functions of the Skeletal System[2]

Bone, or **osseous tissue**, is a hard, dense connective tissue that forms most of the adult skeleton, the support structure of the body. In the areas of the skeleton where bones move (for example, the ribcage and joints), **cartilage**, a semi-rigid form of connective tissue, provides flexibility and smooth surfaces for movement. The **skeletal system** is the body system composed of bones and cartilage and performs the following critical functions for the human body:

- supports the body
- facilitates movement
- protects internal organs
- produces blood cells
- stores and releases minerals and fat

15.2.1 Support, Movement, and Protection

The most apparent functions of the skeletal system are the gross functions—those visible by observation. Simply by looking at a person, you can see how the bones support, facilitate movement, and protect the human body.

Just as the steel beams of a building provide a scaffold to support its weight, the bones and cartilage of your skeletal system compose the scaffold that supports the rest of your body. Without the skeletal system, you would be a limp mass of organs, muscle, and skin.

Bones also facilitate movement by serving as points of attachment for your muscles. While some bones only serve as a support for the muscles, others also transmit the forces produced when your muscles contract. From a mechanical point of view, bones act as levers and joints serve as fulcrums (Figure 15.2 (Bones Support Movement)). Unless a muscle spans a joint and contracts, a bone is not going to move. For information on the interaction of the skeletal and muscular systems, that is, the musculoskeletal system, seek additional content.

[2]This content is available online at <http://cnx.org/content/m58081/1.1/>.

Bones Support Movement

Figure 15.2: Bones act as levers when muscles span a joint and contract. (credit: Benjamin J. DeLong)

Bones also protect internal organs from injury by covering or surrounding them. For example, your ribs protect your lungs and heart, the bones of your vertebral column (spine) protect your spinal cord, and the bones of your cranium (skull) protect your brain (Figure 15.3 (Bones Protect Brain)).

Bones Protect Brain

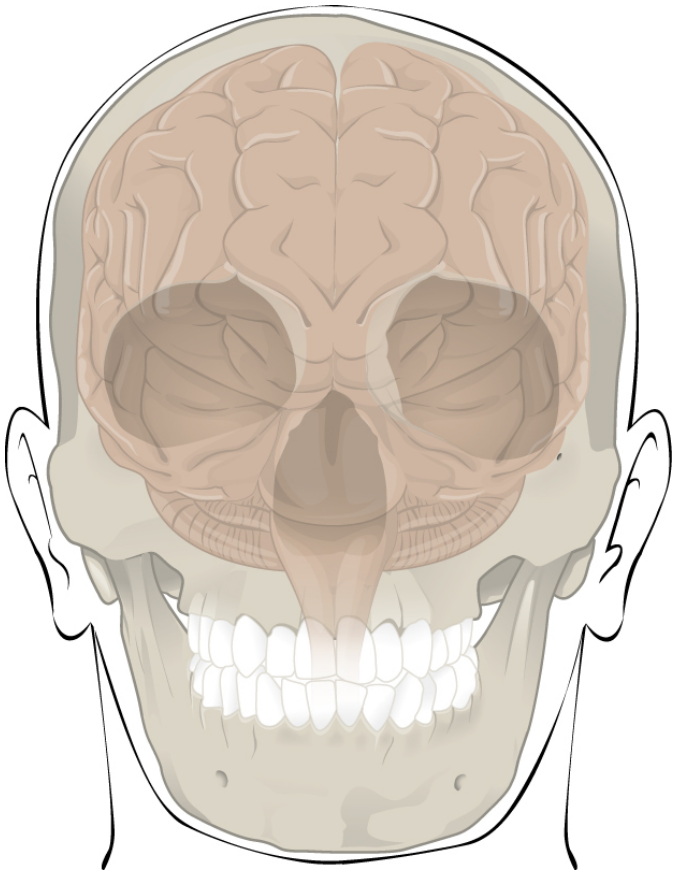

Figure 15.3: The cranium completely surrounds and protects the brain from non-traumatic injury.

: **Orthopedist**

An **orthopedist** is a doctor who specializes in diagnosing and treating disorders and injuries related to the musculoskeletal system. Some orthopedic problems can be treated with medications, exercises, braces, and other devices, but others may be best treated with surgery (Figure 15.4 (Arm Brace)).

Arm Brace

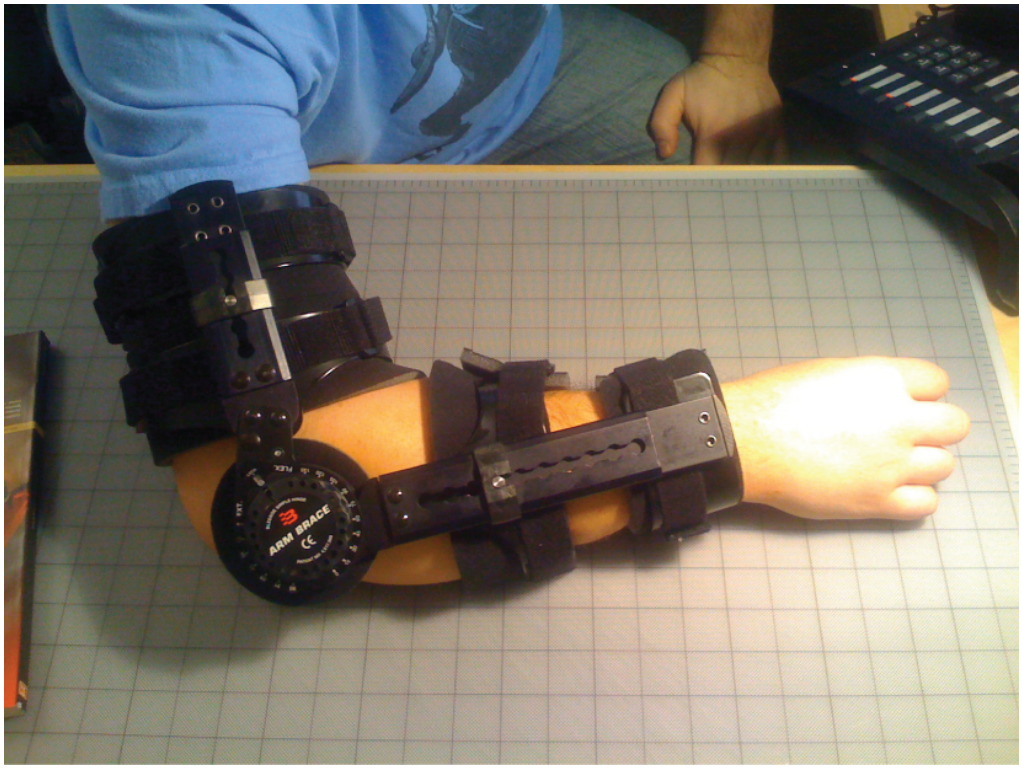

Figure 15.4: An orthopedist will sometimes prescribe the use of a brace that reinforces the underlying bone structure it is being used to support. (credit: Juhan Sonin)

While the origin of the word "orthopedics" (ortho- = "straight"; paed- = "child"), literally means "straightening of the child," orthopedists can have patients who range from pediatric to geriatric. In recent years, orthopedists have even performed prenatal surgery to correct spina bifida, a congenital defect in which the neural canal in the spine of the fetus fails to close completely during embryologic development.

Orthopedists commonly treat bone and joint injuries but they also treat other bone conditions including curvature of the spine. Lateral curvatures (scoliosis) can be severe enough to slip under the shoulder blade (scapula) forcing it up as a hump. Spinal curvatures can also be excessive dorsoventrally (kyphosis) causing a hunch back and thoracic compression. These curvatures often appear in preteens as the result of poor posture, abnormal growth, or indeterminate causes. Mostly, they are readily treated by orthopedists. As people age, accumulated spinal column injuries and diseases like osteoporosis can also lead to curvatures of the spine, hence the stooping you sometimes see in the elderly.

Some orthopedists sub-specialize in sports medicine, which addresses both simple injuries, such as a sprained ankle, and complex injuries, such as a torn rotator cuff in the shoulder. Treatment can range from exercise to surgery.

15.2.2 Mineral Storage, Energy Storage, and Hematopoiesis

On a metabolic level, bone tissue performs several critical functions. For one, the bone matrix acts as a reservoir for a number of minerals important to the functioning of the body, especially calcium, and potassium. These minerals, incorporated into bone tissue, can be released back into the bloodstream to maintain levels needed to support physiological processes. Calcium ions, for example, are essential for muscle contractions and controlling the flow of other ions involved in the transmission of nerve impulses.

Bone also serves as a site for fat storage and blood cell production. The softer connective tissue that fills the interior of most bone is referred to as bone marrow (Figure 15.5 (Head of Femur Showing Red and Yellow Marrow)). There are two types of bone marrow: yellow marrow and red marrow. **Yellow marrow** contains adipose tissue; the triglycerides stored in the adipocytes of the tissue can serve as a source of energy. **Red marrow** is where **hematopoiesis**—the production of blood cells—takes place. Red blood cells, white blood cells, and platelets are all produced in the red marrow.

Head of Femur Showing Red and Yellow Marrow

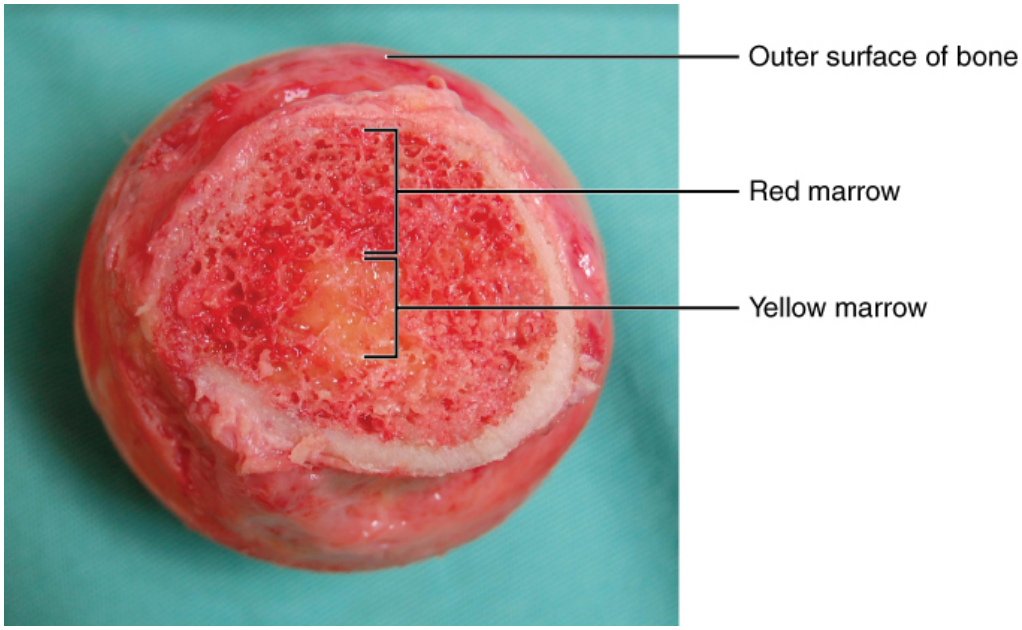

Figure 15.5: The head of the femur contains both yellow and red marrow. Yellow marrow stores fat. Red marrow is responsible for hematopoiesis. (credit: modification of work by "stevenfruitsmaak"/Wikimedia Commons)

15.2.3 Chapter Review

The major functions of the bones are body support, facilitation of movement, protection of internal organs, storage of minerals and fat, and hematopoiesis. Together, the muscular system and skeletal system are known as the musculoskeletal system.

15.2.4 Review Questions

Exercise 15.2.1 *(Solution on p. 340.)*
Which function of the skeletal system would be especially important if you were in a car accident?

a. storage of minerals
b. protection of internal organs
c. facilitation of movement
d. fat storage

Exercise 15.2.2 *(Solution on p. 340.)*
Bone tissue can be described as _____.

a. dead calcified tissue
b. cartilage
c. the skeletal system
d. dense, hard connective tissue

Exercise 15.2.3 *(Solution on p. 340.)*
Without red marrow, bones would not be able to _____.

a. store phosphate
b. store calcium
c. make blood cells
d. move like levers

Exercise 15.2.4 *(Solution on p. 340.)*
Yellow marrow has been identified as _____.

a. an area of fat storage
b. a point of attachment for muscles
c. the hard portion of bone
d. the cause of kyphosis

Exercise 15.2.5 *(Solution on p. 340.)*
Which of the following can be found in areas of movement?

a. hematopoiesis
b. cartilage
c. yellow marrow
d. red marrow

Exercise 15.2.6 *(Solution on p. 340.)*
The skeletal system is made of _____.

a. muscles and tendons
b. bones and cartilage
c. vitreous humor
d. minerals and fat

15.2.5 Critical Thinking Questions

Exercise 15.2.7 *(Solution on p. 340.)*

The skeletal system is composed of bone and cartilage and has many functions. Choose three of these functions and discuss what features of the skeletal system allow it to accomplish these functions.

15.3 Bone Structure[3]

Bone tissue (osseous tissue) differs greatly from other tissues in the body. Bone is hard and many of its functions depend on that characteristic hardness. Later discussions in this chapter will show that bone is also dynamic in that its shape adjusts to accommodate stresses. This section will examine the gross anatomy of bone first and then move on to its histology.

15.3.1 Gross Anatomy of Bone

The structure of a long bone allows for the best visualization of all of the parts of a bone (Figure 15.6 (Anatomy of a Long Bone)). A long bone has two parts: the **diaphysis** and the **epiphysis**. The diaphysis is the tubular shaft that runs between the proximal and distal ends of the bone. The hollow region in the diaphysis is called the **medullary cavity**, which is filled with yellow marrow. The walls of the diaphysis are composed of dense and hard **compact bone**.

[3]This content is available online at <http://cnx.org/content/m58082/1.2/>.

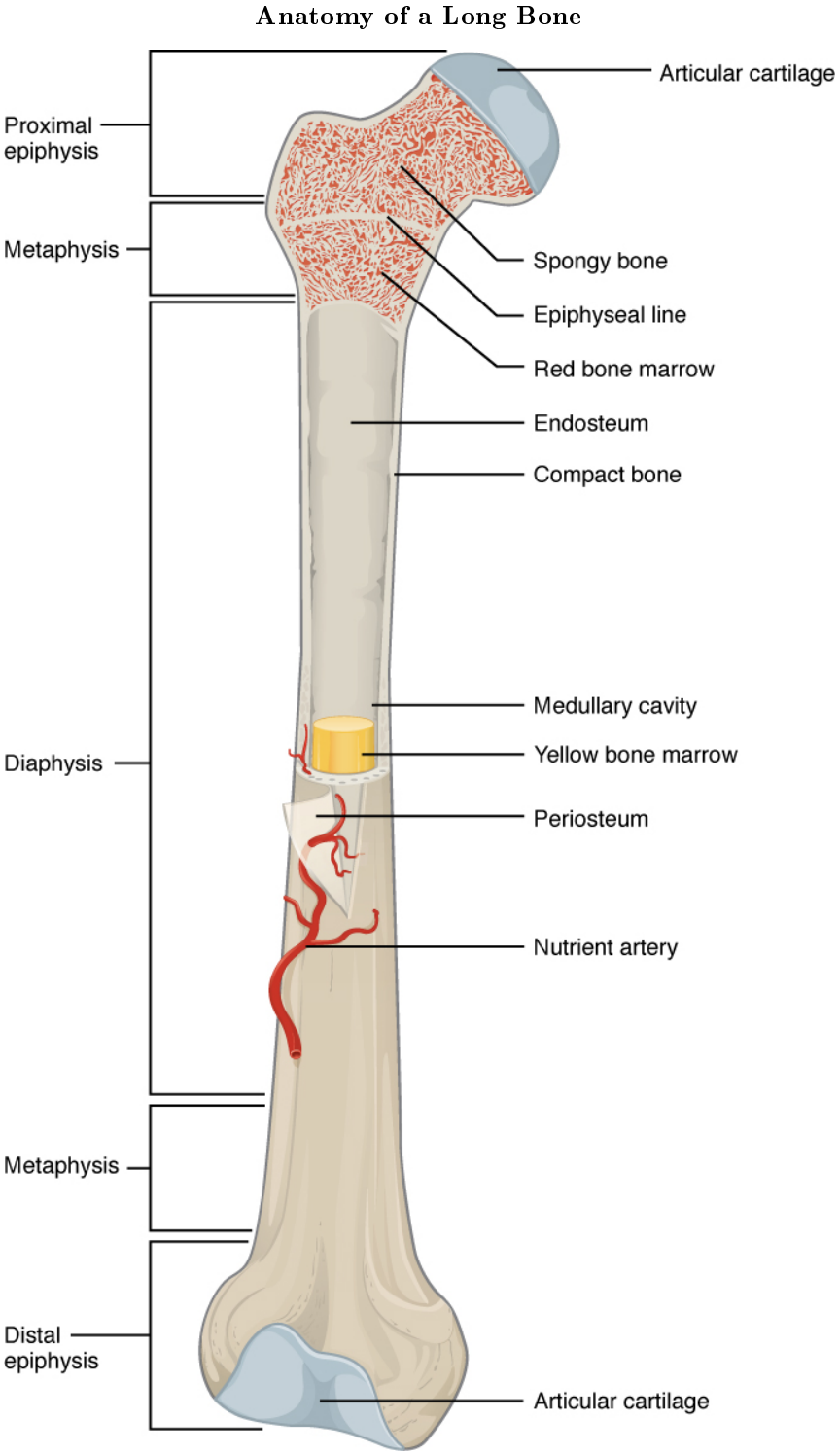

Figure 15.6: A typical long bone shows the gross anatomical characteristics of bone.

The wider section at each end of the bone is called the epiphysis (plural = epiphyses), which is filled with spongy bone. Red marrow fills the spaces in the spongy bone. Each epiphysis meets the diaphysis at the metaphysis, the narrow area that contains the **epiphyseal plate** (growth plate), a layer of hyaline (transparent) cartilage in a growing bone. When the bone stops growing in early adulthood (approximately 18–21 years), the cartilage is replaced by osseous tissue and the epiphyseal plate becomes an epiphyseal line.

15.3.2 Bone Cells and Tissue

Bone contains a relatively small number of cells entrenched in a matrix of collagen fibers that provide a surface for inorganic salt crystals to adhere. These salt crystals form when calcium phosphate and calcium carbonate combine to create hydroxyapatite, which incorporates other inorganic salts like magnesium hydroxide, fluoride, and sulfate as it crystallizes, or calcifies, on the collagen fibers. The hydroxyapatite crystals give bones their hardness and strength, while the collagen fibers give them flexibility so that they are not brittle.

Although bone cells compose a small amount of the bone volume, they are crucial to the function of bones. Four types of cells are found within bone tissue: osteoblasts, osteocytes, osteogenic cells, and osteoclasts (Figure 15.7 (Bone Cells)).

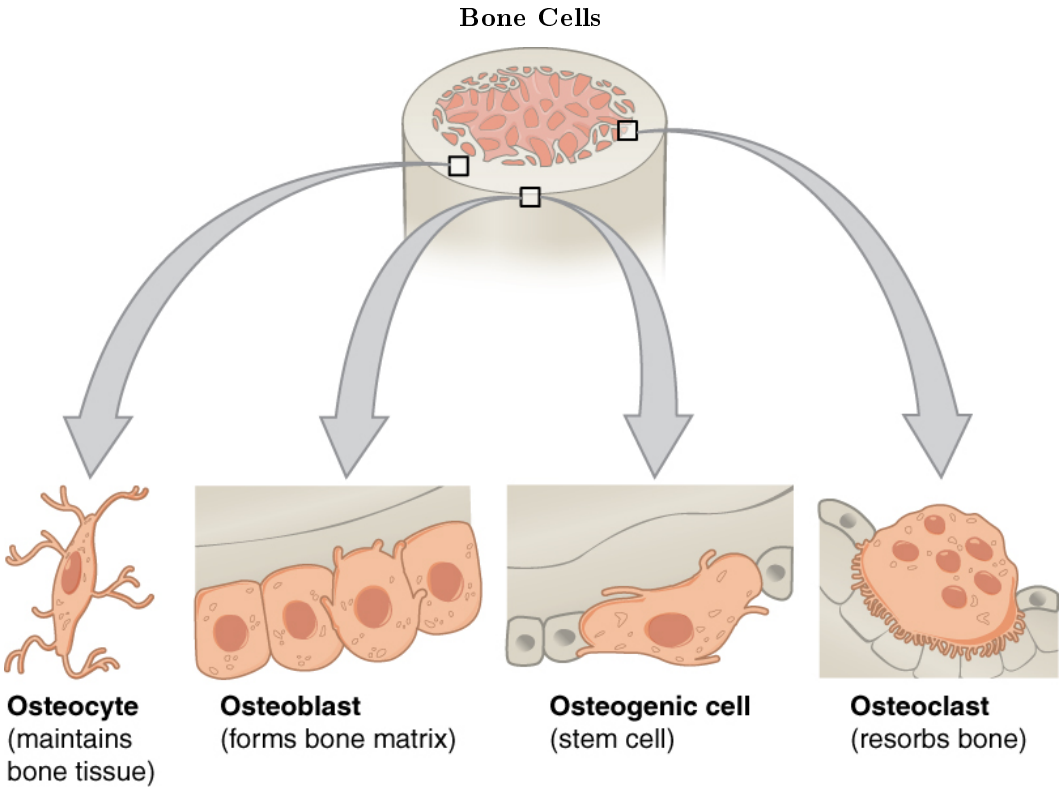

Figure 15.7: Four types of cells are found within bone tissue. Osteogenic cells are undifferentiated and develop into osteoblasts. When osteoblasts get trapped within the calcified matrix, their structure and function changes, and they become osteocytes. Osteoclasts develop from monocytes and macrophages and differ in appearance from other bone cells.

The **osteoblast** is the bone cell responsible for forming new bone and is found in the growing portions of bone, including the periosteum and endosteum. Osteoblasts, which do not divide, synthesize and secrete the collagen matrix and calcium salts. As the secreted matrix surrounding the osteoblast calcifies, the osteoblast become trapped within it; as a result, it changes in structure and becomes an **osteocyte**, the primary cell of mature bone and the most common type of bone cell. Each osteocyte is located in a space called a **lacuna** and is surrounded by bone tissue. Osteocytes maintain the mineral concentration of the matrix via the secretion of enzymes. Like osteoblasts, osteocytes lack mitotic activity. They can communicate with each other and receive nutrients via long cytoplasmic processes that extend through **canaliculi** (singular = canaliculus), channels within the bone matrix.

If osteoblasts and osteocytes are incapable of mitosis, then how are they replenished when old ones die? The answer lies in the properties of a third category of bone cells—the **osteogenic cell**. These osteogenic cells are undifferentiated with high mitotic activity and they are the only bone cells that divide. Immature osteogenic cells are found in the deep layers of the periosteum and the marrow. They differentiate and develop into osteoblasts.

The dynamic nature of bone means that new tissue is constantly formed, and old, injured, or unnecessary bone is dissolved for repair or for calcium release. The cell responsible for bone resorption, or breakdown, is the **osteoclast**. They are found on bone surfaces, are multinucleated, and originate from monocytes and macrophages, two types of white blood cells, not from osteogenic cells. Osteoclasts are continually breaking down old bone while osteoblasts are continually forming new bone. The ongoing balance between osteoblasts and osteoclasts is responsible for the constant but subtle reshaping of bone. Table 15.1 reviews the bone cells, their functions, and locations.

Bone Cells		
Cell type	**Function**	**Location**
Osteogenic cells	Develop into osteoblasts	Deep layers of the periosteum and the marrow
Osteoblasts	Bone formation	Growing portions of bone, including periosteum and endosteum
Osteocytes	Maintain mineral concentration of matrix	Entrapped in matrix
Osteoclasts	Bone resorption	Bone surfaces and at sites of old, injured, or unneeded bone

Table 15.1

15.3.3 Compact and Spongy Bone

The differences between compact and spongy bone are best explored via their histology. Most bones contain compact and spongy osseous tissue, but their distribution and concentration vary based on the bone's overall function. Compact bone is dense so that it can withstand compressive forces, while spongy (cancellous) bone has open spaces and supports shifts in weight distribution.

15.3.3.1 Compact Bone

Compact bone is the denser, stronger of the two types of bone tissue (Figure 15.8 (Diagram of Compact Bone)) and it provides support and protection.

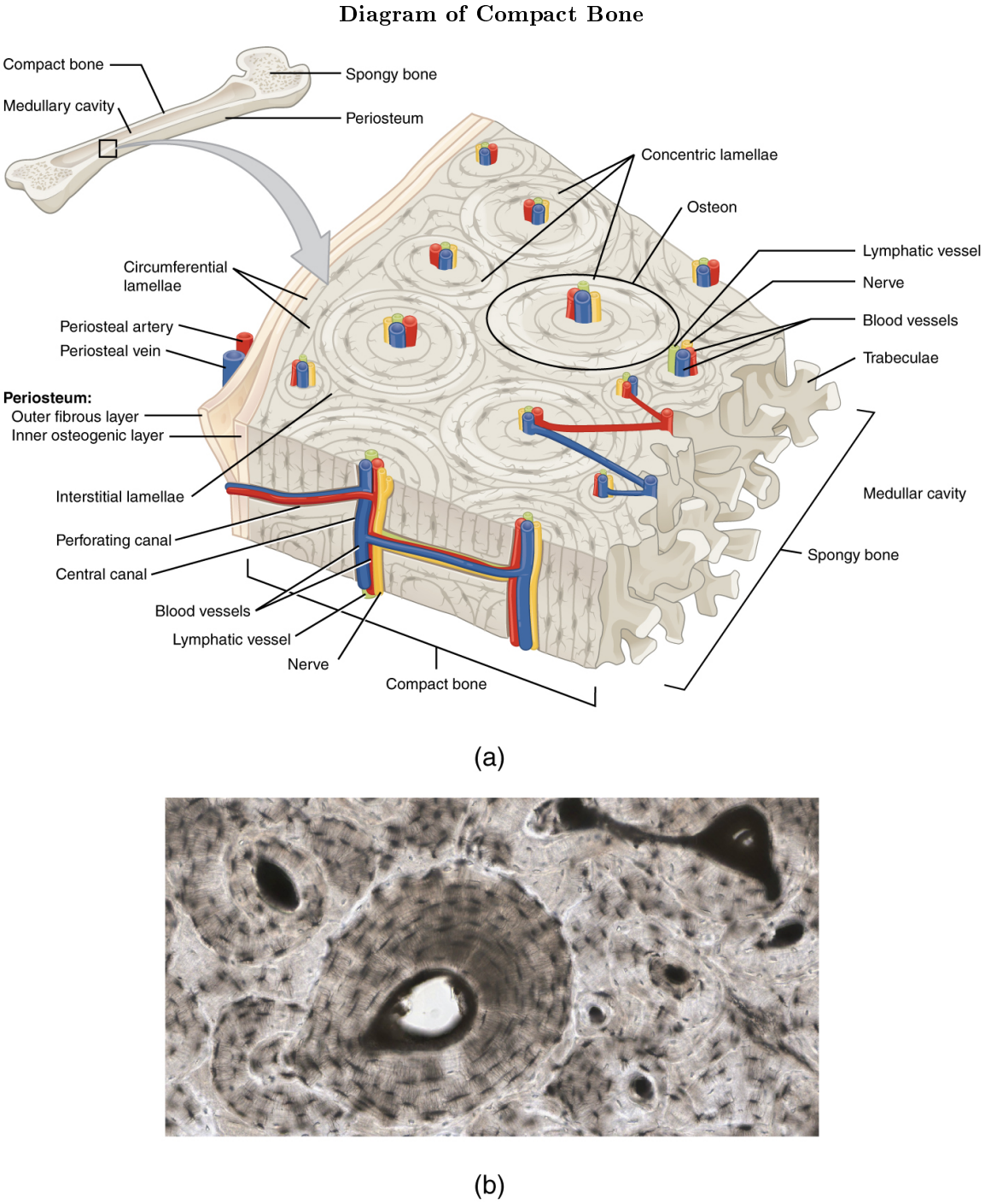

Figure 15.8: (a) This cross-sectional view of compact bone shows the basic structural unit, the osteon. (b) In this micrograph of the osteon, you can clearly see the concentric lamellae and central canals. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School ©2012)

The microscopic structural unit of compact bone is called an **osteon**, or Haversian system. Each osteon is composed of concentric rings of calcified matrix called lamellae (singular = lamella). Running down the center of each osteon is the **central canal**, or Haversian canal, which contains blood vessels, nerves, and lymphatic vessels.

The osteocytes are located inside spaces called lacunae (singular = lacuna), found at the borders of adjacent lamellae. As described earlier, canaliculi connect with the canaliculi of other lacunae and eventually with the central canal. This system allows nutrients to be transported to the osteocytes and wastes to be removed from them.

15.3.3.2 Spongy (Cancellous) Bone

Like compact bone, **spongy bone**, also known as cancellous bone, contains osteocytes housed in lacunae, but they are not arranged in concentric circles. Instead, the lacunae and osteocytes are found in a lattice-like network of matrix spikes called **trabeculae** (singular = trabecula) (Figure 15.9 (Diagram of Spongy Bone)). The trabeculae may appear to be a random network, but each trabecula forms along lines of stress to provide strength to the bone. The spaces of the trabeculated network provide balance to the dense and heavy compact bone by making bones lighter so that muscles can move them more easily. In addition, the spaces in some spongy bones contain red marrow, protected by the trabeculae, where hematopoiesis occurs.

Diagram of Spongy Bone

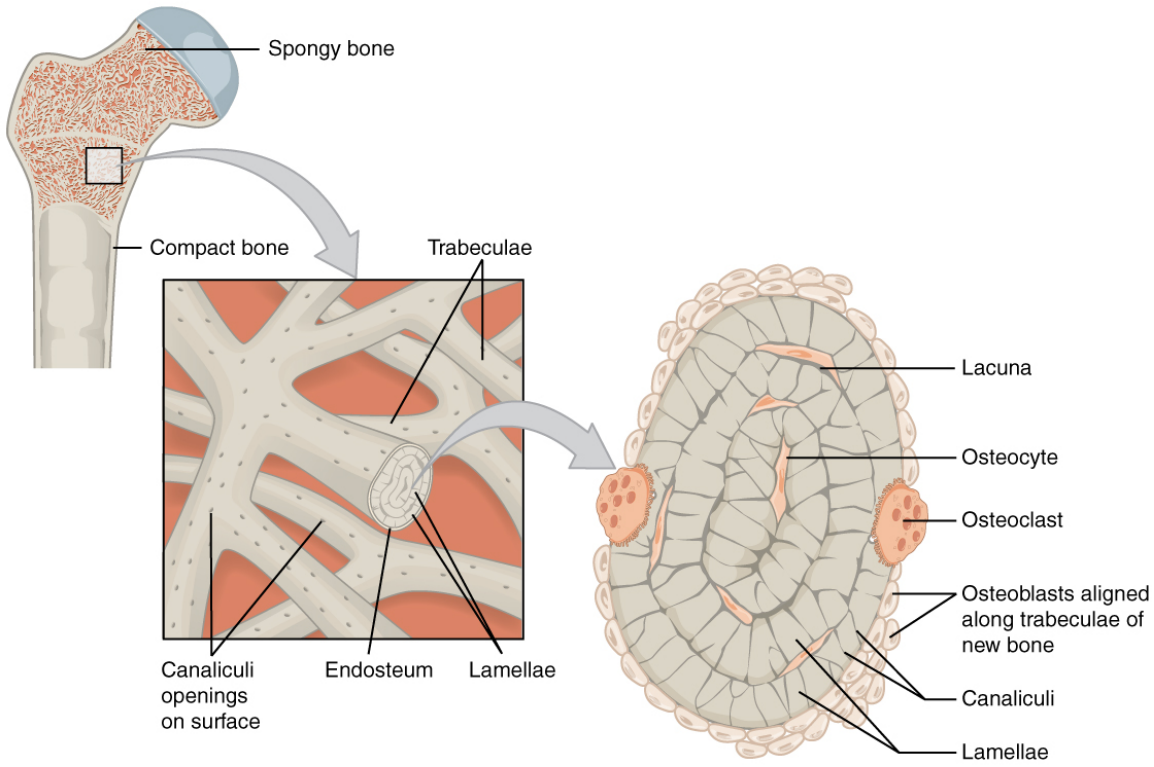

Figure 15.9: Spongy bone is composed of trabeculae that contain the osteocytes. Red marrow fills the spaces in some bones.

: **Skeletal System: Paget's Disease**

Paget's disease usually occurs in adults over age 40. It is a disorder of the bone remodeling process that begins with overactive osteoclasts. This means more bone is resorbed than is laid down. The osteoblasts try to compensate but the new bone they lay down is weak and brittle and therefore prone to fracture.

While some people with Paget's disease have no symptoms, others experience pain, bone fractures, and bone deformities (Figure 15.10 (Paget's Disease)). Bones of the pelvis, skull, spine, and legs are the most commonly affected. When occurring in the skull, Paget's disease can cause headaches and hearing loss.

Paget's Disease

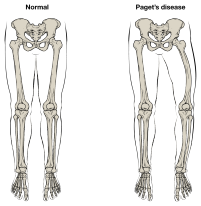

Figure 15.10: Normal leg bones are relatively straight, but those affected by Paget's disease are porous and curved.

What causes the osteoclasts to become overactive? The answer is still unknown, but hereditary factors seem to play a role. Some scientists believe Paget's disease is due to an as-yet-unidentified virus.

Paget's disease is diagnosed via imaging studies and lab tests. X-rays may show bone deformities or areas of bone resorption. Bone scans are also useful. In these studies, a dye containing a radioactive ion is injected into the body. Areas of bone resorption have an affinity for the ion, so they will light up on the scan if the ions are absorbed. In addition, blood levels of an enzyme called alkaline phosphatase are typically elevated in people with Paget's disease.

Bisphosphonates, drugs that decrease the activity of osteoclasts, are often used in the treatment of Paget's disease. However, in a small percentage of cases, bisphosphonates themselves have been linked to an increased risk of fractures because the old bone that is left after bisphosphonates are administered becomes worn out and brittle. Still, most doctors feel that the benefits of bisphosphonates more than outweigh the risk; the medical professional has to weigh the benefits and risks on a case-by-case basis. Bisphosphonate treatment can reduce the overall risk of deformities or fractures, which in turn reduces the risk of surgical repair and its associated risks and complications.

15.3.4 Blood and Nerve Supply

The spongy bone and medullary cavity receive nourishment from arteries that pass through the compact bone. The arteries enter through the **nutrient foramen** (plural = foramina), small openings in the diaphysis (Figure 15.11 (Diagram of Blood and Nerve Supply to Bone)). The osteocytes in spongy bone are nourished by blood vessels of the periosteum that penetrate spongy bone and blood that circulates in the marrow cavities. As the blood passes through the marrow cavities, it is collected by veins, which then pass out of the bone through the foramina.

In addition to the blood vessels, nerves follow the same paths into the bone where they tend to concentrate in the more metabolically active regions of the bone. The nerves sense pain, and it appears the nerves also

play roles in regulating blood supplies and in bone growth, hence their concentrations in metabolically active sites of the bone.

Diagram of Blood and Nerve Supply to Bone

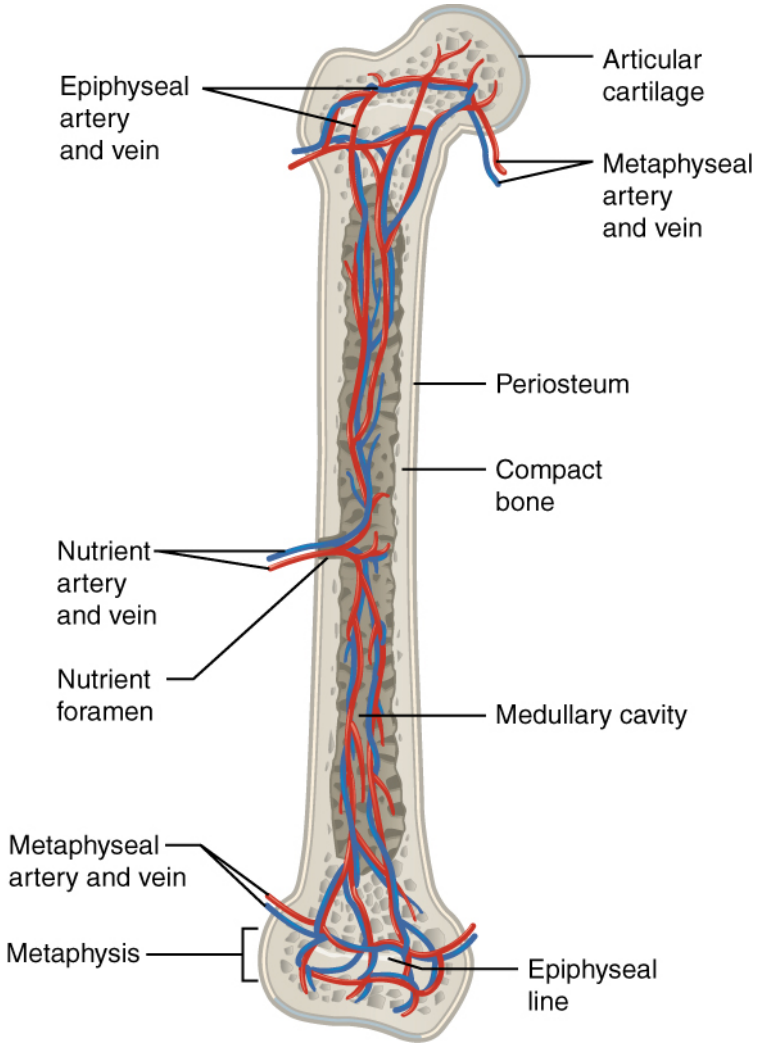

Figure 15.11: Blood vessels and nerves enter the bone through the nutrient foramen.

15.3.5 Chapter Review

A hollow medullary cavity filled with yellow marrow runs the length of the diaphysis of a long bone. The walls of the diaphysis are compact bone. The epiphyses, which are wider sections at each end of a long bone, are filled with spongy bone and red marrow. The epiphyseal plate, a layer of hyaline cartilage, is replaced by osseous tissue as the organ grows in length.

Bone matrix consists of collagen fibers and organic ground substance, primarily hydroxyapatite formed from calcium salts. Osteogenic cells develop into osteoblasts. Osteoblasts are cells that make new bone. They become osteocytes, the cells of mature bone, when they get trapped in the matrix. Osteoclasts engage in bone resorption. Compact bone is dense and composed of osteons, while spongy bone is less dense and made up of trabeculae. Blood vessels and nerves enter the bone through the nutrient foramina to nourish and innervate bones.

15.3.6 Review Questions

Exercise 15.3.1 ***(Solution on p. 340.)***

Which of the following occurs in the spongy bone of the epiphysis?

a. bone growth
b. bone remodeling
c. hematopoiesis
d. shock absorption

Exercise 15.3.2 ***(Solution on p. 340.)***

Which of the following are incapable of undergoing mitosis?

a. osteoblasts and osteoclasts
b. osteocytes and osteoclasts
c. osteoblasts and osteocytes
d. osteogenic cells and osteoclasts

Exercise 15.3.3 ***(Solution on p. 340.)***

Which cells do not originate from osteogenic cells?

a. osteoblasts
b. osteoclasts
c. osteocytes
d. osteoprogenitor cells

Exercise 15.3.4 ***(Solution on p. 340.)***

Which of the following are found in compact bone and cancellous bone?

a. Haversian systems
b. Haversian canals
c. lamellae
d. lacunae

Exercise 15.3.5 ***(Solution on p. 340.)***

Which of the following are *only* found in spongy bone? Hint: See figure 15.9.

a. canaliculi
b. Volkmann's canals
c. trabeculae
d. calcium salts

Exercise 15.3.6 ***(Solution on p. 340.)***

The area of a bone where the nutrient foramen passes forms what kind of bone marking?

a. a hole

b. a facet
c. a canal
d. a fissure

15.3.7 Critical Thinking Questions

Exercise 15.3.7 *(Solution on p. 340.)*

In what ways is the structural makeup of compact and spongy bone well suited to their respective functions?

15.4 Bone Formation and Development[4]

In the early stages of embryonic development, the embryo's skeleton consists of fibrous membranes and hyaline cartilage. By the sixth or seventh week of embryonic life, the actual process of bone development, **ossification**, begins.

15.4.1 Cartilage Templates

Bone is a replacement tissue; that is, it uses a model tissue on which to lay down its mineral matrix. For skeletal development, the most common template is cartilage. During fetal development, a framework is laid down that determines where bones will form. Unlike most connective tissues, cartilage is avascular, meaning that it has no blood vessels supplying nutrients and removing metabolic wastes. All of these functions are carried on by diffusion through the matrix. This is why damaged cartilage does not repair itself as readily as most tissues do.

Throughout fetal development and into childhood growth and development, bone forms on the cartilaginous matrix. By the time a fetus is born, most of the cartilage has been replaced with bone. Some additional cartilage will be replaced throughout childhood, and some cartilage remains in the adult skeleton.

15.4.2 Endochondral Ossification

In **endochondral ossification**, bone develops by *replacing* hyaline cartilage. Cartilage does not become bone. Instead, cartilage serves as a template to be completely replaced by new bone.

In a long bone, for example, at about 6 to 8 weeks after conception, some of the mesenchymal cells differentiate into chondrocytes (cartilage cells) that form the cartilaginous skeletal precursor of the bones.

[4] This content is available online at <http://cnx.org/content/m58083/1.2/>.

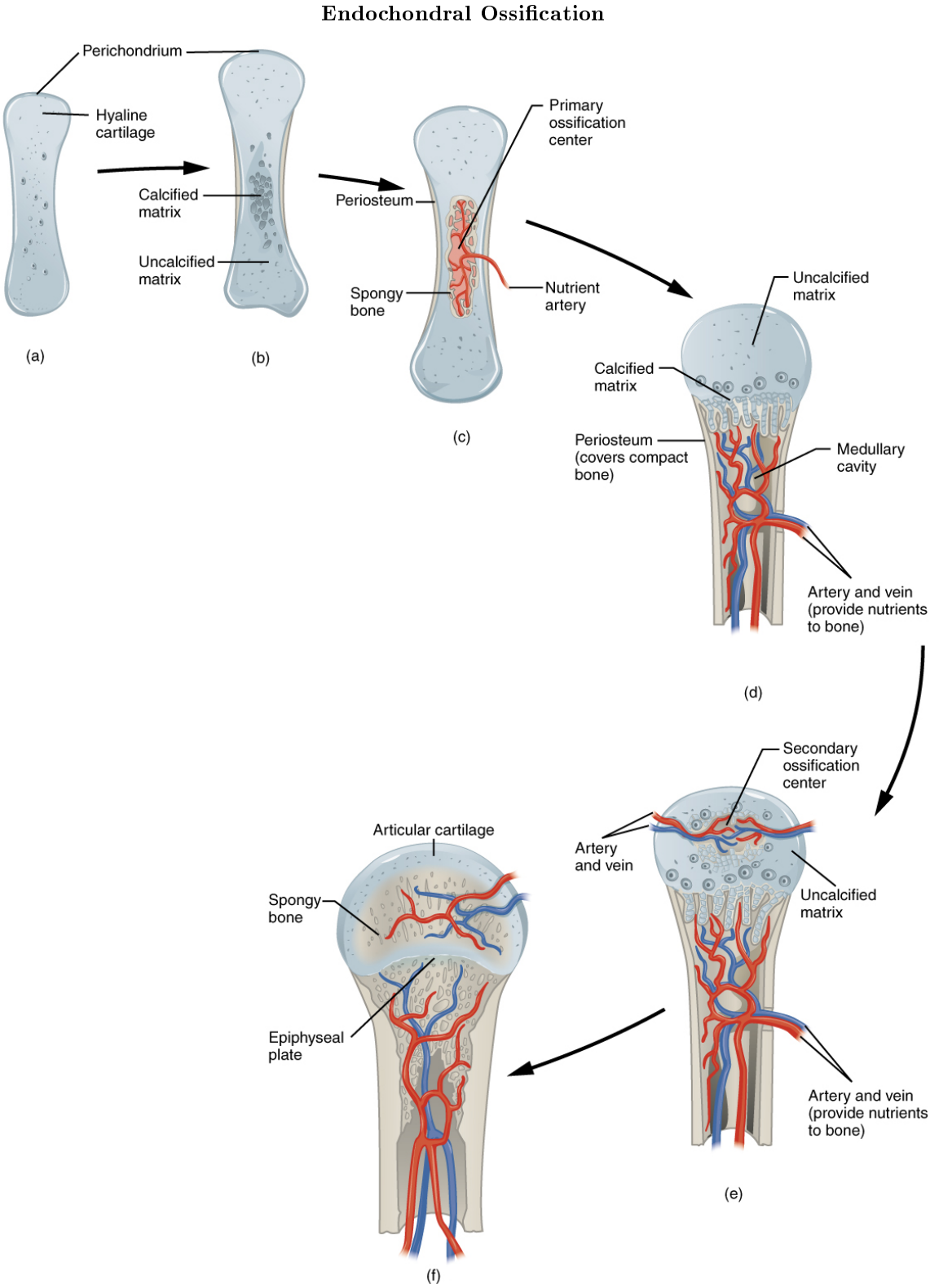

Figure 15.12: Endochondral ossification follows five steps. (a) Mesenchymal cells differentiate into chondrocytes. (b) The cartilage model of the future bony skeleton. (c) Capillaries penetrate cartilage. Primary ossification center develops. (d) Cartilage and chondrocytes continue to grow at ends of the bone. (e) Secondary ossification centers develop. (f) Cartilage remains at epiphyseal (growth) plate and at joint surface as articular cartilage.

Available for free at Connexions <http://cnx.org/content/col11007/1.3>

As more matrix is produced, the chondrocytes in the center of the cartilaginous model grow in size. As the matrix calcifies, nutrients can no longer reach the chondrocytes. This results in their death and the disintegration of the surrounding cartilage. Blood vessels invade the resulting spaces, not only enlarging the cavities but also carrying osteogenic cells with them, many of which will become osteoblasts. These enlarging spaces eventually combine to become the medullary cavity.

As the cartilage grows, capillaries penetrate it. This penetration initiates the transformation of the perichondrium into the bone-producing periosteum. Here, the osteoblasts form a periosteal collar of compact bone around the cartilage of the diaphysis. By the second or third month of fetal life, bone cell development and ossification ramps up and creates the **primary ossification center**, a region deep in the periosteal collar where ossification begins (Figure 15.12 (Endochondral Ossification)**c**).

While these deep changes are occurring, chondrocytes and cartilage continue to grow at the ends of the bone (the future epiphyses), which increases the bone's length at the same time bone is replacing cartilage in the diaphyses. By the time the fetal skeleton is fully formed, cartilage only remains at the joint surface as articular cartilage and between the diaphysis and epiphysis as the epiphyseal plate, the latter of which is responsible for the longitudinal growth of bones. After birth, this same sequence of events (matrix mineralization, death of chondrocytes, invasion of blood vessels from the periosteum, and seeding with osteogenic cells that become osteoblasts) occurs in the epiphyseal regions, and each of these centers of activity is referred to as a **secondary ossification center** (Figure 15.12 (Endochondral Ossification)**e**).

15.4.3 How Bones Grow in Length

The epiphyseal plate is the area of growth in a long bone. It is a layer of hyaline cartilage where ossification occurs in immature bones. On the epiphyseal side of the epiphyseal plate, cartilage is formed. On the diaphyseal side, cartilage is ossified, and the diaphysis grows in length.

Bones continue to grow in length until early adulthood. When the chondrocytes in the epiphyseal plate cease their proliferation and bone replaces the cartilage, longitudinal growth stops. All that remains of the epiphyseal plate is the **epiphyseal line** (Figure 15.13 (Progression from Epiphyseal Plate to Epiphyseal Line)).

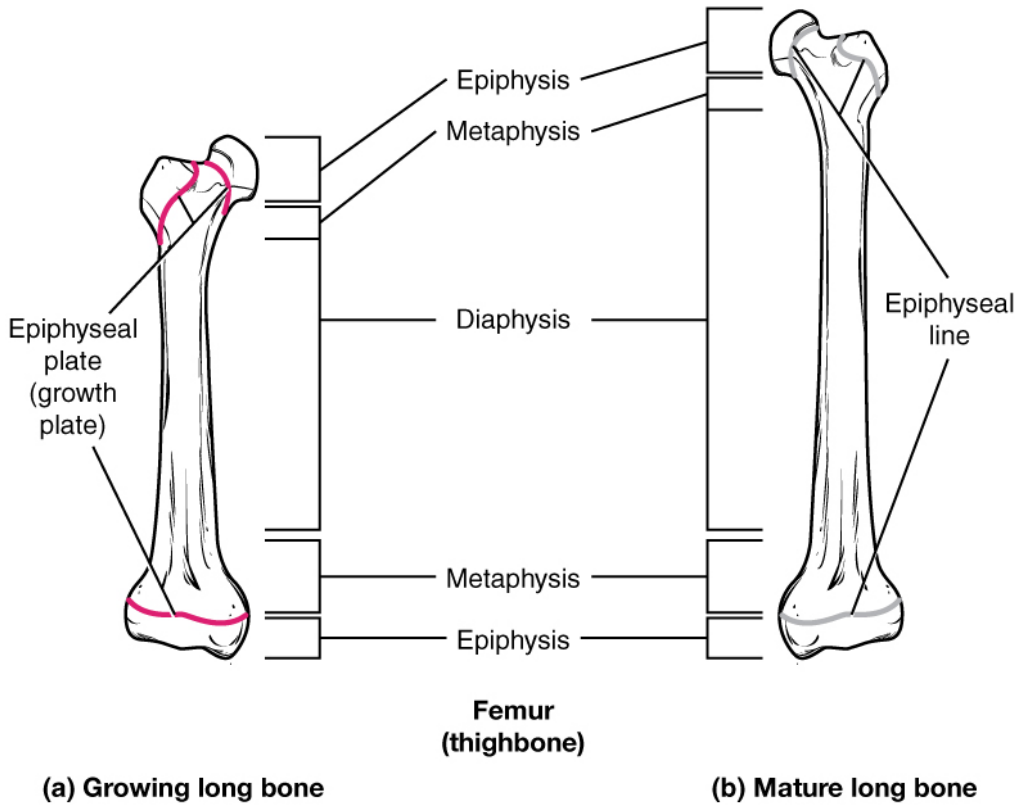

Figure 15.13: As a bone matures, the epiphyseal plate progresses to an epiphyseal line. (a) Epiphyseal plates are visible in a growing bone. (b) Epiphyseal lines are the remnants of epiphyseal plates in a mature bone.

15.4.4 How Bones Grow in Diameter

While bones are increasing in length, they are also increasing in diameter; growth in diameter can continue even after longitudinal growth ceases. This is called appositional growth. Osteoclasts resorb old bone that lines the medullary cavity, while osteoblasts, via intramembranous ossification, produce new bone tissue beneath the periosteum. The erosion of old bone along the medullary cavity and the deposition of new bone beneath the periosteum not only increase the diameter of the diaphysis but also increase the diameter of the medullary cavity. This process is called **modeling**.

15.4.5 Bone Remodeling

The process in which matrix is resorbed on one surface of a bone and deposited on another is known as bone modeling. Modeling primarily takes place during a bone's growth. However, in adult life, bone undergoes **remodeling**, in which resorption of old or damaged bone takes place on the same surface where osteoblasts lay new bone to replace that which is resorbed. Injury, exercise, and other activities lead to remodeling.

Those influences are discussed later in the chapter, but even without injury or exercise, about 5 to 10 percent of the skeleton is remodeled annually just by destroying old bone and renewing it with fresh bone.

: **Skeletal System**

Osteogenesis imperfecta (OI) is a genetic disease in which bones do not form properly and therefore are fragile and break easily. It is also called brittle bone disease. The disease is present from birth and affects a person throughout life.

The genetic mutation that causes OI affects the body's production of collagen, one of the critical components of bone matrix. The severity of the disease can range from mild to severe. Those with the most severe forms of the disease sustain many more fractures than those with a mild form. Frequent and multiple fractures typically lead to bone deformities and short stature. Bowing of the long bones and curvature of the spine are also common in people afflicted with OI. Curvature of the spine makes breathing difficult because the lungs are compressed.

Because collagen is such an important structural protein in many parts of the body, people with OI may also experience fragile skin, weak muscles, loose joints, easy bruising, frequent nosebleeds, brittle teeth, blue sclera, and hearing loss. There is no known cure for OI. Treatment focuses on helping the person retain as much independence as possible while minimizing fractures and maximizing mobility. Toward that end, safe exercises, like swimming, in which the body is less likely to experience collisions or compressive forces, are recommended. Braces to support legs, ankles, knees, and wrists are used as needed. Canes, walkers, or wheelchairs can also help compensate for weaknesses.

When bones do break, casts, splints, or wraps are used. In some cases, metal rods may be surgically implanted into the long bones of the arms and legs. Research is currently being conducted on using bisphosphonates to treat OI. Smoking and being overweight are especially risky in people with OI, since smoking is known to weaken bones, and extra body weight puts additional stress on the bones.

15.4.6 Chapter Review

All bone formation is a replacement process. Embryos develop a cartilaginous skeleton and various membranes. During development, these are replaced by bone during the ossification process. In endochondral ossification, bone develops by replacing hyaline cartilage. Activity in the epiphyseal plate enables bones to grow in length. Modeling allows bones to grow in diameter. Remodeling occurs as bone is resorbed and replaced by new bone. Osteogenesis imperfecta is a genetic disease in which collagen production is altered, resulting in fragile, brittle bones.

15.4.7 Review Questions

Exercise 15.4.1 *(Solution on p. 340.)*

Why is cartilage slow to heal?

a. because it eventually develops into bone
b. because it is semi-solid and flexible
c. because it does not have a blood supply
d. because endochondral ossification replaces all cartilage with bone

Exercise 15.4.2 *(Solution on p. 340.)*

Bones grow in length due to activity in the _ _ _ _ _ _ _ _.

a. epiphyseal plate
b. perichondrium

c. periosteum
d. medullary cavity

Solutions to Exercises in Chapter 15

to Exercise 15.2.1 (p. 324)
B
to Exercise 15.2.2 (p. 324)
D
to Exercise 15.2.3 (p. 324)
C
to Exercise 15.2.4 (p. 324)
A
to Exercise 15.2.5 (p. 324)
B
to Exercise 15.2.6 (p. 324)
B
to Exercise 15.2.7 (p. 325)
It supports the body. The rigid, yet flexible skeleton acts as a framework to support the other organs of the body.

It facilitates movement. The movable joints allow the skeleton to change shape and positions; that is, move.

It protects internal organs. Parts of the skeleton enclose or partly enclose various organs of the body including our brain, ears, heart, and lungs. Any trauma to these organs has to be mediated through the skeletal system.

It produces blood cells. The central cavity of long bones is filled with marrow. The red marrow is responsible for forming red and white blood cells.

It stores and releases minerals and fat. The mineral component of bone, in addition to providing hardness to bone, provides a mineral reservoir that can be tapped as needed. Additionally, the yellow marrow, which is found in the central cavity of long bones along with red marrow, serves as a storage site for fat.
to Exercise 15.3.1 (p. 333)
C
to Exercise 15.3.2 (p. 333)
C
to Exercise 15.3.3 (p. 333)
D
to Exercise 15.3.4 (p. 333)
C
to Exercise 15.3.5 (p. 333)
C
to Exercise 15.3.6 (p. 333)
A
to Exercise 15.3.7 (p. 334)
The densely packed concentric rings of matrix in compact bone are ideal for resisting compressive forces, which is the function of compact bone. The open spaces of the trabeculated network of spongy bone allow spongy bone to support shifts in weight distribution, which is the function of spongy bone.
to Exercise 15.4.1 (p. 338)
C
to Exercise 15.4.2 (p. 338)
A

Chapter 16

Muscles and Movement

16.1 Muscle Contraction and Locomotion[1]

Muscle cells are specialized for contraction. Muscles allow for motions such as walking, and they also facilitate bodily processes such as respiration and digestion. The body contains three types of muscle tissue: skeletal muscle, cardiac muscle, and smooth muscle (Figure 16.1).

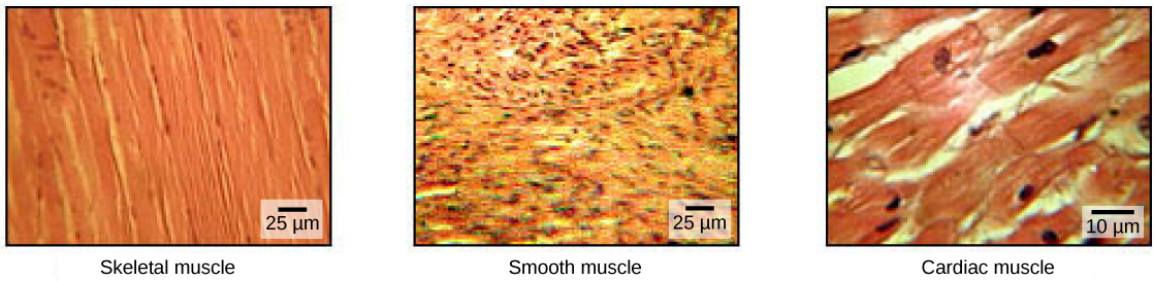

Figure 16.1: The body contains three types of muscle tissue: skeletal muscle, smooth muscle, and cardiac muscle, visualized here using light microscopy. Skeletal muscle cells are long, striated, and multinucleate. Smooth muscle cells are short, tapered at each end, and have only one plump nucleus in each. Cardiac muscle cells are branched and striated, but short. They also can have more than one nucleus per cell. (credit: modification of work by NCI, NIH; scale-bar data from Matt Russell)

Skeletal muscle tissue forms skeletal muscles, which attach to bones or skin and control locomotion and any movement that can be consciously controlled. Because it can be controlled by thought, skeletal muscle is also called voluntary muscle. Skeletal muscles are long and cylindrical in appearance; when viewed under a microscope, skeletal muscle tissue has a striped or striated appearance. The striations are caused by the regular arrangement of contractile proteins (actin and myosin). **Actin** is a filamentous contractile protein that interacts with another filamentous protein called **myosin** for muscle contraction to occur. Skeletal muscle also has multiple nuclei present in a single cell.

Smooth muscle tissue occurs in the walls of hollow organs such as the intestines, stomach, and urinary bladder, and around passages such as the respiratory tract and blood vessels. Smooth muscle has no

[1] This content is available online at <http://cnx.org/content/m58084/1.3/>.

striations, is not under voluntary control, has only one nucleus per cell, is tapered at both ends, and is called involuntary muscle.

Cardiac muscle tissue is only found in the heart, and cardiac contractions pump blood throughout the body and maintain blood pressure. Like skeletal muscle, cardiac muscle is striated, but unlike skeletal muscle, cardiac muscle cannot be consciously controlled and is called involuntary muscle. Cardiac muscle cells can have more than one nucleus per cell, are branched, and are distinguished by the presence of intercalated disks.

16.1.1 Skeletal Muscle Fiber Structure

Each skeletal muscle fiber is a skeletal muscle cell. These cells are incredibly large, with diameters of up to 100 μm and lengths of up to 30 cm. The plasma membrane of a skeletal muscle fiber is called the **sarcolemma**. The sarcolemma is the site of action potential conduction, which triggers muscle contraction. Within each muscle fiber are **myofibrils**—long cylindrical structures that lie parallel to the muscle fiber. Myofibrils run the entire length of the muscle fiber, and because they are only approximately 1.2 μm in diameter, hundreds to thousands can be found inside one muscle fiber. They attach to the sarcolemma at their ends, so that as myofibrils shorten, the entire muscle cell contracts (Figure 16.2).

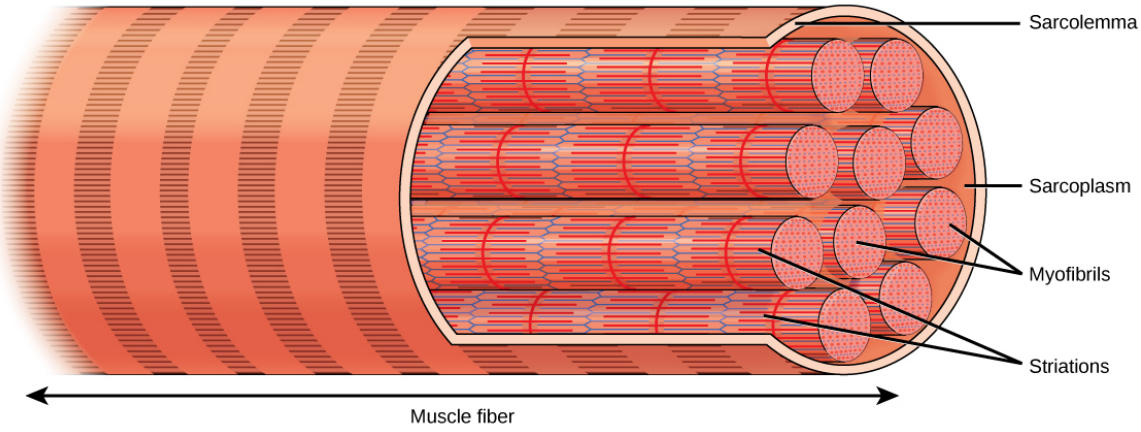

Figure 16.2: A skeletal muscle cell is surrounded by a plasma membrane called the sarcolemma with a cytoplasm called the sarcoplasm. A muscle fiber is composed of many fibrils, packaged into orderly units.

The striated appearance of skeletal muscle tissue is a result of repeating bands of the proteins actin and myosin that are present along the length of myofibrils. The alignment of myofibrils in the cell causes the entire cell to appear striated or banded.

The Z lines mark the border of units called **sarcomeres**, which are the functional units of skeletal muscle. A myofibril is composed of many sarcomeres running along its length, and as the sarcomeres individually contract, the myofibrils and muscle cells shorten (Figure 16.3).

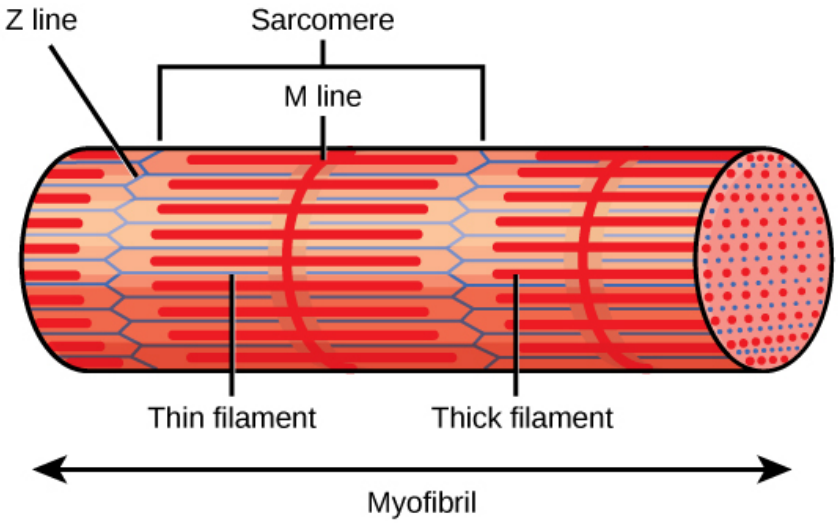

Figure 16.3: A sarcomere is the region from one Z line to the next Z line. Many sarcomeres are present in a myofibril, resulting in the striation pattern characteristic of skeletal muscle.

Myofibrils are composed of smaller structures called **myofilaments**. There are two main types of filaments: thick filaments and thin filaments; each has different compositions and locations. **Thick filaments** (composed of the protein myosin) and **Thin filaments** (composed of the protein actin).

The myosin thick filaments contain two regions designated as the head and the tail. These regions are important in the process of muscle contraction and will be discussed in more detail. Two components of the thin filaments are tropomyosin and troponin. Actin has binding sites for myosin attachment. Strands of tropomyosin block the binding sites and prevent actin–myosin interactions when the muscles are at rest. Troponin consists of three globular subunits. One subunit binds to tropomyosin, one subunit binds to actin, and one subunit binds Ca^{2+} ions.

16.1.2 Sliding Filament Model of Contraction

For a muscle cell to contract, the sarcomere must shorten. However, thick and thin filaments—the components of sarcomeres—do not shorten. Instead, they slide by one another, causing the sarcomere to shorten while the filaments remain the same length. The sliding filament theory of muscle contraction was developed to fit the differences observed in the named bands on the sarcomere at different degrees of muscle contraction and relaxation. The mechanism of contraction is the binding of myosin to actin, forming cross-bridges that generate filament movement (Figure 16.4).

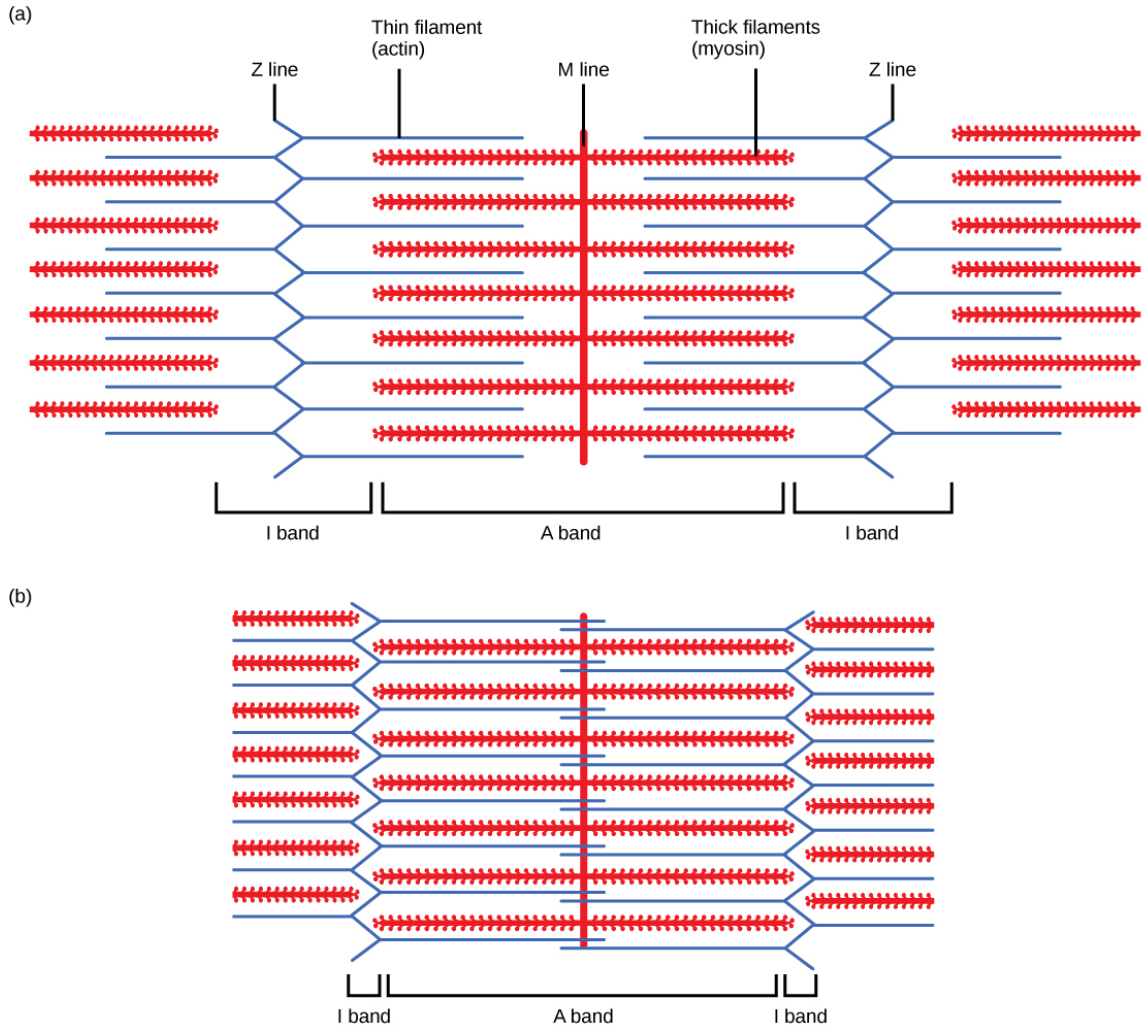

Figure 16.4: When (a) a sarcomere (b) contracts, the Z lines move closer together and the I band gets smaller. The A band stays the same width and, at full contraction, the thin filaments overlap.

When a sarcomere shortens, some regions shorten whereas others stay the same length. A sarcomere is defined as the distance between two consecutive Z lines; when a muscle contracts, the distance between the Z lines is reduced. Thin filaments are pulled by the thick filaments toward the center of the sarcomere until the Z lines approach the thick filaments. The zone of overlap, in which thin filaments and thick filaments occupy the same area, increases as the thin filaments move inward.

16.1.3 ATP and Muscle Contraction

The motion of muscle shortening occurs as myosin heads bind to actin and pull the actin inwards. This action requires energy, which is provided by ATP. Myosin binds to actin at a binding site on the actin protein. Myosin has another binding site for ATP at which enzymatic activity hydrolyzes ATP to ADP, releasing an

inorganic phosphate molecule and energy.

ATP binding causes myosin to release actin, allowing actin and myosin to detach from each other. After this happens, the newly bound ATP is converted to ADP and inorganic phosphate, P_i. The enzyme at the binding site on myosin is called ATPase. The energy released during ATP hydrolysis changes the angle of the myosin head into a "cocked" position. The myosin head is then in a position for further movement, possessing potential energy, but ADP and P_i are still attached. If actin binding sites are covered and unavailable, the myosin will remain in the high energy configuration with ATP hydrolyzed, but still attached.

If the actin binding sites are uncovered, a cross-bridge will form; that is, the myosin head spans the distance between the actin and myosin molecules. P_i is then released, allowing myosin to expend the stored energy as a conformational change. The myosin head moves toward the M line, pulling the actin along with it. As the actin is pulled, the filaments move approximately 10 nm toward the M line. This movement is called the power stroke, as it is the step at which force is produced. As the actin is pulled toward the M line, the sarcomere shortens and the muscle contracts.

When the myosin head is "cocked," it contains energy and is in a high-energy configuration. This energy is expended as the myosin head moves through the power stroke; at the end of the power stroke, the myosin head is in a low-energy position. After the power stroke, ADP is released; however, the cross-bridge formed is still in place, and actin and myosin are bound together. ATP can then attach to myosin, which allows the cross-bridge cycle to start again and further muscle contraction can occur (Figure 16.5).

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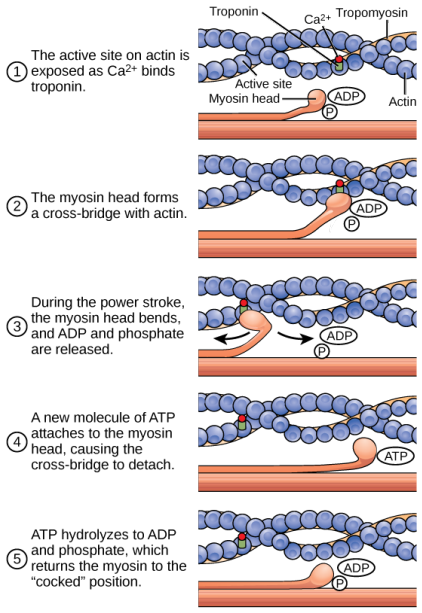

Figure 16.5: The cross-bridge muscle contraction cycle, which is triggered by Ca^{2+} binding to the actin active site, is shown. With each contraction cycle, actin moves relative to myosin.

16.1.4 Regulatory Proteins

When a muscle is in a resting state, actin and myosin are separated. To keep actin from binding to the active site on myosin, regulatory proteins block the molecular binding sites. **Tropomyosin** blocks myosin binding sites on actin molecules, preventing cross-bridge formation and preventing contraction in a muscle

without nervous input. **Troponin** binds to tropomyosin and helps to position it on the actin molecule; it also binds calcium ions.

To enable a muscle contraction, tropomyosin must change conformation, uncovering the myosin-binding site on an actin molecule and allowing cross-bridge formation. This can only happen in the presence of calcium, which is kept at extremely low concentrations in the sarcoplasm. If present, calcium ions bind to troponin, causing conformational changes in troponin that allow tropomyosin to move away from the myosin binding sites on actin. Once the tropomyosin is removed, a cross-bridge can form between actin and myosin, triggering contraction. Cross-bridge cycling continues until Ca^{2+} ions and ATP are no longer available and tropomyosin again covers the binding sites on actin.

16.1.5 Excitation–Contraction Coupling

Excitation–contraction coupling is the link (transduction) between the action potential generated in the sarcolemma and the start of a muscle contraction. The trigger for calcium release from the sarcoplasmic reticulum into the sarcoplasm is a neural signal. Each skeletal muscle fiber is controlled by a motor neuron, which conducts signals from the brain or spinal cord to the muscle. The area of the sarcolemma on the muscle fiber that interacts with the neuron is called the **motor end plate**. The end of the neuron's axon is called the synaptic terminal, and it does not actually contact the motor end plate. A small space called the synaptic cleft separates the synaptic terminal from the motor end plate. Electrical signals travel along the neuron's axon, which branches through the muscle and connects to individual muscle fibers at a neuromuscular junction.

The ability of cells to communicate electrically requires that the cells expend energy to create an electrical gradient across their cell membranes. This charge gradient is carried by ions, which are differentially distributed across the membrane. Each ion exerts an electrical influence and a concentration influence. Just as milk will eventually mix with coffee without the need to stir, ions also distribute themselves evenly, if they are permitted to do so. In this case, they are not permitted to return to an evenly mixed state.

Transport proteins called sodium-potassium pumps use cellular energy (ATP) to pump two K^+ ions inside the cell and three Na^+ ions outside at the same time. Therefore, a concentration gradient for both ions exists across the plasma membrane. This alone accumulates a small electrical charge, but a big concentration gradient. There is lots of K^+ in the cell and lots of Na^+ outside the cell. Potassium is able to leave the cell through K^+ channels that are open 90% of the time, and it does. However, Na^+ channels are rarely open, so Na^+ remains outside the cell. When K^+ leaves the cell, obeying its concentration gradient, that effectively leaves a negative charge behind. So at rest, there is a large concentration gradient for Na^+ to enter the cell, and there is an accumulation of negative charges left behind in the cell. This is the resting membrane potential. Potential in this context means a separation of electrical charge that is capable of doing work. It is measured in volts, just like a battery. However, the transmembrane potential is considerably smaller (0.07 V); therefore, the small value is expressed as millivolts (mV) or 70 mV. Because the inside of a cell is negative compared with the outside, a minus sign signifies the excess of negative charges inside the cell, -70 mV.

If an event changes the permeability of the membrane to Na^+ ions, they will enter the cell. That will change the voltage. This is an electrical event, called an action potential, that can be used as a cellular signal. Communication occurs between nerves and muscles through neurotransmitters. Neuron action potentials cause the release of neurotransmitters from the synaptic terminal into the synaptic cleft, where they can then diffuse across the synaptic cleft and bind to a receptor molecule on the motor end plate. The motor end plate possesses junctional folds—folds in the sarcolemma that create a large surface area for the neurotransmitter to bind to receptors. The receptors are actually sodium channels that open to allow the passage of Na^+ into the cell when they receive neurotransmitter signal.

Acetylcholine (ACh) is a neurotransmitter released by motor neurons that binds to receptors in the motor end plate. Neurotransmitter release occurs when an action potential travels down the motor neuron's axon, resulting in altered permeability of the synaptic terminal membrane and an influx of calcium. The Ca^{2+} ions allow synaptic vesicles to move to and bind with the presynaptic membrane (on the neuron), and release neurotransmitter from the vesicles into the synaptic cleft. Once released by the synaptic terminal,

ACh diffuses across the synaptic cleft to the motor end plate, where it binds with ACh receptors. As a neurotransmitter binds, these ion channels open, and Na^+ ions cross the membrane into the muscle cell. This reduces the voltage difference between the inside and outside of the cell, which is called depolarization. As ACh binds at the motor end plate, this depolarization is called an end-plate potential. The depolarization then spreads along the sarcolemma, creating an action potential as sodium channels adjacent to the initial depolarization site sense the change in voltage and open. The action potential moves across the entire cell, creating a wave of depolarization.

ACh is broken down by the enzyme **acetylcholinesterase** (AChE) into acetyl and choline. AChE resides in the synaptic cleft, breaking down ACh so that it does not remain bound to ACh receptors, which would cause unwanted extended muscle contraction (Figure 16.6).

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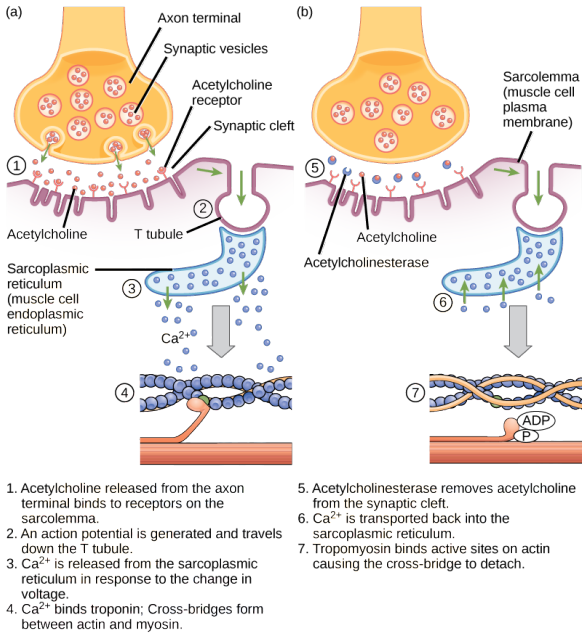

Figure 16.6: This diagram shows excitation-contraction coupling in a skeletal muscle contraction and contains details not included in the text. Therefore, it is essential that you read it carefully and study each step. The sarcoplasmic reticulum (SR) is a specialized endoplasmic reticulum found in muscle cells that stores calcium ions. The action potential within skeletal muscle travels down the T (Transverse) tubules and triggers the release of calcium ions from the SR. The calcium ions bind with troponin/tropomyosin to uncover the myosin binding sites so that contraction can occur.

After depolarization, the membrane returns to its resting state. This is called repolarization, during which voltage-gated sodium channels close. Potassium channels continue at 90% conductance. Because the plasma membrane sodium–potassium ATPase always transports ions, the resting state (negatively charged inside relative to the outside) is restored. The period immediately following the transmission of an impulse in a nerve or muscle, in which a neuron or muscle cell regains its ability to transmit another impulse, is called the refractory period. During the refractory period, the membrane cannot generate another action potential. . The refractory period allows the voltage-sensitive ion channels to return to their resting configurations. The sodium potassium ATPase continually moves Na^+ back out of the cell and K^+ back into the cell, and the K^+ leaks out leaving negative charge behind. Very quickly, the membrane repolarizes, so that it can again be depolarized.

16.1.6 Control of Muscle Tension

Neural control initiates the formation of actin–myosin cross-bridges, leading to the sarcomere shortening involved in muscle contraction. These contractions extend from the muscle fiber through connective tissue to pull on bones, causing skeletal movement. The pull exerted by a muscle is called tension, and the amount of force created by this tension can vary. This enables the same muscles to move very light objects and very heavy objects. In individual muscle fibers, the amount of tension produced depends on the cross-sectional area of the muscle fiber and the frequency of neural stimulation.

The number of cross-bridges formed between actin and myosin determine the amount of tension that a muscle fiber can produce. Cross-bridges can only form where thick and thin filaments overlap, allowing myosin to bind to actin. If more cross-bridges are formed, more myosin will pull on actin, and more tension will be produced.

The ideal length of a sarcomere during production of maximal tension occurs when thick and thin filaments overlap to the greatest degree. If a sarcomere at rest is stretched past an ideal resting length, thick and thin filaments do not overlap to the greatest degree, and fewer cross-bridges can form. This results in fewer myosin heads pulling on actin, and less tension is produced. As a sarcomere is shortened, the zone of overlap is reduced as the thin filaments reach the H zone, which is composed of myosin tails. Because it is myosin heads that form cross-bridges, actin will not bind to myosin in this zone, reducing the tension produced by this myofiber. If the sarcomere is shortened even more, thin filaments begin to overlap with each other—reducing cross-bridge formation even further, and producing even less tension. Conversely, if the sarcomere is stretched to the point at which thick and thin filaments do not overlap at all, no cross-bridges are formed and no tension is produced. This amount of stretching does not usually occur because accessory proteins, internal sensory nerves, and connective tissue oppose extreme stretching.

The primary variable determining force production is the number of myofibers within the muscle that receive an action potential from the neuron that controls that fiber. When using the biceps to pick up a pencil, the motor cortex of the brain only signals a few neurons of the biceps, and only a few myofibers respond. In vertebrates, each myofiber responds fully if stimulated. When picking up a piano, the motor cortex signals a majority of the neurons in the biceps and most myofibers participate. This is close to the maximum force the muscle can produce. As mentioned above, increasing the frequency of action potentials (the number of signals per second) can increase the force a bit more, because the tropomyosin is flooded with calcium. Even at maximum voluntary contraction, not all motor units are active simultaneously; at any given moment, some of them are at rest on a rotational basis.

16.1.7 Section Summary

The body contains three types of muscle tissue: skeletal muscle, cardiac muscle, and smooth muscle. Skeletal muscle tissue is composed of sarcomeres, the functional units of muscle tissue. Muscle contraction occurs when sarcomeres shorten, as thick and thin filaments slide past each other, which is called the sliding filament model of muscle contraction. ATP provides the energy for cross-bridge formation and filament sliding. Regulatory proteins, such as troponin and tropomyosin, control cross-bridge formation. Excitation–contraction coupling transduces the electrical signal of the neuron, via acetylcholine, to an electrical signal on the muscle membrane, which initiates force production. The number of muscle fibers contracting determines how much force the whole muscle produces.

16.1.8 Art Connections

Exercise 16.1.1 ***(Solution on p. 350.)***

Figure 16.5 Which of the following statements about muscle contraction is true?

a. The power stroke occurs when ATP is hydrolyzed to ADP and phosphate.
b. The power stroke occurs when ADP and phosphate dissociate from the myosin head.
c. The power stroke occurs when ADP and phosphate dissociate from the actin active site.

d. The power stroke occurs when Ca^{2+} binds the calcium head.

Exercise 16.1.2 *(Solution on p. 350.)*
Figure 16.6 The deadly nerve gas Sarin irreversibly inhibits acetycholinesterase. What effect would Sarin have on muscle contraction?

16.1.9 Review Questions

Exercise 16.1.3 *(Solution on p. 350.)*
In relaxed muscle, the myosin-binding site on actin is blocked by _____.

a. titin
b. troponin
c. myoglobin
d. tropomyosin

Exercise 16.1.4 *(Solution on p. 350.)*
The cell membrane of a muscle fiber is called a _____.

a. myofibril
b. sarcolemma
c. sarcoplasm
d. myofilament

Exercise 16.1.5 *(Solution on p. 350.)*
The muscle relaxes if no new nerve signal arrives. However the neurotransmitter from the previous stimulation is still present in the synapse. The activity of _____ helps to remove this neurotransmitter.

a. myosin
b. action potential
c. tropomyosin
d. acetylcholinesterase

16.1.10 Free Response

Exercise 16.1.6 *(Solution on p. 350.)*
How would muscle contractions be affected if ATP was completely depleted in a muscle fiber?

Solutions to Exercises in Chapter 16

to Exercise 16.1.1 (p. 348)
Figure 16.5 B
to Exercise 16.1.2 (p. 349)
Figure 16.6 In the presence of Sarin, acetycholine is not removed from the synapse, resulting in continuous stimulation of the muscle plasma membrane. At first, muscle activity is intense and uncontrolled, but the ion gradients dissipate, so electrical signals in the T-tubules are no longer possible. The result is paralysis, leading to death by asphyxiation.
to Exercise 16.1.3 (p. 349)
D
to Exercise 16.1.4 (p. 349)
B
to Exercise 16.1.5 (p. 349)
D
to Exercise 16.1.6 (p. 349)
Because ATP is required for myosin to release from actin, muscles would remain rigidly contracted until more ATP was available for the myosin cross-bridge release. This is why dead vertebrates undergo rigor mortis.

Chapter 17

Nervous System

17.1 Introduction to the Nervous System[1]

Figure 17.1: An athlete's nervous system is hard at work during the planning and execution of a movement as precise as a high jump. Parts of the nervous system are involved in determining how hard to push off and when to turn, as well as controlling the muscles throughout the body that make this complicated movement possible without knocking the bar down—all in just a few seconds. (credit: modification of work by Shane T. McCoy, U.S. Navy)

When you're reading this book, your nervous system is performing several functions simultaneously. The visual system is processing what is seen on the page; the motor system controls the turn of the pages (or click of the mouse); the prefrontal cortex maintains attention. Even fundamental functions, like breathing

[1] This content is available online at <http://cnx.org/content/m58085/1.1/>.

and regulation of body temperature, are controlled by the nervous system. A nervous system is an organism's control center: it processes sensory information from outside (and inside) the body and controls all behaviors—from eating to sleeping to finding a mate.

17.2 Neurons and Glial Cells[2]

The nervous system is made up of **neurons**, specialized cells that can receive and transmit chemical or electrical signals, and **glia**, cells that provide support functions for the neurons by playing an information processing role that is complementary to neurons. A neuron can be compared to an electrical wire—it transmits a signal from one place to another. Glia can be compared to the workers at the electric company who make sure wires go to the right places, maintain the wires, and take down wires that are broken. Although glia have been compared to workers, recent evidence suggests that also usurp some of the signaling functions of neurons.

There is great diversity in the types of neurons and glia that are present in different parts of the nervous system. There are four major types of neurons, and they share several important cellular components.

17.2.1 Neurons

The nervous system of the common laboratory fly, *Drosophila melanogaster*, contains around 100,000 neurons, the same number as a lobster. This number compares to 75 million in the mouse and 300 million in the octopus. A human brain contains around 86 billion neurons. Despite these very different numbers, the nervous systems of these animals control many of the same behaviors—from basic reflexes to more complicated behaviors like finding food and courting mates. The ability of neurons to communicate with each other as well as with other types of cells underlies all of these behaviors.

Most neurons share the same cellular components. But neurons are also highly specialized—different types of neurons have different sizes and shapes that relate to their functional roles.

17.2.1.1 Parts of a Neuron

Like other cells, each neuron has a cell body that contains a nucleus, smooth and rough endoplasmic reticulum, Golgi apparatus, mitochondria, and other cellular components. Neurons also contain unique structures, illustrated in Figure 17.2 for receiving and sending the electrical signals that make neuronal communication possible. **Dendrites** are tree-like structures that extend away from the cell body to receive messages from other neurons at specialized junctions called **synapses**. Although some neurons do not have any dendrites, some types of neurons have multiple dendrites. Dendrites can have small protrusions called dendritic spines, which further increase surface area for possible synaptic connections.

Once a signal is received by the dendrite, it then travels passively to the cell body. The cell body contains a specialized structure, the **axon hillock** that integrates signals from multiple synapses and serves as a junction between the cell body and an **axon**. An axon is a tube-like structure that propagates the integrated signal to specialized endings called **axon terminals**. These terminals in turn synapse on other neurons, muscle, or target organs. Chemicals released at axon terminals allow signals to be communicated to these other cells. Neurons usually have one or two axons, but some neurons, like amacrine cells in the retina, do not contain any axons. Some axons are covered with **myelin**, which acts as an insulator to minimize dissipation of the electrical signal as it travels down the axon, greatly increasing the speed on conduction. This insulation is important as the axon from a human motor neuron can be as long as a meter—from the base of the spine to the toes. The myelin sheath is not actually part of the neuron. Myelin is produced by glial cells. Along the axon there are periodic gaps in the myelin sheath. These gaps are called **nodes of Ranvier** and are sites where the signal is "recharged" as it travels along the axon.

It is important to note that a single neuron does not act alone—neuronal communication depends on the connections that neurons make with one another (as well as with other cells, like muscle cells). Dendrites

[2]This content is available online at <http://cnx.org/content/m58086/1.3/>.

from a single neuron may receive synaptic contact from many other neurons. For example, dendrites from a Purkinje cell in the cerebellum are thought to receive contact from as many as 200,000 other neurons.

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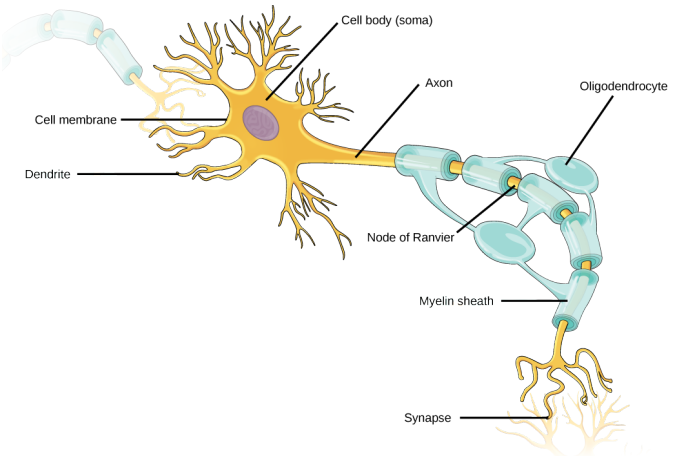

Figure 17.2: Neurons contain organelles common to many other cells, such as a nucleus and mitochondria. They also have more specialized structures, including dendrites and axons.

17.2.1.2 Types of Neurons

There are different types of neurons, and the functional role of a given neuron is intimately dependent on its structure. There is an amazing diversity of neuron shapes and sizes found in different parts of the nervous system (and across species), as illustrated by the neurons shown in Figure 17.3.

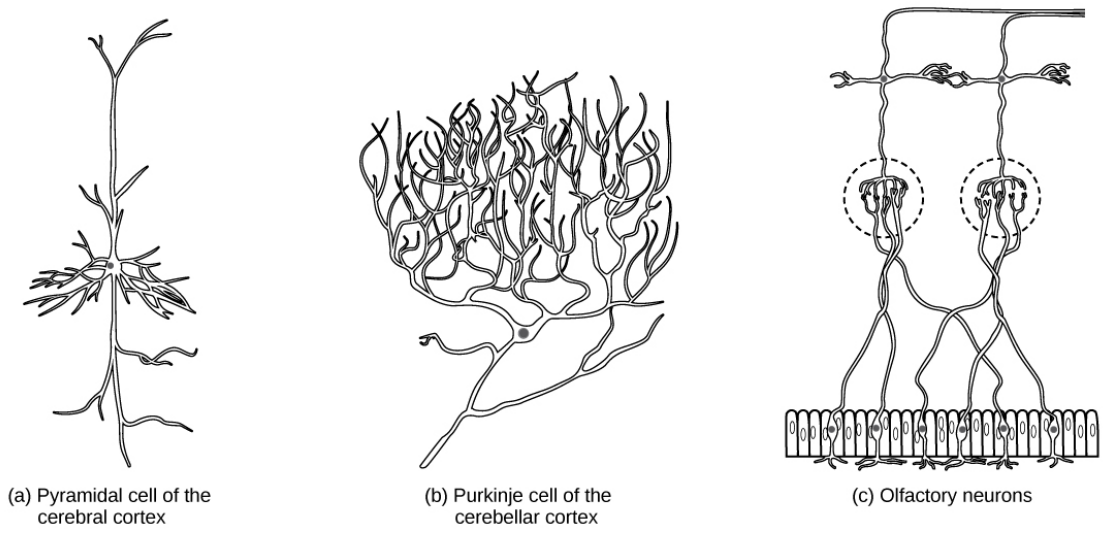

Figure 17.3: There is great diversity in the size and shape of neurons throughout the nervous system. Examples include (a) a pyramidal cell from the cerebral cortex, (b) a Purkinje cell from the cerebellar cortex, and (c) olfactory cells from the olfactory epithelium and olfactory bulb.

Multipolar neurons are the most common type of neuron. Each multipolar neuron contains one axon and multiple dendrites. Multipolar neurons can be found in the central nervous system (brain and spinal cord). An example of a multipolar neuron is a Purkinje cell in the cerebellum, which has many branching dendrites but only one axon.

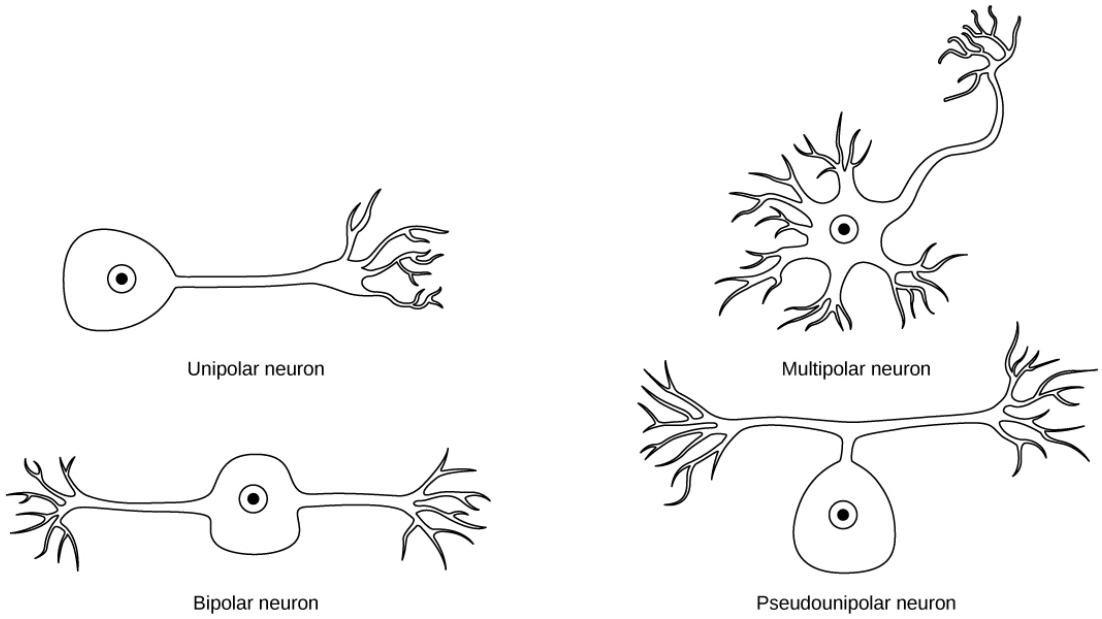

Figure 17.4: Neurons are broadly divided into four main types based on the number and placement of axons: (1) unipolar, (2) bipolar, (3) multipolar, and (4) pseudounipolar.

: **Neurogenesis**

At one time, scientists believed that people were born with all the neurons they would ever have. Research performed during the last few decades indicates that neurogenesis, the birth of new neurons, continues into adulthood. Neurogenesis was first discovered in songbirds that produce new neurons while learning songs. For mammals, new neurons also play an important role in learning: about 1000 new neurons develop in the hippocampus (a brain structure involved in learning and memory) each day. While most of the new neurons will die, researchers found that an increase in the number of surviving new neurons in the hippocampus correlated with how well rats learned a new task. Interestingly, both exercise and some antidepressant medications also promote neurogenesis in the hippocampus. Stress has the opposite effect. While neurogenesis is quite limited compared to regeneration in other tissues, research in this area may lead to new treatments for disorders such as Alzheimer's, stroke, and epilepsy.

How do scientists identify new neurons? A researcher can inject a compound called bromodeoxyuridine (BrdU) into the brain of an animal. While all cells will be exposed to BrdU, BrdU will only be incorporated into the DNA of newly generated cells that are in S phase. A technique called immunohistochemistry can be used to attach a fluorescent label to the incorporated BrdU, and a researcher can use fluorescent microscopy to visualize the presence of BrdU, and thus new neurons, in brain tissue. Figure 17.5 is a micrograph which shows fluorescently labeled neurons in the hippocampus of a rat.

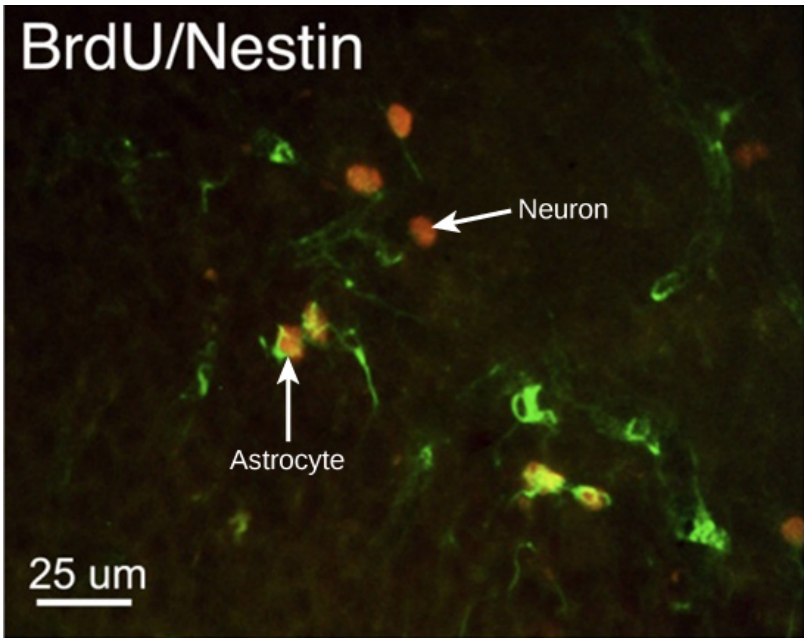

Figure 17.5: This micrograph shows fluorescently labeled new neurons in a rat hippocampus. Cells that are actively dividing have bromodoxyuridine (BrdU) incorporated into their DNA and are labeled in red. Cells that express glial fibrillary acidic protein (GFAP) are labeled in green. Astrocytes, but not neurons, express GFAP. Thus, cells that are labeled both red and green are actively dividing astrocytes, whereas cells labeled red only are actively dividing neurons. (credit: modification of work by Dr. Maryam Faiz, et. al., University of Barcelona; scale-bar data from Matt Russell)

17.2.2 Glia

While glia are often thought of as the supporting cast of the nervous system, the number of glial cells in the brain actually outnumbers the number of neurons by a factor of ten. Neurons would be unable to function without the vital roles that are fulfilled by these glial cells. Glia guide developing neurons to their destinations, buffer ions and chemicals that would otherwise harm neurons, and provide myelin sheaths around axons. Scientists have recently discovered that they also play a role in responding to nerve activity and modulating communication between nerve cells. When glia do not function properly, the result can be disastrous—most brain tumors are caused by mutations in glia.

17.2.3 Section Summary

The nervous system is made up of neurons and glia. Neurons are specialized cells that are capable of sending electrical as well as chemical signals. Most neurons contain dendrites, which receive these signals, and axons that send signals to other neurons or tissues. There are four main types of neurons: unipolar, bipolar, multipolar, and pseudounipolar neurons. Glia are non-neuronal cells in the nervous system that support neuronal development and signaling. There are several types of glia that serve different functions.

17.2.4 Review Questions

Exercise 17.2.1 *(Solution on p. 378.)*
Neurons contain _____, which can receive signals from other neurons.

a. axons
b. mitochondria
c. dendrites
d. Golgi bodies

Exercise 17.2.2 *(Solution on p. 378.)*
A(n) _____ neuron has one axon and multiple dendrites.

a. unipolar
b. bipolar
c. multipolar
d. pseudounipolar

17.2.5 Free Response

Exercise 17.2.3 *(Solution on p. 378.)*
How are neurons similar to other cells? How are they unique?

Exercise 17.2.4 *(Solution on p. 378.)*
Multiple sclerosis causes demyelination of axons in the brain and spinal cord. Why is this problematic?

17.3 How Neurons Communicate[3]

All functions performed by the nervous system—from a simple motor reflex to more advanced functions like making a memory or a decision—require neurons to communicate with one another. While humans use words and body language to communicate, neurons use electrical and chemical signals. Just like a person in a committee, one neuron usually receives and synthesizes messages from multiple other neurons before "making the decision" to send the message on to other neurons.

17.3.1 Nerve Impulse Transmission within a Neuron

For the nervous system to function, neurons must be able to send and receive signals. These signals are possible because each neuron has a charged cellular membrane (a voltage difference between the inside and the outside), and the charge of this membrane can change in response to neurotransmitter molecules released from other neurons and environmental stimuli. To understand how neurons communicate, one must first understand the basis of the baseline or 'resting' membrane charge.

[3]This content is available online at <http://cnx.org/content/m58087/1.2/>.

17.3.1.1 Neuronal Charged Membranes

The lipid bilayer membrane that surrounds a neuron is impermeable to charged molecules or ions. To enter or exit the neuron, ions must pass through special proteins called ion channels that span the membrane. Ion channels have different configurations: open, closed, and inactive, as illustrated in Figure 17.6. Some ion channels need to be activated in order to open and allow ions to pass into or out of the cell. These ion channels are sensitive to the environment and can change their shape accordingly. Ion channels that change their structure in response to voltage changes are called voltage-gated ion channels. Voltage-gated ion channels regulate the relative concentrations of different ions inside and outside the cell. The difference in total charge between the inside and outside of the cell is called the **membrane potential**.

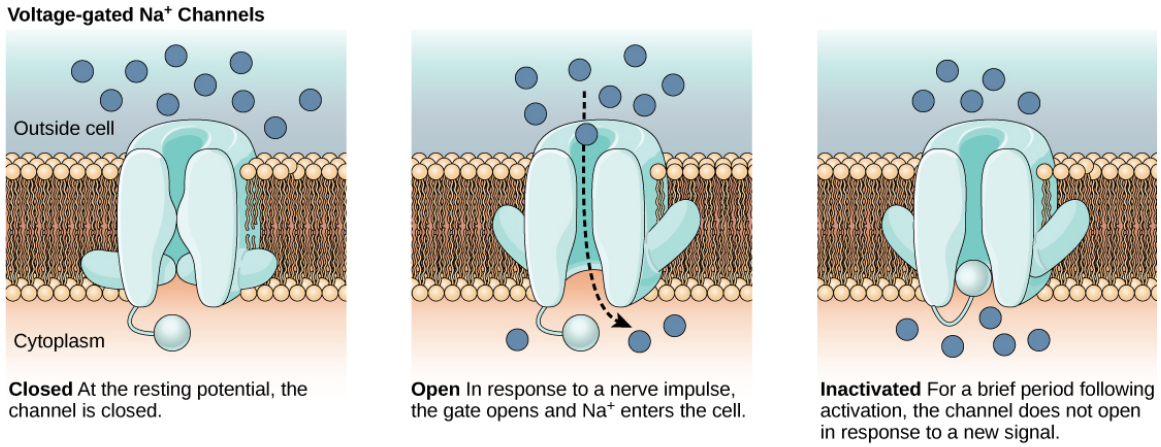

Figure 17.6: Voltage-gated ion channels open in response to changes in membrane voltage. After activation, they become inactivated for a brief period and will no longer open in response to a signal.

17.3.1.2 Resting Membrane Potential

A neuron at rest is negatively charged: the inside of a cell is approximately 70 millivolts more negative than the outside (-70 mV, note that this number varies by neuron type and by species). This voltage is called the resting membrane potential; it is caused by differences in the concentrations of ions inside and outside the cell. If the membrane were equally permeable to all ions, each type of ion would flow across the membrane and the system would reach equilibrium. Because ions cannot simply cross the membrane at will, there are different concentrations of several ions inside and outside the cell, as shown in Table 17.1. The difference in the number of positively charged potassium ions (K^+) inside and outside the cell dominates the resting membrane potential (Figure 17.7). When the membrane is at rest, K^+ ions accumulate inside the cell due to a net movement with the concentration gradient. The negative resting membrane potential is created and maintained by increasing the concentration of cations outside the cell (in the extracellular fluid) relative to inside the cell (in the cytoplasm). The negative charge within the cell is created by the cell membrane being more permeable to potassium ion movement than sodium ion movement. In neurons, potassium ions are maintained at high concentrations within the cell while sodium ions are maintained at high concentrations outside of the cell. The cell possesses potassium and sodium leakage channels that allow the two cations to diffuse down their concentration gradient. However, the neurons have far more potassium leakage channels

than sodium leakage channels. Therefore, potassium diffuses out of the cell at a much faster rate than sodium leaks in. Because more cations are leaving the cell than are entering, this causes the interior of the cell to be negatively charged relative to the outside of the cell. The actions of the sodium potassium pump help to maintain the resting potential, once established. Recall that sodium potassium pumps brings two K^+ ions into the cell while removing three Na^+ ions per ATP consumed. As more cations are expelled from the cell than taken in, the inside of the cell remains negatively charged relative to the extracellular fluid. It should be noted that calcium ions (Ca^{+2}) tend to accumulate outside of the cell because they are repelled by negatively-charged proteins within the cytoplasm.

Ion Concentration Inside and Outside Neurons			
Ion	**Extracellular concentration (mM)**	**Intracellular concentration (mM)**	**Ratio outside/inside**
Na^+	145	12	12
K+	4	155	0.026
Cl^-	120	4	30
Organic anions (A−)	—	100	

Table 17.1: The resting membrane potential is a result of different concentrations inside and outside the cell.

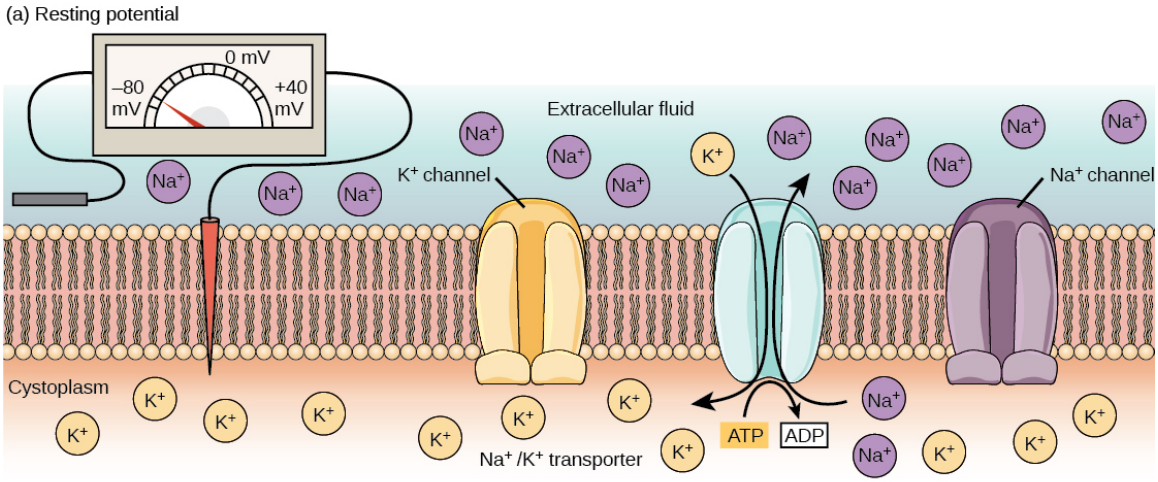

Figure 17.7: Available for free at Connexions <http://cnx.org/content/col11903/1.3> The (a) resting membrane potential is a result of different concentrations of Na^+ and K^+ ions inside and outside the cell. A nerve impulse causes Na^+ to enter the cell, resulting in (b) depolarization. At the peak action potential, K^+ channels open and the cell becomes (c) hyperpolarized.

17.3.1.3 Action Potential

A neuron can receive input from other neurons and, if this input is strong enough, send the signal to downstream neurons. Transmission of a signal between neurons is generally carried by a chemical called a neurotransmitter. Transmission of a signal within a neuron (from dendrite to axon terminal) is carried by a brief reversal of the resting membrane potential called an **action potential**. When neurotransmitter molecules bind to receptors located on a neuron's dendrites, ion channels open. At excitatory synapses, this opening allows positive ions to enter the neuron and results in **depolarization** of the membrane—a decrease in the difference in voltage between the inside and outside of the neuron. A stimulus from a sensory cell or another neuron depolarizes the target neuron to its threshold potential (-55 mV). Na^+ channels in the axon hillock open, allowing positive ions to enter the cell (Figure 17.7 and Figure 17.8). Once the sodium channels open, the neuron completely depolarizes to a membrane potential of about +40 mV. Action potentials are considered an "all-or nothing" event, in that, once the threshold potential is reached, the neuron always completely depolarizes. Once depolarization is complete, the cell must now "reset" its membrane voltage back to the resting potential. To accomplish this, the Na^+ channels close and cannot be opened. This begins the neuron's **refractory period**, in which it cannot produce another action potential because its sodium channels will not open. At the same time, voltage-gated K^+ channels open, allowing K^+ to leave the cell. As K^+ ions leave the cell, the membrane potential once again becomes negative. The diffusion of K^+ out of the cell actually **hyperpolarizes** the cell, in that the membrane potential becomes more negative than the cell's normal resting potential. At this point, the sodium channels will return to their resting state, meaning they are ready to open again if the membrane potential again exceeds the threshold potential. Eventually the extra K^+ ions diffuse out of the cell through the potassium leakage channels, bringing the cell from its hyperpolarized state, back to its resting membrane potential. The sodium-potassium pumps function to restore the original ion concentrations associated with the maintenance of the resting membrane potential.

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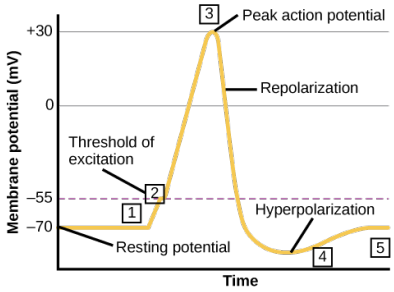

Figure 17.8: The formation of an action potential can be divided into five steps: (1) A stimulus from a sensory cell or another neuron causes the target cell to depolarize toward the threshold potential. (2) If the threshold of excitation is reached, all Na^+ channels open and the membrane depolarizes. (3) At the peak action potential, K^+ channels open and K^+ begins to leave the cell. At the same time, Na^+ channels close. (4) The membrane becomes hyperpolarized as K^+ ions continue to leave the cell. The hyperpolarized membrane is in a refractory period and cannot fire. (5) The K^+ channels close and the Na^+/K^+ transporter restores the resting potential.

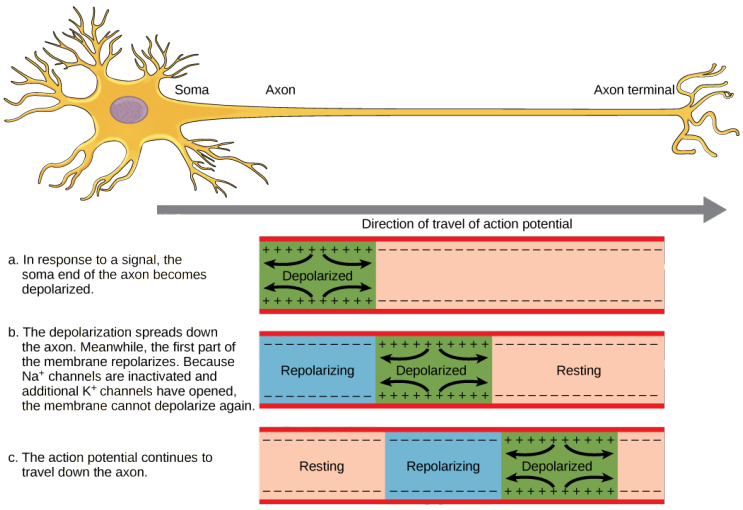

Figure 17.9: The action potential is conducted down the axon as the axon membrane depolarizes, then repolarizes.

17.3.1.4 Myelin and the Propagation of the Action Potential

For an action potential to communicate information to another neuron, it must travel along the axon and reach the axon terminals where it can initiate neurotransmitter release. The speed of conduction of an action potential along an axon is influenced by both the diameter of the axon and the axon's resistance to ion leakage. Myelin acts as an insulator that prevents current from leaving the axon; this increases the speed of action potential conduction. In demyelinating diseases like multiple sclerosis, action potential conduction slows because ions leak from previously insulated axon areas. The nodes of Ranvier, illustrated in Figure 17.10 are gaps in the myelin sheath along the axon. These unmyelinated spaces are about one micrometer long and contain voltage gated Na^+ and K^+ channels. Flow of ions through these channels, particularly the Na^+ channels, regenerates the action potential over and over again along the axon. This 'jumping' of the action potential from one node to the next is called **saltatory conduction**. If nodes of Ranvier were not present along an axon, the action potential would propagate very slowly since Na^+ and K^+ channels would have to continuously regenerate action potentials at every point along the axon instead of at specific points. Nodes of Ranvier also save energy for the neuron since the channels only need to be present at the nodes and not along the entire axon.

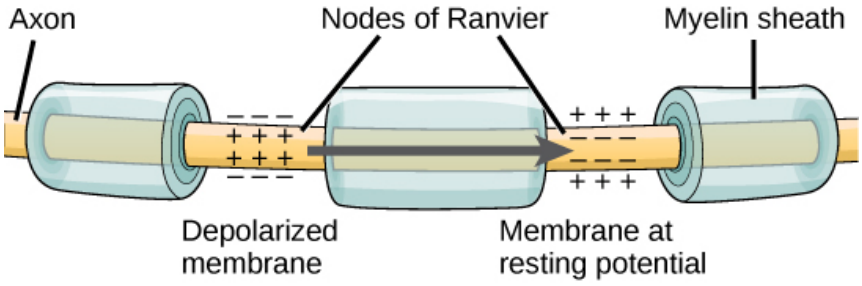

Figure 17.10: Nodes of Ranvier are gaps in myelin coverage along axons. Nodes contain voltage-gated K^+ and Na^+ channels. Action potentials travel down the axon by jumping from one node to the next.

17.3.2 Synaptic Transmission

The synapse or "gap" is the place where information is transmitted from one neuron to another. Synapses usually form between axon terminals and dendritic spines, but this is not universally true. There are also axon-to-axon, dendrite-to-dendrite, and axon-to-cell body synapses. The neuron transmitting the signal is called the presynaptic neuron, and the neuron receiving the signal is called the postsynaptic neuron. Note that these designations are relative to a particular synapse—most neurons are both presynaptic and postsynaptic. There are two types of synapses: chemical and electrical.

17.3.2.1 Chemical Synapse

When an action potential reaches the axon terminal it depolarizes the membrane and opens voltage-gated Na^+ channels. Na^+ ions enter the cell, further depolarizing the presynaptic membrane. This depolarization causes voltage-gated Ca^{2+} channels to open. Calcium ions entering the cell initiate a signaling cascade that causes small membrane-bound vesicles, called **synaptic vesicles**, containing neurotransmitter molecules to fuse with the presynaptic membrane. Synaptic vesicles are shown in Figure 17.11, which is an image from a scanning electron microscope.

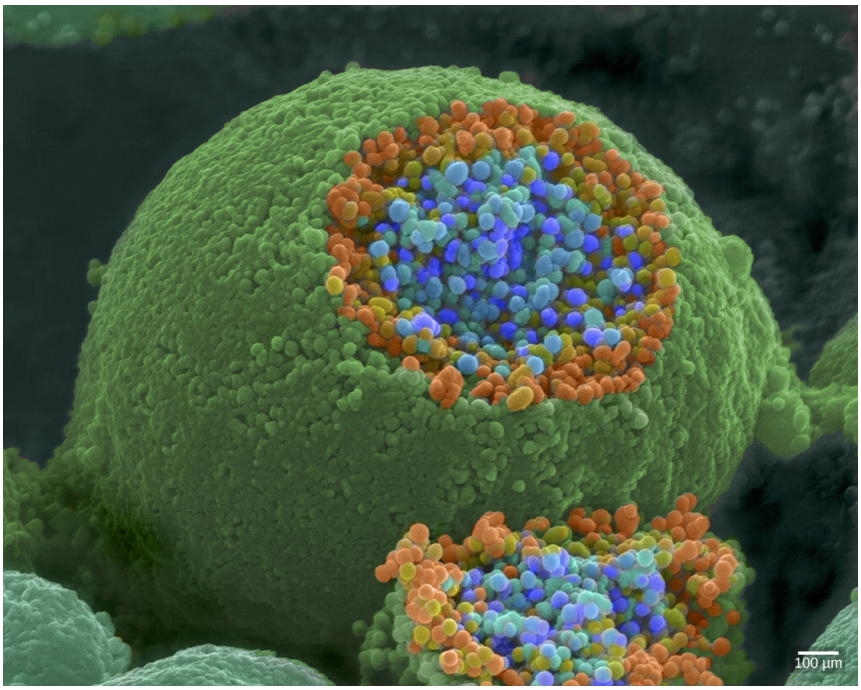

Figure 17.11: This pseudocolored image taken with a scanning electron microscope shows an axon terminal that was broken open to reveal synaptic vesicles (blue and orange) inside the neuron. (credit: modification of work by Tina Carvalho, NIH-NIGMS; scale-bar data from Matt Russell)

Fusion of a vesicle with the presynaptic membrane causes neurotransmitter to be released into the **synaptic cleft**, the extracellular space between the presynaptic and postsynaptic membranes, as illustrated in Figure 17.12. The neurotransmitter diffuses across the synaptic cleft and binds to receptor proteins on the postsynaptic membrane.

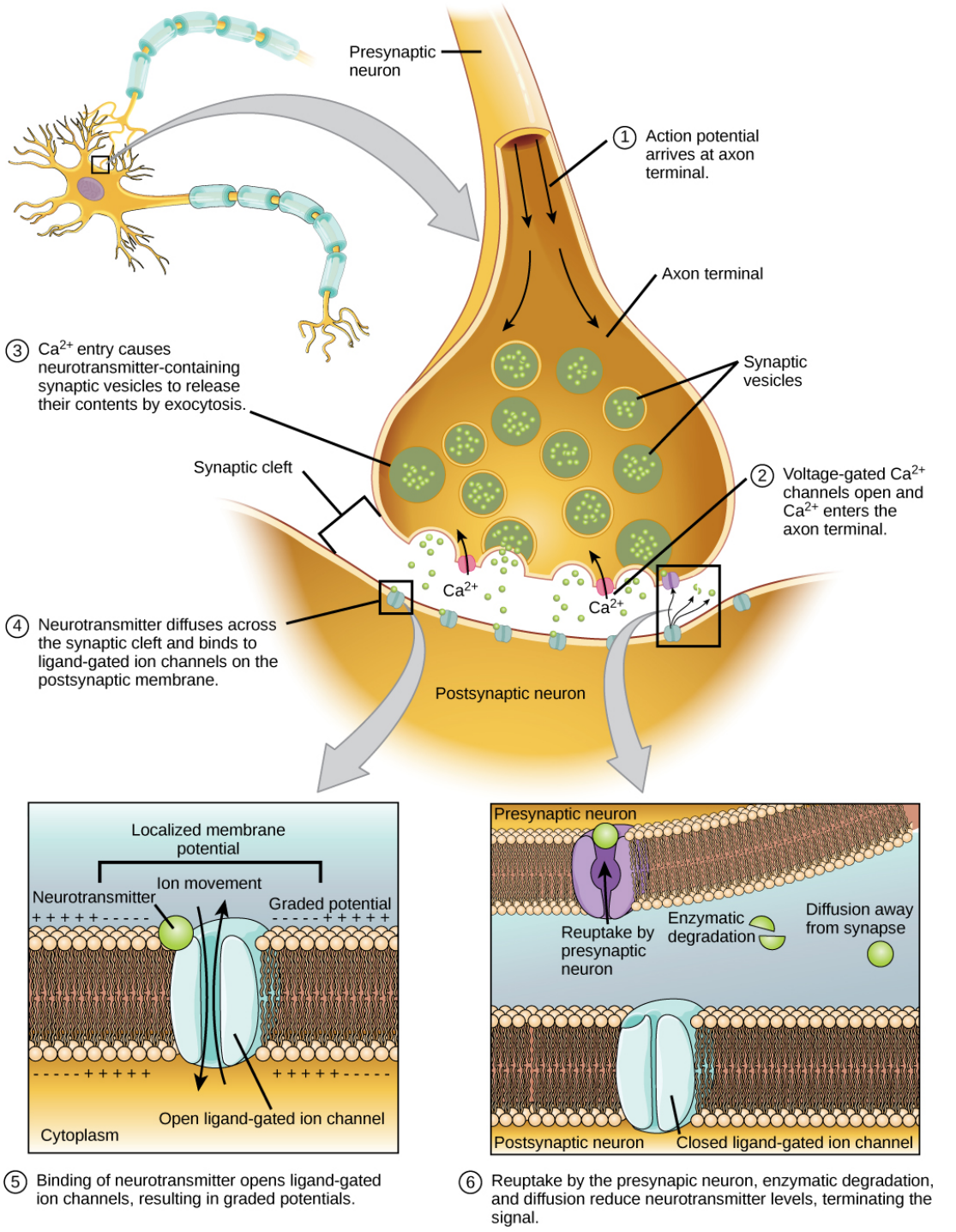

Figure 17.12: Communication at chemical synapses requires release of neurotransmitters. When the presynaptic membrane is depolarized, voltage-gated Ca^{2+} channels open and allow Ca^{2+} to enter the cell. The calcium entry causes synaptic vesicles to fuse with the membrane and release neurotransmitter molecules into the synaptic cleft. The neurotransmitter diffuses across the synaptic cleft and binds to ligand-gated ion channels in the postsynaptic membrane, resulting in a localized depolarization or hyperpolarization of the postsynaptic neuron.

The binding of a specific neurotransmitter causes particular ion channels, in this case chemically-gated channels, on the postsynaptic membrane to open. Neurotransmitters can either have excitatory or inhibitory effects on the postsynaptic membrane, as detailed in Table 17.1. For example, when acetylcholine is released at the synapse between a nerve and muscle (called the neuromuscular junction) by a presynaptic neuron, it causes postsynaptic Na^+ channels to open. Na^+ enters the postsynaptic cell and causes the postsynaptic membrane to depolarize. This depolarization is called an **excitatory postsynaptic potential (EPSP)** and makes the postsynaptic neuron more likely to fire an action potential. Release of neurotransmitter at inhibitory synapses causes **inhibitory postsynaptic potentials (IPSPs)**, a hyperpolarization of the presynaptic membrane. For example, when the neurotransmitter GABA (gamma-aminobutyric acid) is released from a presynaptic neuron, it binds to and opens Cl^- channels. Cl^- ions enter the cell and hyperpolarizes the membrane, making the neuron less likely to fire an action potential.

Once neurotransmission has occurred, the neurotransmitter must be removed from the synaptic cleft so the postsynaptic membrane can "reset" and be ready to receive another signal. This can be accomplished in three ways: the neurotransmitter can diffuse away from the synaptic cleft, it can be degraded by enzymes in the synaptic cleft, or it can be recycled (sometimes called reuptake) by the presynaptic neuron. Several drugs act at this step of neurotransmission. For example, some drugs that are given to Alzheimer's patients work by inhibiting acetylcholinesterase, the enzyme that degrades acetylcholine. This inhibition of the enzyme essentially increases neurotransmission at synapses that release acetylcholine. Once released, the acetylcholine stays in the cleft and can continually bind and unbind to postsynaptic receptors.

Neurotransmitter Function and Location		
Neurotransmitter	**Example**	**Location**
Acetylcholine	—	CNS and/or PNS
Biogenic amine	Dopamine, serotonin, norepinephrine	CNS and/or PNS
Amino acid	Glycine, glutamate, aspartate, gamma aminobutyric acid	CNS
Neuropeptide	Substance P, endorphins	CNS and/or PNS

Table 17.2

17.3.3 Signal Summation

Sometimes a single EPSP is strong enough to induce an action potential in the postsynaptic neuron, but often multiple presynaptic inputs must create EPSPs around the same time for the postsynaptic neuron to be sufficiently depolarized to fire an action potential. This process is called **summation** and occurs at the axon hillock, as illustrated in Figure 17.13. Additionally, one neuron often has inputs from many presynaptic neurons—some excitatory and some inhibitory—so IPSPs can cancel out EPSPs and vice versa. It is the net change in postsynaptic membrane voltage that determines whether the postsynaptic cell has reached its threshold of excitation needed to fire an action potential. Together, synaptic summation and the threshold for excitation act as a filter so that random "noise" in the system is not transmitted as important information.

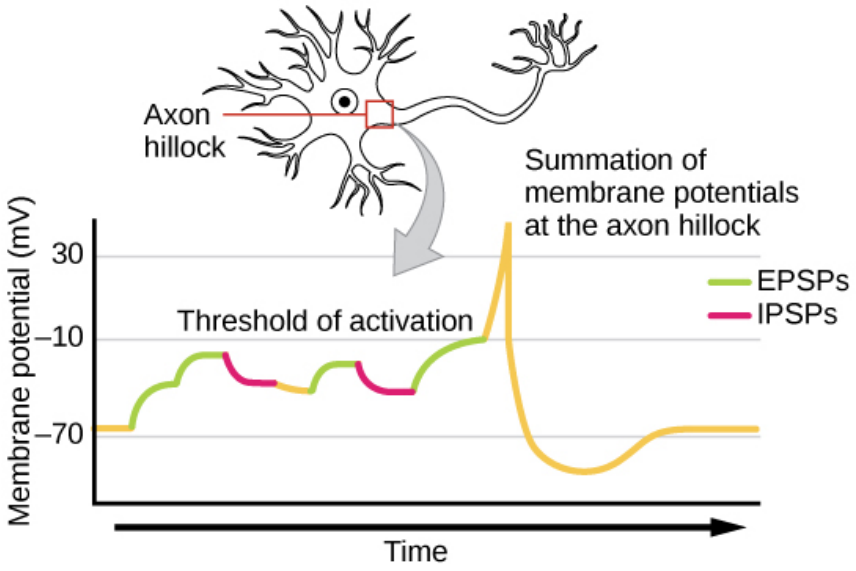

Figure 17.13: A single neuron can receive both excitatory and inhibitory inputs from multiple neurons, resulting in local membrane depolarization (EPSP input) and hyperpolarization (IPSP input). All these inputs are added together at the axon hillock. If the EPSPs are strong enough to overcome the IPSPs and reach the threshold of excitation, the neuron will fire.

17.3.4 Section Summary

Neurons have charged membranes because there are different concentrations of ions inside and outside of the cell. Voltage-gated ion channels control the movement of ions into and out of a neuron. When a neuronal membrane is depolarized to at least the threshold of excitation, an action potential is fired. The action potential is then propagated along an axon to the axon terminals. In a chemical synapse, the action potential causes release of neurotransmitter molecules into the synaptic cleft. Through binding to postsynaptic receptors, the neurotransmitter can cause excitatory or inhibitory postsynaptic potentials by depolarizing or hyperpolarizing, respectively, the postsynaptic membrane.

17.3.5 Art Connections

Exercise 17.3.1 *(Solution on p. 378.)*

Figure 17.8 Potassium channel blockers, such as amiodarone and procainamide, which are used to treat abnormal electrical activity in the heart, called cardiac dysrhythmia, impede the movement of K+ through voltage-gated K+ channels. Which part of the action potential would you expect potassium channels to affect?

17.3.6 Review Questions

Exercise 17.3.2 *(Solution on p. 378.)*

For a neuron to fire an action potential, its membrane must reach _ _ _ _ _ _ _ _.

a. hyperpolarization
b. the threshold of excitation
c. the refractory period
d. inhibitory postsynaptic potential

Exercise 17.3.3 *(Solution on p. 378.)*
After an action potential, the opening of additional voltage-gated _____ channels and the inactivation of sodium channels, cause the membrane to return to its resting membrane potential.

a. sodium
b. potassium
c. calcium
d. chloride

17.3.7 Free Response

Exercise 17.3.4 *(Solution on p. 378.)*
How does myelin aid propagation of an action potential along an axon? How do the nodes of Ranvier help this process?

Exercise 17.3.5 *(Solution on p. 378.)*
What are the main steps in chemical neurotransmission?

17.4 The Central and Peripheral Nervous Systems[4]

17.4.1 The Central Nervous System

The **central nervous system (CNS)** is made up of the brain and spinal cord and is covered with three layers of protective coverings called **meninges** ("meninges" is derived from the Greek and means "membranes") (Figure 17.14). The outermost layer is the dura mater, the middle layer is the web-like arachnoid mater, and the inner layer is the pia mater, which directly contacts and covers the brain and spinal cord. The space between the arachnoid and pia maters is filled with **cerebrospinal fluid (CSF)**. The brain floats in CSF, which acts as a cushion and shock absorber.

[4] This content is available online at <http://cnx.org/content/m58090/1.2/>.

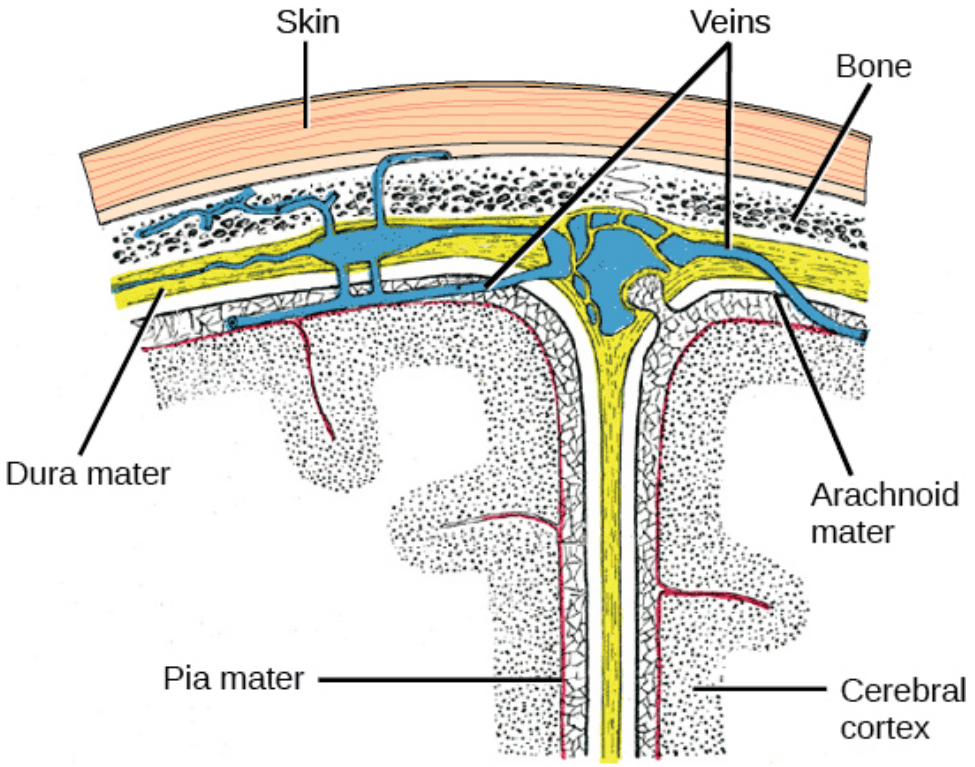

Figure 17.14: The cerebral cortex is covered by three layers of meninges: the dura, arachnoid, and pia maters. (credit: modification of work by Gray's Anatomy)

17.4.2 The Brain

The brain is the part of the central nervous system that is contained in the cranial cavity of the skull. It includes the cerebral cortex, limbic system, basal ganglia, thalamus, hypothalamus, cerebellum, brainstem, and retinas. The outermost part of the brain is a thick piece of nervous system tissue called the **cerebral cortex**. The cerebral cortex, limbic system, and basal ganglia make up the two cerebral hemispheres. A thick fiber bundle called the **corpus callosum** (corpus = "body"; callosum = "tough") connects the two hemispheres. Although there are some brain functions that are localized more to one hemisphere than the other, the functions of the two hemispheres are largely redundant. In fact, sometimes (very rarely) an entire hemisphere is removed to treat severe epilepsy. While patients do suffer some deficits following the surgery, they can have surprisingly few problems, especially when the surgery is performed on children who have very immature nervous systems.

In other surgeries to treat severe epilepsy, the corpus callosum is cut instead of removing an entire hemisphere. This causes a condition called split-brain, which gives insights into unique functions of the two hemispheres. For example, when an object is presented to patients' left visual field, they may be unable to verbally name the object (and may claim to not have seen an object at all). This is because the visual input from the left visual field crosses and enters the right hemisphere and cannot then signal to the speech center, which generally is found in the left side of the brain. Remarkably, if a split-brain patient is asked to pick up

a specific object out of a group of objects with the left hand, the patient will be able to do so but will still be unable to verbally identify it.

Each hemisphere contains regions called lobes that are involved in different functions. Each hemisphere of the mammalian cerebral cortex can be broken down into four functionally and spatially defined lobes: frontal, parietal, temporal, and occipital (Figure 17.15).

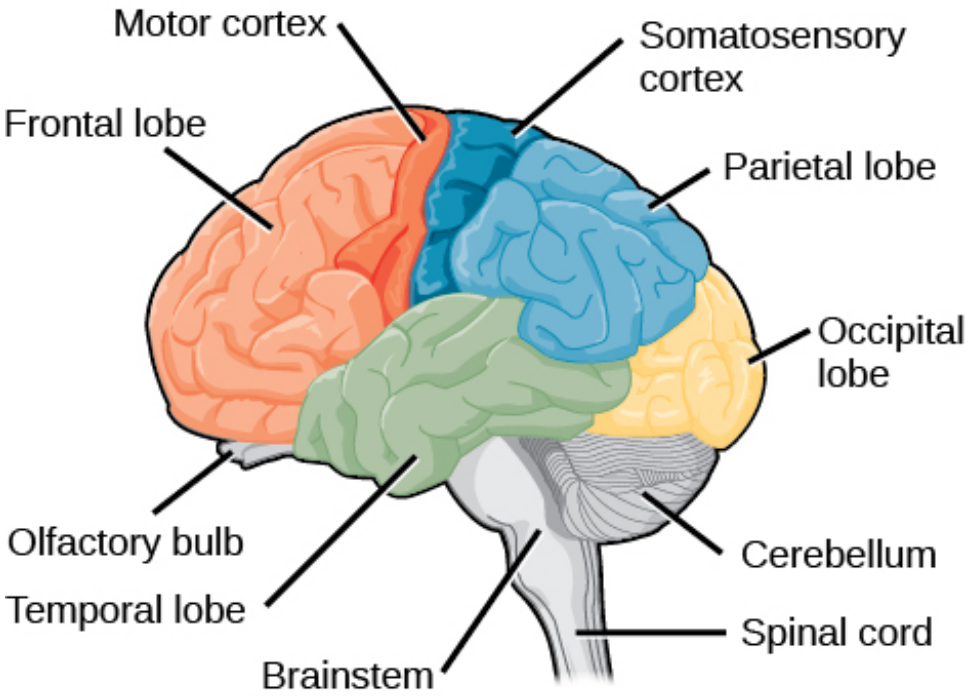

Figure 17.15: The human cerebral cortex includes the frontal, parietal, temporal, and occipital lobes.

The **frontal lobe** is located at the front of the brain, over the eyes. This lobe contains the olfactory bulb, which processes smells. The frontal lobe also contains the motor cortex, which is important for planning and implementing movement. Areas within the motor cortex map to different muscle groups. Neurons in the frontal lobe also control cognitive functions like maintaining attention, speech, and decision-making. Studies of humans who have damaged their frontal lobes show that parts of this area are involved in personality, socialization, and assessing risk. The **parietal lobe** is located at the top of the brain. Neurons in the parietal lobe are involved in speech and also reading. Two of the parietal lobe's main functions are processing somatosensation—touch sensations like pressure, pain, heat, cold—and processing proprioception—the sense of how parts of the body are oriented in space. The parietal lobe contains a somatosensory map of the body similar to the motor cortex. The **occipital lobe** is located at the back of the brain. It is primarily involved in vision—seeing, recognizing, and identifying the visual world. The **temporal lobe** is located at the base of the brain and is primarily involved in processing and interpreting sounds. It also contains the **hippocampus** (named from the Greek for "seahorse," which it resembles in shape) a structure that processes memory formation. The role of the hippocampus in memory was partially determined by studying one famous epileptic patient, HM, who had both sides of his hippocampus removed in an attempt to cure his epilepsy. His seizures went away, but he could no longer form new memories (although he could remember

some facts from before his surgery and could learn new motor tasks).

Interconnected brain areas called the **basal ganglia** play important roles in movement control and posture. The basal ganglia also regulate motivation.

The **thalamus** acts as a gateway to and from the cortex. Sensory and motor impulses go through it from the brain to the effectors in the peripheral nervous system. It also receives feedback from the cortex. This feedback mechanism can modulate conscious awareness of sensory and motor inputs depending on the attention and arousal state of the animal. The thalamus helps regulate consciousness, arousal, and sleep states.

Below the thalamus is the **hypothalamus**. The hypothalamus controls the endocrine system by sending signals to the pituitary gland. Among other functions, the hypothalamus is the body's thermostat—it makes sure the body temperature is kept at appropriate levels. Neurons within the hypothalamus also regulate circadian rhythms, sometimes called sleep cycles.

The **limbic system** is a connected set of structures that regulates emotion, as well as behaviors related to fear and motivation. It plays a role in memory formation and includes parts of the thalamus and hypothalamus as well as the hippocampus. One important structure within the limbic system is a temporal lobe structure called the **amygdala**. The two amygdala (one on each side) are important both for the sensation of fear and for recognizing fearful faces.

The **cerebellum** (cerebellum = "little brain") sits at the base of the brain on top of the brainstem. The cerebellum controls balance and aids in coordinating movement and learning new motor tasks. The cerebellum of birds is large compared to other vertebrates because of the coordination required by flight.

The **brainstem** connects the rest of the brain with the spinal cord and regulates some of the most important and basic functions of the nervous system including breathing, swallowing, digestion, sleeping, walking, and sensory and motor information integration.

17.4.3 Spinal cord

Connecting to the brainstem and extending down the body through the spinal column is the spinal cord. The spinal cord is a thick bundle of nerve tissue that carries information about the body to the brain and from the brain to the body. The spinal cord is contained within the meninges and the bones of the vertebral column but is able to communicate signals to and from the body through its connections with spinal nerves (part of the peripheral nervous system). A cross-section of the spinal cord looks like a white oval containing a gray butterfly-shape (Figure 17.16). Myelinated axons make up the "white matter" and neuron and glia cell bodies (and interneurons) make up the "gray matter." Axons and cell bodies in the dorsal spinal cord convey mostly sensory information from the body to the brain. Axons and cell bodies in the ventral spinal cord primarily transmit signals controlling movement from the brain to the body.

The spinal cord also controls motor reflexes. These reflexes are quick, unconscious movements—like automatically removing a hand from a hot object. Reflexes are so fast because they involve local synaptic connections. For example, the knee reflex that a doctor tests during a routine physical is controlled by a single synapse between a sensory neuron and a motor neuron. While a reflex may only require the involvement of one or two synapses, synapses with interneurons in the spinal column transmit information to the brain to convey what happened (the knee jerked, or the hand was hot).

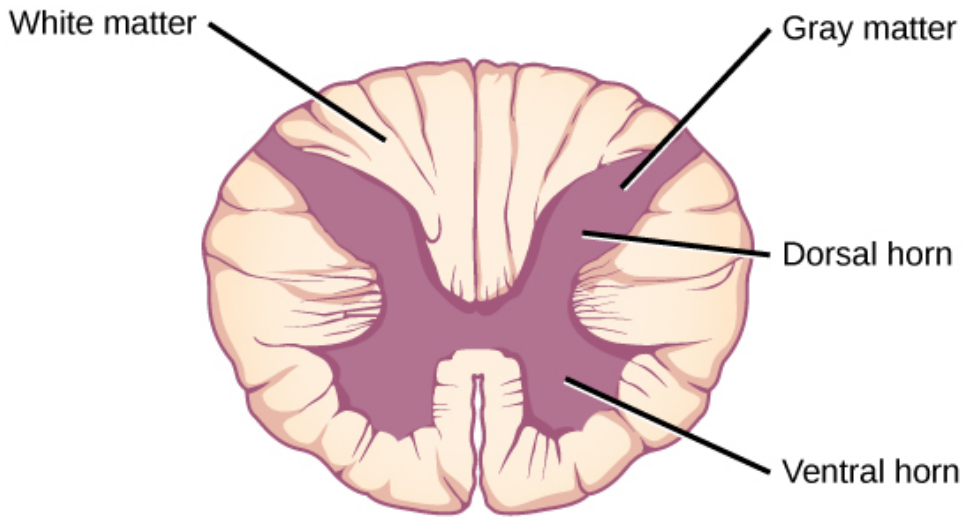

Figure 17.16: A cross-section of the spinal cord shows gray matter (containing cell bodies and interneurons) and white matter (containing myelinated axons).

17.4.4 The Peripheral Nervous System

The **peripheral nervous system (PNS)** is the connection between the central nervous system and the rest of the body. The PNS can be broken down into the **autonomic nervous system**, which controls bodily functions without conscious control, and the **sensory-somatic nervous system**, which transmits sensory information from the skin, muscles, and sensory organs to the CNS and sends motor commands from the CNS to the muscles.

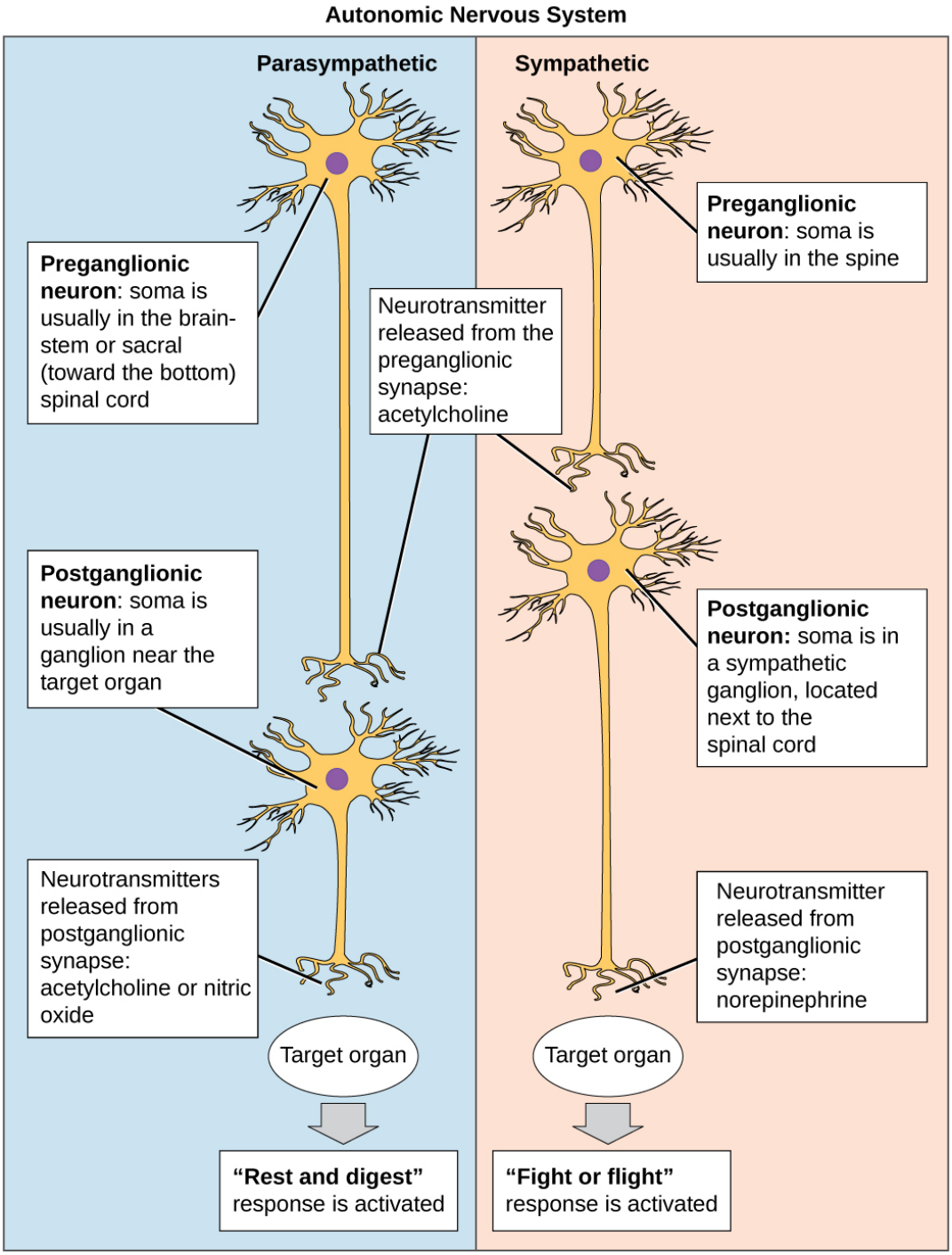

Figure 17.17: In the autonomic nervous system, a preganglionic neuron (originating in the thoracolumbar region of the spinal cord) synapses to a neuron in a ganglion that, in turn, synapses on a target organ. Activation of the sympathetic nervous system causes release of norepinephrine on the target organ. Activation of the parasympathetic nervous system causes release of acetylcholine on the target organ.

The autonomic nervous system serves as the relay between the CNS and the internal organs. It controls the lungs, the heart, smooth muscle, and exocrine and endocrine glands and vicera of the abdominal cavity. The autonomic nervous system controls these organs largely without conscious control; it can continuously monitor the conditions of these different systems and implement changes as needed. Signaling to the target tissue usually involves two synapses: a preganglionic neuron (originating in the CNS) synapses to a neuron in a ganglion that, in turn, synapses on the target organ (Figure 17.17). There are two divisions of the autonomic nervous system that often have opposing effects: the sympathetic nervous system and the parasympathetic nervous system.

The **sympathetic nervous system** is responsible for the immediate responses an animal makes when it encounters a dangerous situation. One way to remember this is to think of the "fight-or-flight" response a person feels when encountering a snake ("snake" and "sympathetic" both begin with "s"). Examples of functions controlled by the sympathetic nervous system include an accelerated heart rate and inhibited digestion. These functions help prepare an organism's body for the physical strain required to escape a potentially dangerous situation or to fend off a predator.

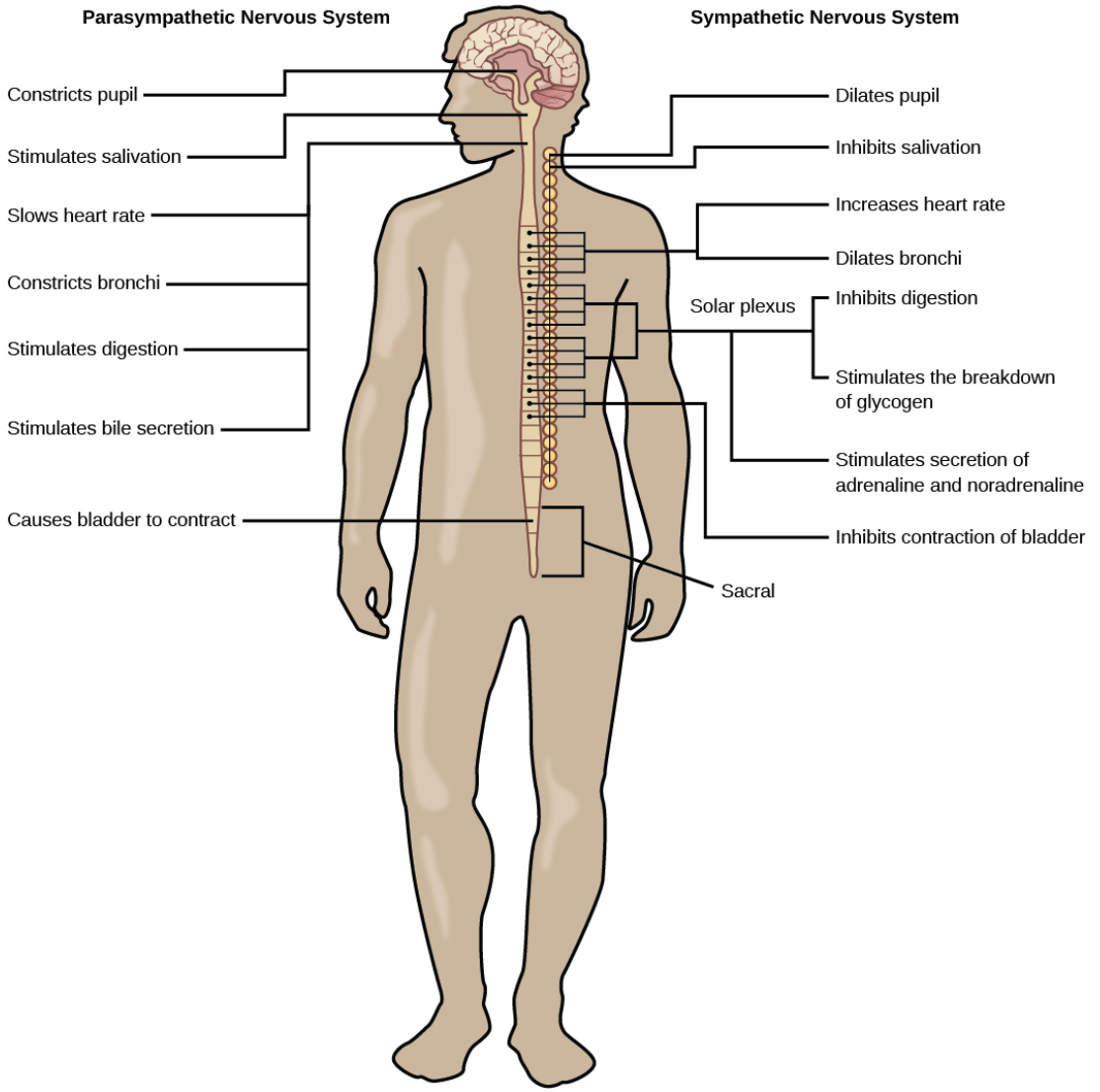

Figure 17.18: The sympathetic and parasympathetic nervous systems often have opposing effects on target organs.

While the sympathetic nervous system is activated in stressful situations, the **parasympathetic nervous system** allows an animal to "rest and digest." One way to remember this is to think that during a restful situation like a picnic, the parasympathetic nervous system is in control ("picnic" and "parasympathetic" both start with "p"). Parasympathetic preganglionic neurons have cell bodies located in the brainstem and in the sacral (toward the bottom) spinal cord (Figure 17.18). The parasympathetic nervous system resets organ function after the sympathetic nervous system is activated including slowing of heart rate, lowered blood pressure, and stimulation of digestion.

The sensory-somatic nervous system is made up of cranial and spinal nerves and contains both sensory

and motor neurons. Sensory neurons transmit sensory information from the skin, skeletal muscle, and sensory organs to the CNS. Motor neurons transmit messages about desired movement from the CNS to the muscles to make them contract. Without its sensory-somatic nervous system, an animal would be unable to process any information about its environment (what it sees, feels, hears, and so on) and could not control motor movements. Unlike the autonomic nervous system, which usually has two synapses between the CNS and the target organ, sensory and motor neurons usually have only one synapse—one ending of the neuron is at the organ and the other directly contacts a CNS neuron.

17.4.5 Section Summary

The vertebrate central nervous system contains the brain and the spinal cord, which are covered and protected by three meninges. The brain contains structurally and functionally defined regions. In mammals, these include the cortex (which can be broken down into four primary functional lobes: frontal, temporal, occipital, and parietal), basal ganglia, thalamus, hypothalamus, limbic system, cerebellum, and brainstem—although structures in some of these designations overlap. While functions may be primarily localized to one structure in the brain, most complex functions, like language and sleep, involve neurons in multiple brain regions. The spinal cord is the information superhighway that connects the brain with the rest of the body through its connections with peripheral nerves. It transmits sensory input and motor output and also controls motor reflexes.

The peripheral nervous system contains both the autonomic and sensory-somatic nervous systems. The autonomic nervous system provides unconscious control over visceral functions and has two divisions: the sympathetic and parasympathetic nervous systems. The sympathetic nervous system is activated in stressful situations to prepare the animal for a "fight-or-flight" response. The parasympathetic nervous system is active during restful periods. The sensory-somatic nervous system is made of cranial and spinal nerves that transmit sensory information from skin and muscle to the CNS and motor commands from the CNS to the muscles.

17.4.6 Review Questions

Exercise 17.4.1 *(Solution on p. 378.)*

The part of the brain that is responsible for coordination during movement is the _____.

a. limbic system
b. thalamus
c. cerebellum
d. parietal lobe

Exercise 17.4.2 *(Solution on p. 378.)*

Which part of the nervous system directly controls the digestive system?

a. parasympathetic nervous system
b. central nervous system
c. spinal cord
d. sensory-somatic nervous system

17.4.7 Free Response

Exercise 17.4.3 *(Solution on p. 378.)*

What are the main functions of the spinal cord?

Exercise 17.4.4 *(Solution on p. 378.)*

What are the main differences between the sympathetic and parasympathetic branches of the autonomic nervous system?

Exercise 17.4.5 *(Solution on p. 378.)*

What are the main functions of the sensory-somatic nervous system?

Solutions to Exercises in Chapter 17

to Exercise 17.2.1 (p. 357)
C
to Exercise 17.2.2 (p. 357)
C
to Exercise 17.2.3 (p. 357)
Neurons contain organelles common to all cells, such as a nucleus and mitochondria. They are unique because they contain dendrites, which can receive signals from other neurons, and axons that can send these signals to other cells.
to Exercise 17.2.4 (p. 357)
Myelin provides insulation for signals traveling along axons. Without myelin, signal transmission can slow down and degrade over time. This would slow down neuronal communication across the nervous system and affect all downstream functions.
to Exercise 17.3.1 (p. 367)
Figure 17.8 Potassium channel blockers slow the repolarization phase, but have no effect on depolarization.
to Exercise 17.3.2 (p. 367)
B
to Exercise 17.3.3 (p. 368)
B
to Exercise 17.3.4 (p. 368)
Myelin prevents the leak of current from the axon. Nodes of Ranvier allow the action potential to be regenerated at specific points along the axon. They also save energy for the cell since voltage-gated ion channels and sodium-potassium transporters are not needed along myelinated portions of the axon.
to Exercise 17.3.5 (p. 368)
An action potential travels along an axon until it depolarizes the membrane at an axon terminal. Depolarization of the membrane causes voltage-gated Ca^{2+} channels to open and Ca^{2+} to enter the cell. The intracellular calcium influx causes synaptic vesicles containing neurotransmitter to fuse with the presynaptic membrane. The neurotransmitter diffuses across the synaptic cleft and binds to receptors on the postsynaptic membrane. Depending on the specific neurotransmitter and postsynaptic receptor, this action can cause positive (excitatory postsynaptic potential) or negative (inhibitory postsynaptic potential) ions to enter the cell.
to Exercise 17.4.1 (p. 376)
C
to Exercise 17.4.2 (p. 376)
A
to Exercise 17.4.3 (p. 376)
The spinal cord transmits sensory information from the body to the brain and motor commands from the brain to the body through its connections with peripheral nerves. It also controls motor reflexes.
to Exercise 17.4.4 (p. 376)
The sympathetic nervous system prepares the body for "fight or flight," whereas the parasympathetic nervous system allows the body to "rest and digest." Sympathetic neurons release norepinephrine onto target organs; parasympathetic neurons release acetylcholine. Sympathetic neuron cell bodies are located in sympathetic ganglia. Parasympathetic neuron cell bodies are located in the brainstem and sacral spinal cord. Activation of the sympathetic nervous system increases heart rate and blood pressure and decreases digestion and blood flow to the skin. Activation of the parasympathetic nervous system decreases heart rate and blood pressure and increases digestion and blood flow to the skin.
to Exercise 17.4.5 (p. 377)
The sensory-somatic nervous system transmits sensory information from the skin, muscles, and sensory organs to the CNS. It also sends motor commands from the CNS to the muscles, causing them to contract.

Chapter 18

Special Senses

18.1 Introduction to the Special Senses[1]

Figure 18.1: 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

[1] This content is available online at <http://cnx.org/content/m58112/1.1/>.

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.

18.2 Taste and Smell[2]

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.

18.2.1 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.

18.2.2 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 18.2). 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.

[2]This content is available online at <http://cnx.org/content/m58098/1.1/>.

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.

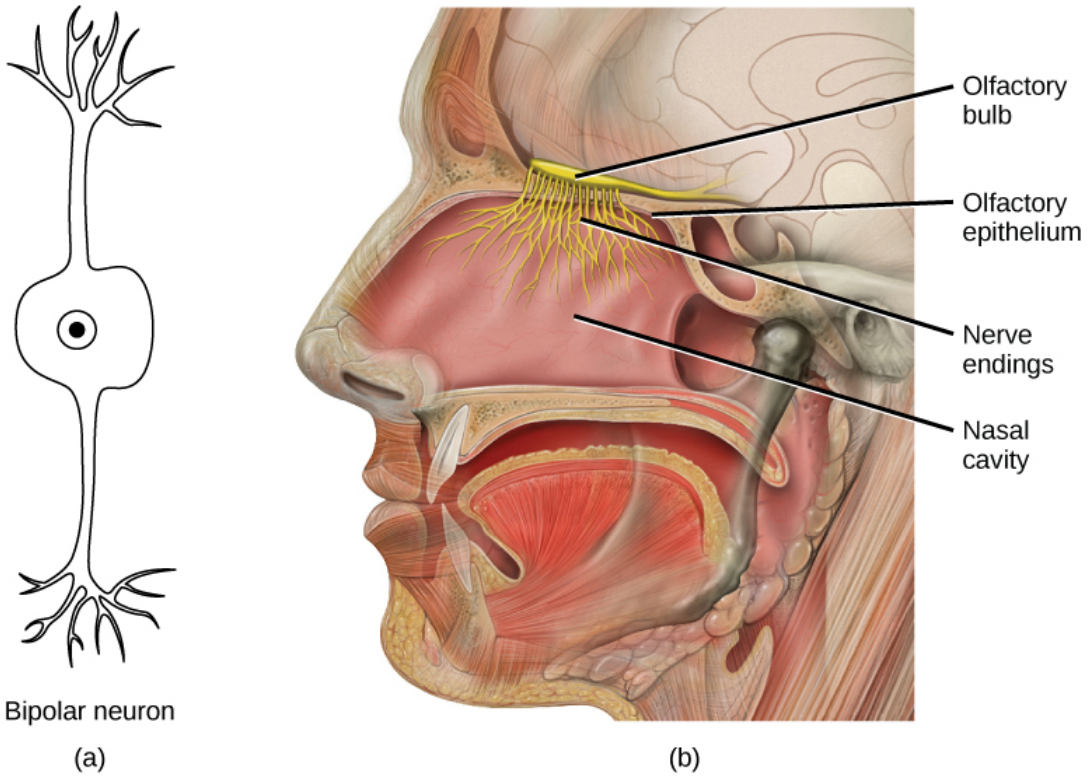

Figure 18.2: In the human olfactory system, (a) bipolar olfactory neurons extend from (b) the olfactory epithelium, where olfactory receptors are located, to the olfactory bulb. (credit: modification of work by Patrick J. Lynch, medical illustrator; C. Carl Jaffe, MD, cardiologist)

: **Pheromones**

A **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 18.3), 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 18.3: 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)

18.2.2.1 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 18.4). 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.

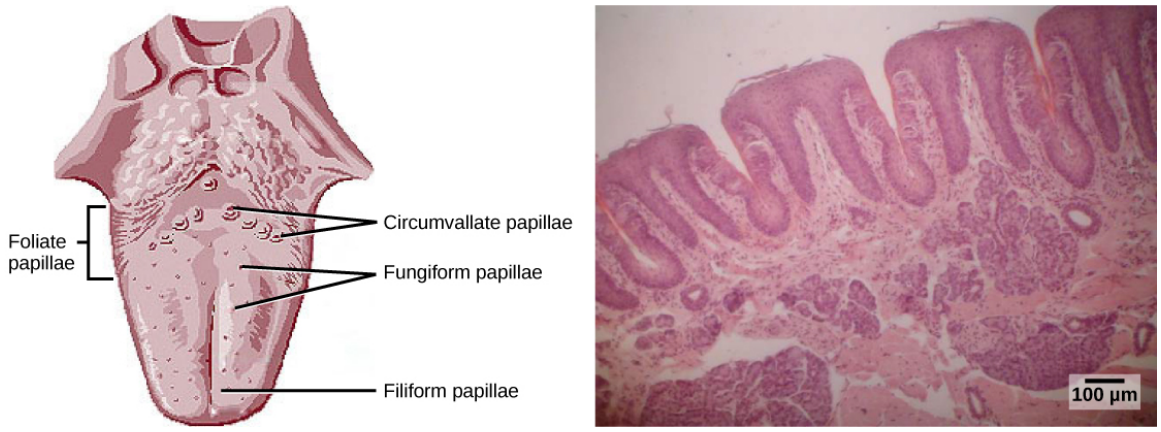

Figure 18.4: (a) Foliate, circumvallate, and fungiform papillae are located on different regions of the tongue. (b) Foliate papillae are prominent protrusions on this light micrograph. (credit a: modification of work by NCI; scale-bar data from Matt Russell)

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 18.4 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 18.5). 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.

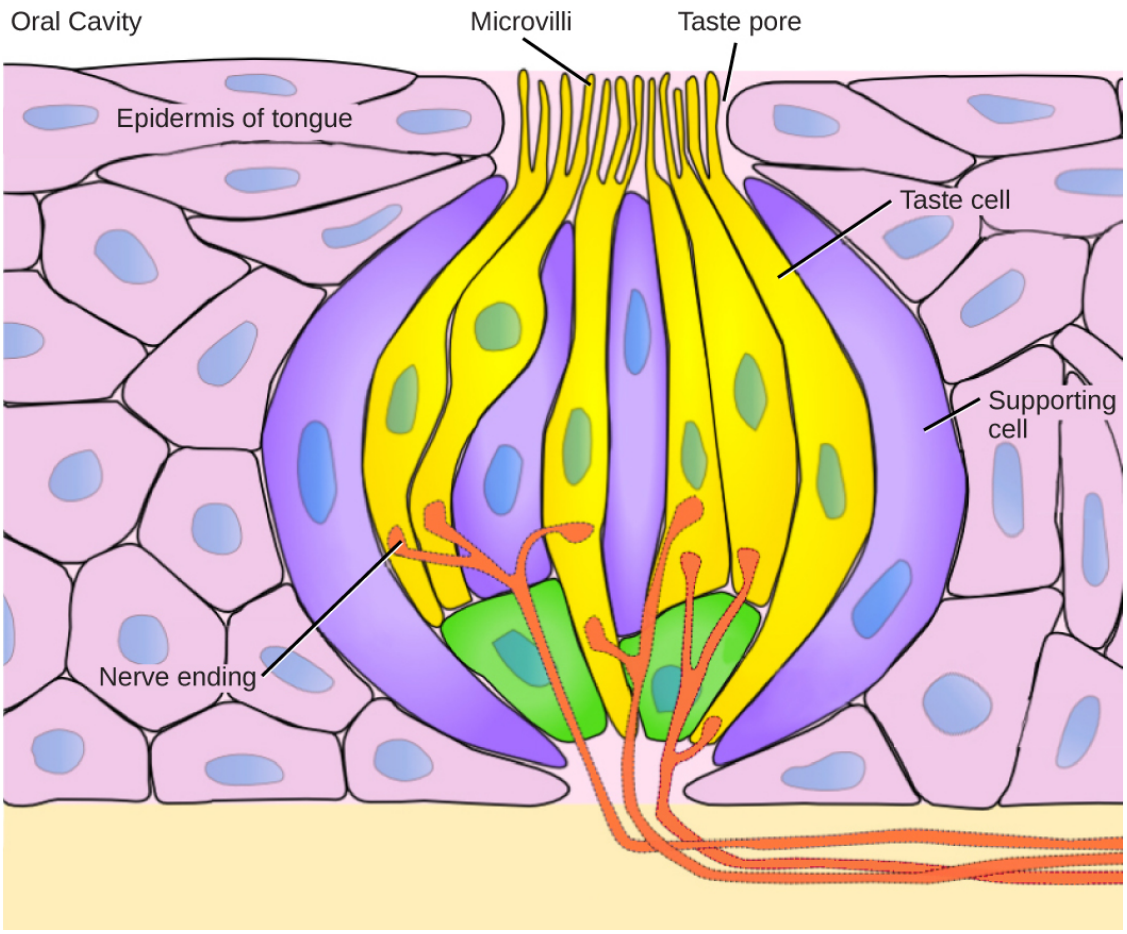

Figure 18.5: Pores in the tongue allow tastants to enter taste pores in the tongue. (credit: modification of work by Vincenzo Rizzo)

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.

18.2.3 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.

18.2.4 Review Questions

Exercise 18.2.1 *(Solution on p. 400.)*

Which of the following has the fewest taste receptors?

a. fungiform papillae
b. circumvallate papillae
c. foliate papillae
d. filiform papillae

Exercise 18.2.2 *(Solution on p. 400.)*

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

Exercise 18.2.3 *(Solution on p. 400.)*

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

18.2.5 Free Response

Exercise 18.2.4 *(Solution on p. 400.)*

From the perspective of the recipient of the signal, in what ways do pheromones differ from other odorants?

Exercise 18.2.5 *(Solution on p. 400.)*

What might be the effect on an animal of not being able to perceive taste?

18.3 Hearing and Vestibular Sensation[3]

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.

18.3.1 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 ($\geq$15.000Hz) sounds are higher-pitched (short wavelength) than low-frequency (long wavelengths; $\leq$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 18.6. 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.

[3]This content is available online at <http://cnx.org/content/m58109/1.2/>.

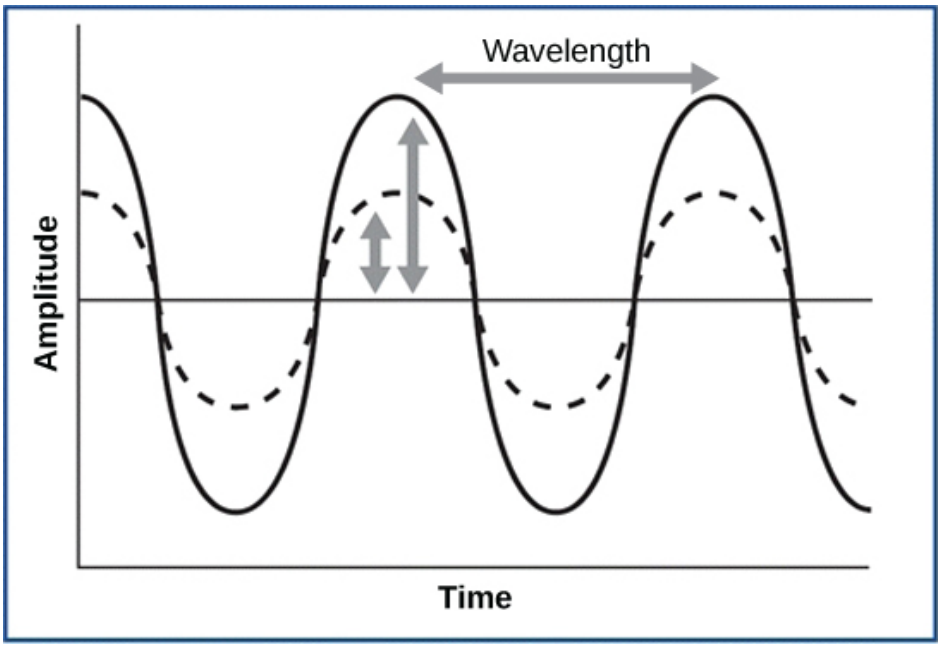

Figure 18.6: For sound waves, wavelength corresponds to pitch. Amplitude of the wave corresponds to volume. The sound wave shown with a dashed line is softer in volume than the sound wave shown with a solid line. (credit: NIH)

18.3.2 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 18.7). 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.

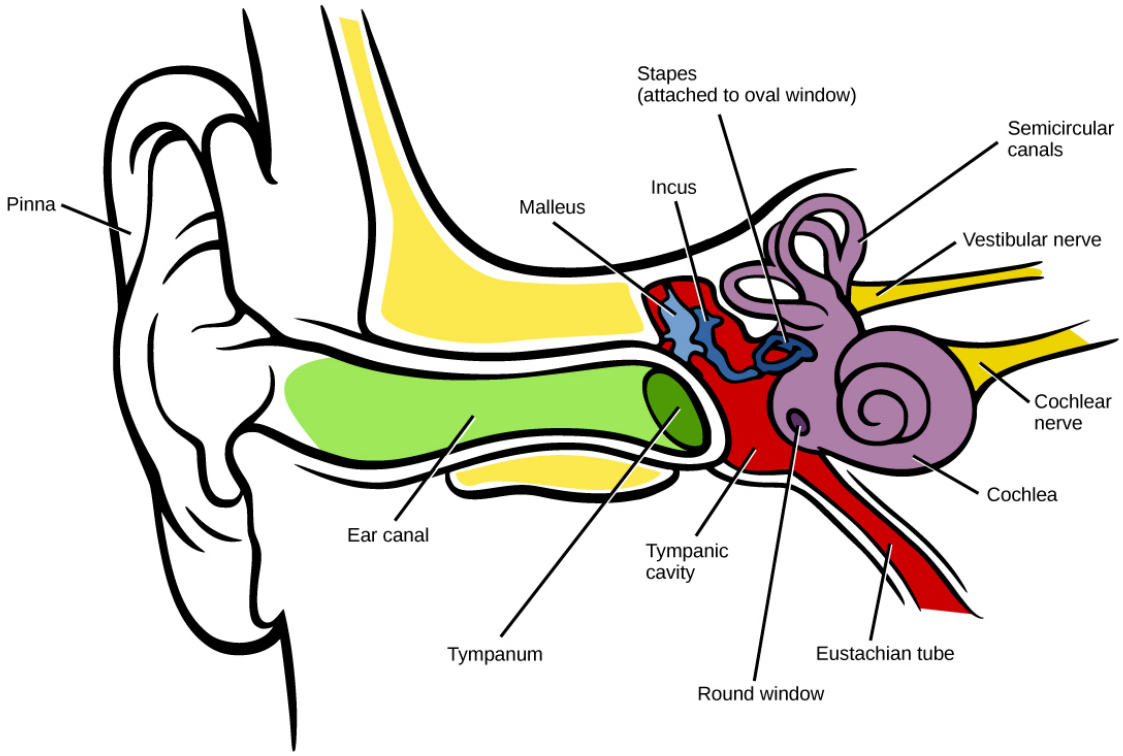

Figure 18.7: Sound travels through the outer ear to the middle ear, which is bounded on its exterior by the tympanic membrane. The middle ear contains three bones called ossicles that transfer the sound wave to the oval window, the exterior boundary of the inner ear. The organ of Corti, which is the organ of sound transduction, lies inside the cochlea. (credit: modification of work by Lars Chittka, Axel Brockmann)

18.3.3 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 18.8). 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**.

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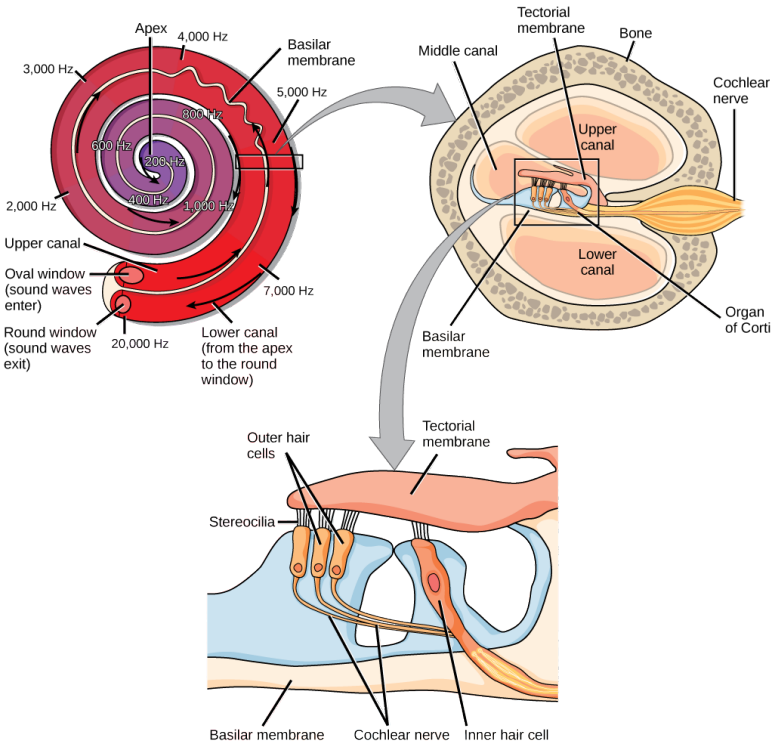

Figure 18.8: In the human ear, sound waves cause the stapes to press against the oval window. Vibrations travel up the fluid-filled interior of the cochlea. The basilar membrane that lines the cochlea gets continuously thinner toward the apex of the cochlea. Different thicknesses of membrane vibrate 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.

: Watch an animation[4] of sound entering the outer ear, moving through the ear structure, stimulating cochlear nerve impulses, and eventually sending signals to the temporal lobe.

18.3.3.1 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.

18.3.4 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 recep-

[4] http://openstaxcollege.org/l/hearing

tive 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 18.9. 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.

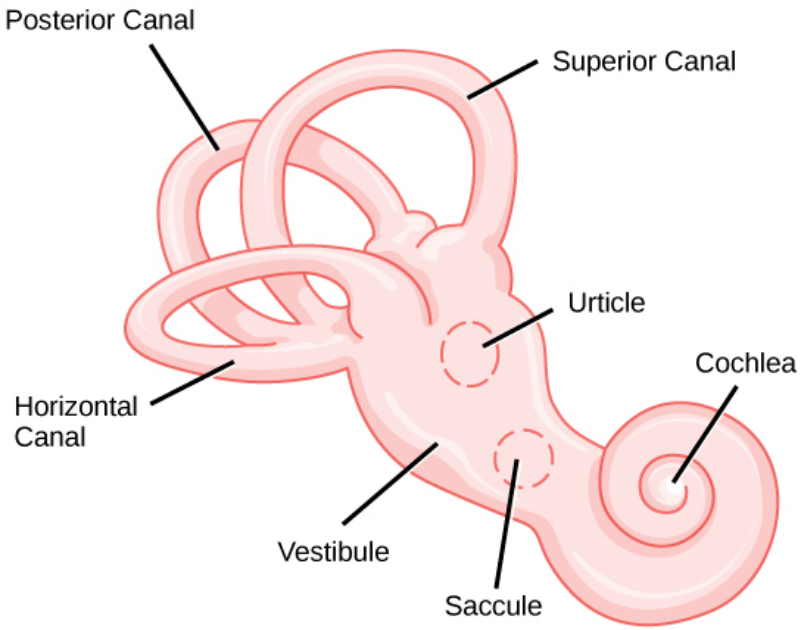

Figure 18.9: The structure of the vestibular labyrinth is shown. (credit: modification of work by NIH)

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 18.9. 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.

18.3.4.1 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.

: Click through this interactive tutorial[5] to review the parts of the ear and how they function to process sound.

18.3.5 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.

18.3.6 Art Connections

Exercise 18.3.1 ***(Solution on p. 400.)***

Figure 18.8 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

[5] http://openstaxcollege.org/l/ear_anatomy

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.

18.3.7 Review Questions

Exercise 18.3.2 *(Solution on p. 400.)*
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)

Exercise 18.3.3 *(Solution on p. 400.)*
Auditory hair cells are indirectly anchored to the _____.

a. basilar membrane
b. oval window
c. tectorial membrane
d. ossicles

Exercise 18.3.4 *(Solution on p. 400.)*
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

18.3.8 Free Response

Exercise 18.3.5 *(Solution on p. 400.)*
How would a rise in altitude likely affect the speed of a sound transmitted through air? Why?

Exercise 18.3.6 *(Solution on p. 400.)*
How might being in a place with less gravity than Earth has (such as Earth's moon) affect vestibular sensation, and why?

18.4 Vision[6]

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.

18.4.1 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 18.10). 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).

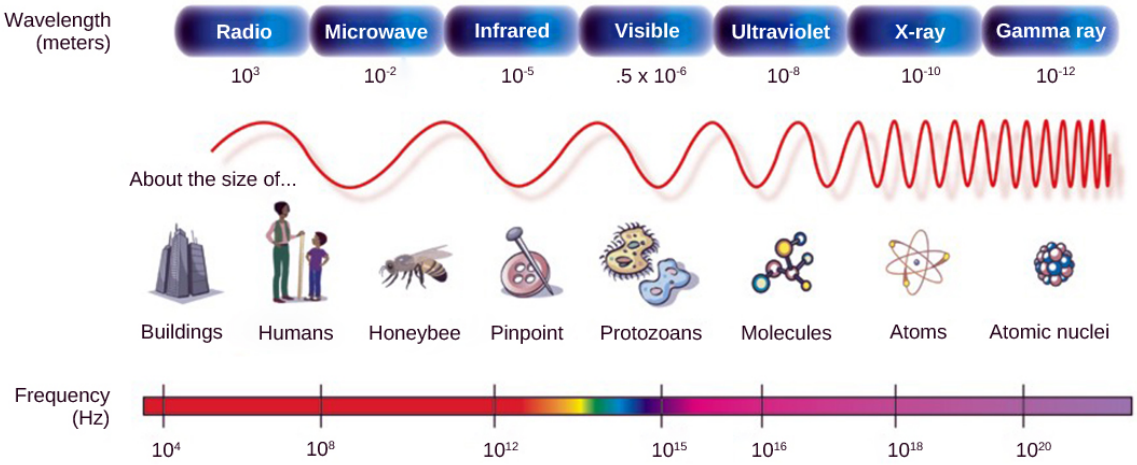

Figure 18.10: In the electromagnetic spectrum, visible light lies between 380 nm and 740 nm. (credit: modification of work by NASA)

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.

[6]This content is available online at <http://cnx.org/content/m58111/1.2/>.

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.

18.4.2 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 18.11) 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 18.11**b**). 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.

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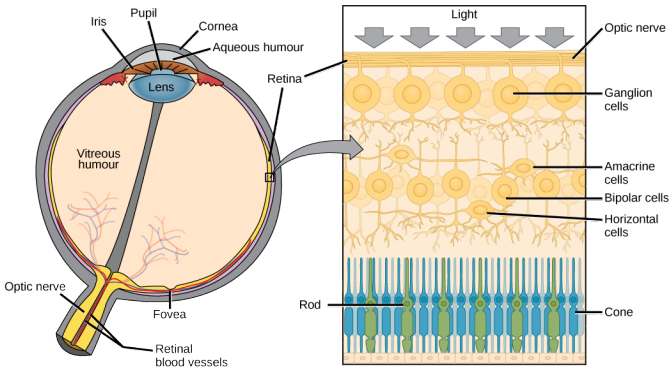

Figure 18.11: (a) The human eye is shown in cross section. (b) A blowup shows the layers of the retina.

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 18.12. 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.

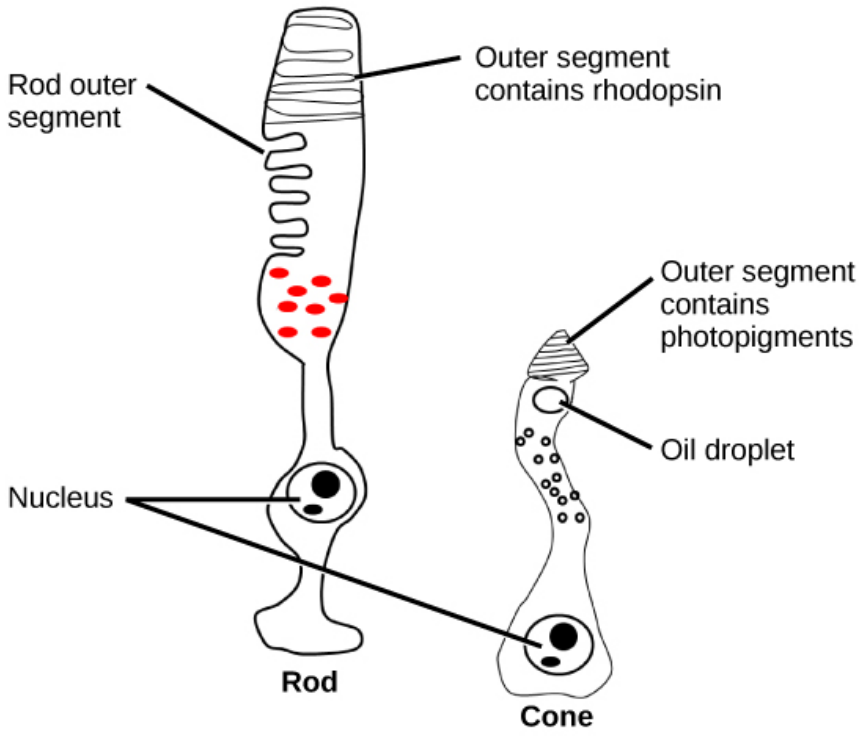

Figure 18.12: Rods and cones are photoreceptors in the retina. Rods respond in low light and can detect only shades of gray. Cones respond in intense light and are responsible for color vision. (credit: modification of work by Piotr Sliwa)

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.

: Review the anatomical structure[7] of the eye, clicking on each part to practice identification.

18.4.3 Processing Visual Input

18.4.3.1 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 18.13. 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.

[7] http://openstaxcollege.org/l/eye_diagram

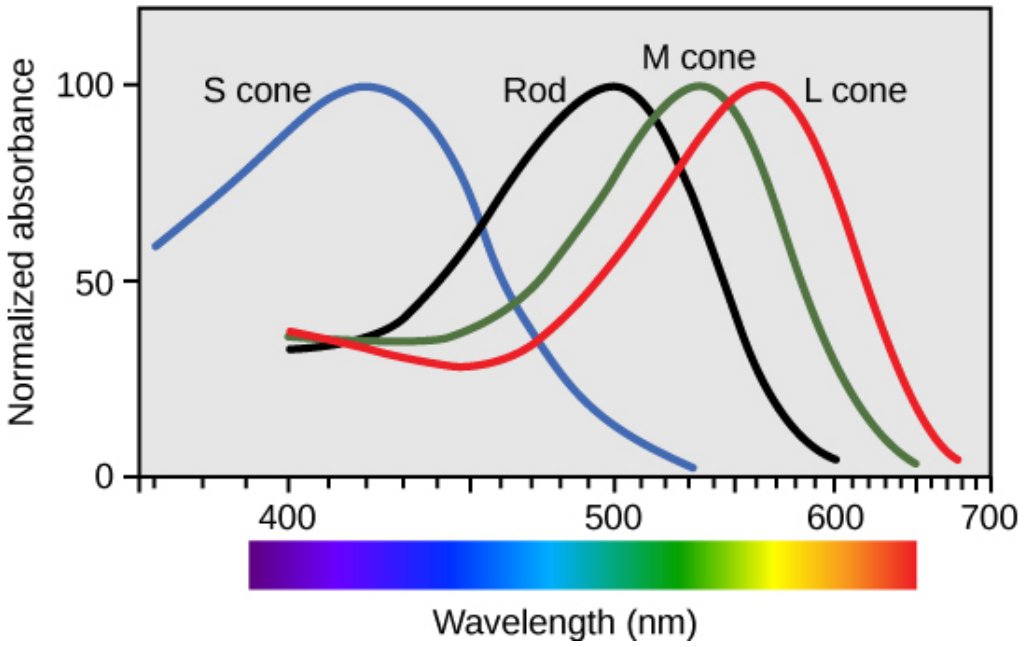

Figure 18.13: Human rod cells and the different types of cone cells each have an optimal wavelength. However, there is considerable overlap in the wavelengths of light detected.

18.4.3.2 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.

18.4.4 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.

18.4.5 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.

18.4.6 Art Connections

Exercise 18.4.1 ***(Solution on p. 400.)***

Figure 18.11 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.

18.4.7 Review Questions

Exercise 18.4.2 ***(Solution on p. 400.)***

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.

Exercise 18.4.3 ***(Solution on p. 400.)***

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.

Solutions to Exercises in Chapter 18

to Exercise 18.2.1 (p. 385)
D
to Exercise 18.2.2 (p. 385)
A
to Exercise 18.2.3 (p. 385)
A
to Exercise 18.2.4 (p. 385)
Pheromones may not be consciously perceived, and pheromones can have direct physiological and behavioral effects on their recipients.
to Exercise 18.2.5 (p. 385)
The animal might not be able to recognize the differences in food sources and thus might not be able to discriminate between spoiled food and safe food or between foods that contain necessary nutrients, such as proteins, and foods that do not.
to Exercise 18.3.1 (p. 392)
Figure 18.8 B
to Exercise 18.3.2 (p. 393)
D
to Exercise 18.3.3 (p. 393)
A
to Exercise 18.3.4 (p. 393)
B
to Exercise 18.3.5 (p. 393)
The sound would slow down, because it is transmitted through the particles (gas) and there are fewer particles (lower density) at higher altitudes.
to Exercise 18.3.6 (p. 393)
Because vestibular sensation relies on gravity's effects on tiny crystals in the inner ear, a situation of reduced gravity would likely impair vestibular sensation.
to Exercise 18.4.1 (p. 399)
Figure 18.11 A
to Exercise 18.4.2 (p. 399)
B
to Exercise 18.4.3 (p. 399)
C

Chapter 19

Immune System

19.1 Introduction to the Immune System[1]

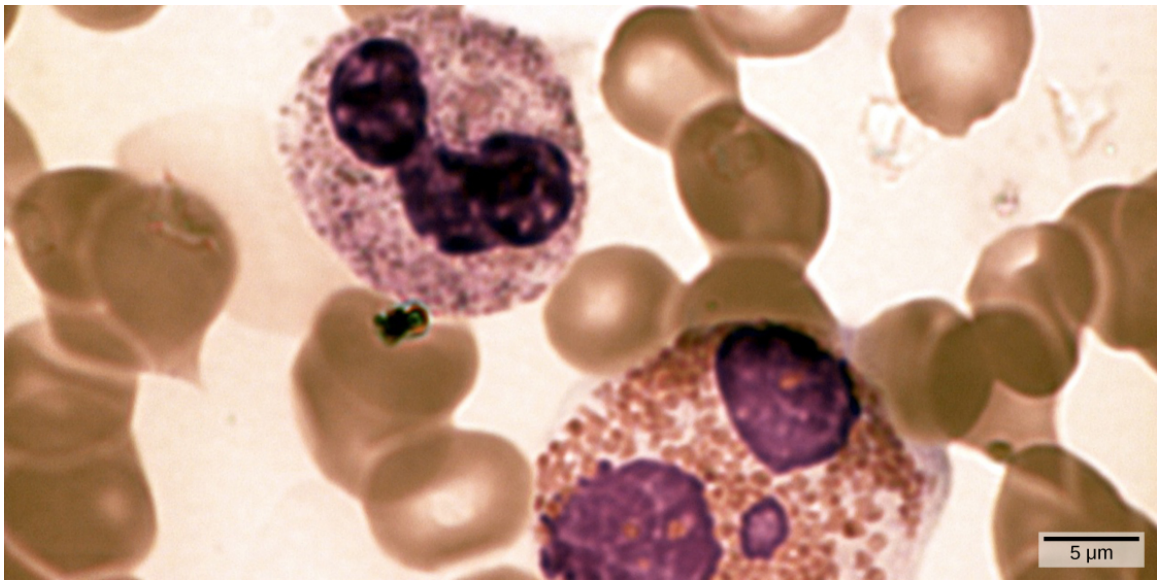

Figure 19.1: In this compound light micrograph purple-stained neutrophil (upper left) and eosinophil (lower right) are white blood cells that float among red blood cells in this blood smear. Neutrophils provide an early, rapid, and nonspecific defense against invading pathogens. Eosinophils play a variety of roles in the immune response. Red blood cells are about 7–8 μm in diameter, and a neutrophil is about 10–12μm. (credit: modification of work by Dr. David Csaba)

The environment consists of numerous **pathogens**, which are agents, usually microorganisms, that cause diseases in their hosts. A **host** is the organism that is invaded and often harmed by a pathogen. Pathogens include bacteria, protists, fungi and other infectious organisms. We are constantly exposed to pathogens

[1] This content is available online at <http://cnx.org/content/m58113/1.1/>.

in food and water, on surfaces, and in the air. Mammalian immune systems evolved for protection from such pathogens; they are composed of an extremely diverse array of specialized cells and soluble molecules that coordinate a rapid and flexible defense system capable of providing protection from a majority of these disease agents.

Components of the immune system constantly search the body for signs of pathogens. When pathogens are found, immune factors are mobilized to the site of an infection. The immune factors identify the nature of the pathogen, strengthen the corresponding cells and molecules to combat it efficiently, and then halt the immune response after the infection is cleared to avoid unnecessary host cell damage. The immune system can remember pathogens to which it has been exposed to create a more efficient response upon re-exposure. This memory can last several decades. Features of the immune system, such as pathogen identification, specific response, amplification, retreat, and remembrance are essential for survival against pathogens. The immune response can be classified as either innate or active. The innate immune response is always present and attempts to defend against all pathogens rather than focusing on specific ones. Conversely, the adaptive immune response stores information about past infections and mounts pathogen-specific defenses.

19.2 Innate Immunity[2]

The human immune system is a complex, multilayered system for defending against external and internal threats to the integrity of the body. The system can be divided into two types of defense systems: the innate immune system, which is nonspecific toward a particular kind of pathogen, and the adaptive immune system, which is specific (Figure 19.2). **Innate immunity** is not caused by an infection or vaccination and depends initially on physical and chemical barriers that work on all pathogens, sometimes called the first line of defense. The second line of defense of the innate system includes chemical signals that produce inflammation and fever responses as well as mobilizing protective cells and other chemical defenses. The adaptive immune system mounts a highly specific response to substances and organisms that do not belong in the body. The adaptive system takes longer to respond and has a memory system that allows it to respond with greater intensity should the body reencounter a pathogen even years later.

Vertebrate Immunity		
Innate Immune System		Adaptive Immune System
Physical Barriers	Internal Defenses	
• Skin, hair, cilia • Mucus membranes • Mucus and chemical secretions • Digestive enzymes in mouth • Stomach acid	• Inflammatory response • Complement proteins • Phagocytic cells • Natural killer (NK) cells	• Antibodies and the humoral immune response • Cell-mediated immune response • Memory response

Figure 19.2: There are two main parts to the vertebrate immune system. The innate immune system, which is made up of physical barriers and internal defenses, responds to all pathogens. The adaptive immune system is highly specific.

[2]This content is available online at <http://cnx.org/content/m58114/1.2/>.

19.2.1 External and Chemical Barriers

The body has significant physical barriers to potential pathogens. The skin contains the protein keratin, which resists physical entry into cells. Other body surfaces, particularly those associated with body openings, are protected by the mucous membranes. The sticky mucus provides a physical trap for pathogens, preventing their movement deeper into the body. The openings of the body, such as the nose and ears, are protected by hairs that catch pathogens, and the mucous membranes of the upper respiratory tract have cilia that constantly move pathogens trapped in the mucus coat up to the mouth.

The skin and mucous membranes also create a chemical environment that is hostile to many microorganisms. The surface of the skin is acidic, which prevents bacterial growth. Saliva, mucus, and the tears of the eye contain an enzyme that breaks down bacterial cell walls. The stomach secretions create a highly acidic environment, which kills many pathogens entering the digestive system.

Finally, the surface of the body and the lower digestive system have a community of microorganisms such as bacteria, archaea, and fungi that coexist without harming the body. There is evidence that these organisms are highly beneficial to their host, combating disease-causing organisms and outcompeting them for nutritional resources provided by the host body. Despite these defenses, pathogens may enter the body through skin abrasions or punctures, or by collecting on mucosal surfaces in large numbers that overcome the protections of mucus or cilia.

19.2.2 Internal Defenses

When pathogens enter the body, the innate immune system responds with a variety of internal defenses. These include the inflammatory response, phagocytosis, natural killer cells, and the complement system. White blood cells in the blood and lymph recognize pathogens as foreign to the body. A **white blood cell** is larger than a red blood cell, is nucleated, and is typically able to move using amoeboid locomotion. Because they can move on their own, white blood cells can leave the blood to go to infected tissues. For example, a **monocyte** is a type of white blood cell that circulates in the blood and lymph and develops into a macrophage after it moves into infected tissue. A **macrophage** is a large cell that engulfs foreign particles and pathogens. **Mast cells** are produced in the same way as white blood cells, but unlike circulating white blood cells, mast cells take up residence in connective tissues and especially mucosal tissues. They are responsible for releasing chemicals in response to physical injury. They also play a role in the allergic response, which will be discussed later in the chapter.

When a pathogen is recognized as foreign, chemicals called cytokines are released. A **cytokine** is a chemical messenger that regulates cell differentiation (form and function), proliferation (production), and gene expression to produce a variety of immune responses. Approximately 40 types of cytokines exist in humans. In addition to being released from white blood cells after pathogen recognition, cytokines are also released by the infected cells and bind to nearby uninfected cells, inducing those cells to release cytokines. This positive feedback loop results in a burst of cytokine production.

One class of early-acting cytokines is the interferons, which are released by infected cells as a warning to nearby uninfected cells. An **interferon** is a small protein that signals a viral infection to other cells. The interferons stimulate uninfected cells to produce compounds that interfere with viral replication. Interferons also activate macrophages and other cells.

19.2.2.1 The Inflammatory Response and Phagocytosis

The first cytokines to be produced encourage **inflammation**, a localized redness, swelling, heat, and pain. Inflammation is a response to physical trauma, such as a cut or a blow, chemical irritation, and infection by pathogens (viruses, bacteria, or fungi). The chemical signals that trigger an inflammatory response enter the extracellular fluid and cause capillaries to dilate (expand) and capillary walls to become more permeable, or leaky. The serum and other compounds leaking from capillaries cause swelling of the area, which in turn causes pain. Various kinds of white blood cells are attracted to the area of inflammation. The types of white blood cells that arrive at an inflamed site depend on the nature of the injury or infecting pathogen. For

example, a **neutrophil** is an early arriving white blood cell that engulfs and digests pathogens. Neutrophils are the most abundant white blood cells of the immune system (Figure 19.3). Macrophages follow neutrophils and take over the phagocytosis function and are involved in the resolution of an inflamed site, cleaning up cell debris and pathogens.

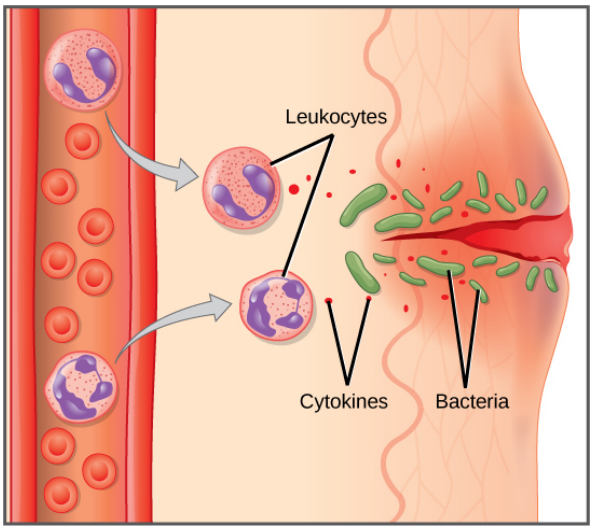

Figure 19.3: White blood cells (leukocytes) release chemicals to stimulate the inflammatory response following a cut in the skin.

Cytokines also send feedback to cells of the nervous system to bring about the overall symptoms of feeling sick, which include lethargy, muscle pain, and nausea. Cytokines also increase the core body temperature, causing a fever. The elevated temperatures of a fever inhibit the growth of pathogens and speed up cellular repair processes. For these reasons, suppression of fevers should be limited to those that are dangerously high.

: Check out this 23-second, stop-motion video[3] showing a neutrophil that searches and engulfs fungus spores during an elapsed time of 79 minutes.

[3] http://openstaxcollege.org/l/neutrophil

19.2.2.2 Natural Killer Cells

A **lymphocyte** is a white blood cell that contains a large nucleus (Figure 19.4). Most lymphocytes are associated with the adaptive immune response, but infected cells are identified and destroyed by natural killer cells, the only lymphocytes of the innate immune system. A **natural killer (NK) cell** is a lymphocyte that can kill cells infected with viruses (or cancerous cells). NK cells identify intracellular infections, especially from viruses, by the altered expression of **major histocompatibility class (MHC) I molecules** on the surface of infected cells. MHC class I molecules are proteins on the surfaces of all nucleated cells that provide a sample of the cell's internal environment at any given time. Unhealthy cells, whether infected or cancerous, display an altered MHC class I complement on their cell surfaces.

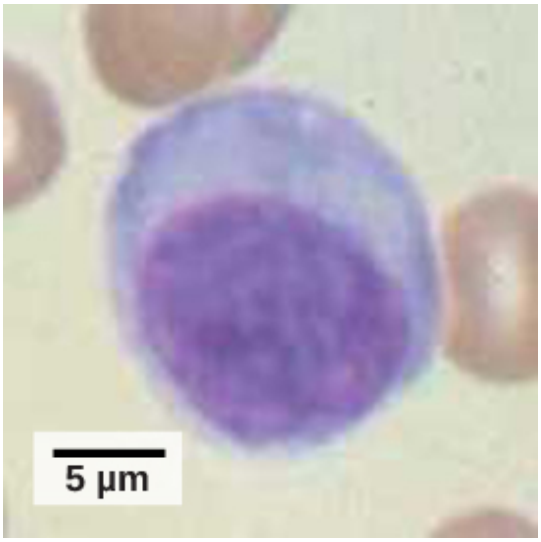

Figure 19.4: Lymphocytes, such as NK cells, are characterized by their large nuclei that actively absorb Wright stain and therefore appear dark colored under a microscope. (credit: scale-bar data from Matt Russell)

After the NK cell detects an infected or tumor cell, it induces programmed cell death, or apoptosis. Phagocytic cells then come along and digest the cell debris left behind. NK cells are constantly patrolling the body and are an effective mechanism for controlling potential infections and preventing cancer progression. The various types of immune cells are shown in Figure 19.5.

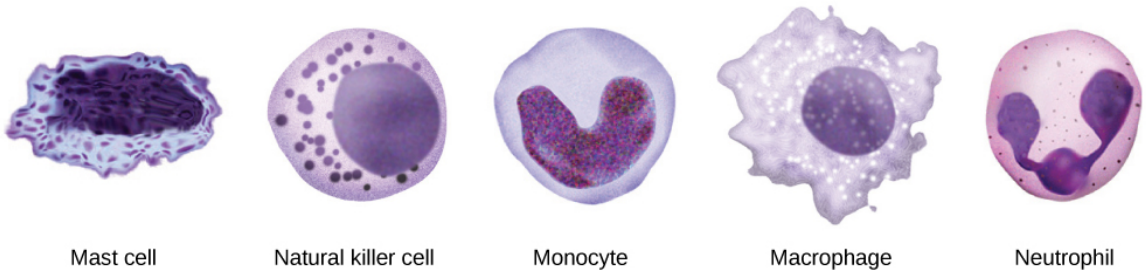

Figure 19.5: Cells involved in the innate immune response include mast cells, natural killer cells, and white blood cells, such as monocytes, macrophages and neutrophils.

19.2.2.3 Complement

An array of approximately 20 types of proteins, called a **complement system**, is also activated by infection or the activity of the cells of the adaptive immune system and functions to destroy extracellular pathogens. Liver cells and macrophages synthesize inactive forms of complement proteins continuously; these proteins are abundant in the blood serum and are capable of responding immediately to infecting microorganisms. The complement system is so named because it is complementary to the innate and adaptive immune system. Complement proteins bind to the surfaces of microorganisms and are particularly attracted to pathogens that are already tagged by the adaptive immune system. This "tagging" involves the attachment of specific proteins called antibodies (discussed in detail later) to the pathogen. When they attach, the antibodies change shape providing a binding site for one of the complement proteins. After the first few complement proteins bind, a cascade of binding in a specific sequence of proteins follows in which the pathogen rapidly becomes coated in complement proteins.

Complement proteins perform several functions, one of which is to serve as a marker to indicate the presence of a pathogen to phagocytic cells and enhance engulfment. Certain complement proteins can combine to open pores in microbial cell membranes and cause lysis of the cells.

19.2.3 Section Summary

The innate immune system consists first of physical and chemical barriers to infection including the skin and mucous membranes and their secretions, ciliated surfaces, and body hairs. The second line of defense is an internal defense system designed to counter pathogenic threats that bypass the physical and chemical barriers of the body. Using a combination of cellular and molecular responses, the innate immune system identifies the nature of a pathogen and responds with inflammation, phagocytosis, cytokine release, destruction by NK cells, or the complement system.

19.2.4 Review Questions

Exercise 19.2.1 *(Solution on p. 420.)*

Which of the following is a barrier against pathogens provided by the skin?

a. low pH
b. mucus
c. tears
d. cilia

Exercise 19.2.2 *(Solution on p. 420.)*
Although interferons have several effects, they are particularly useful against infections with which type of pathogen?

a. bacteria
b. viruses
c. fungi
d. helminths

Exercise 19.2.3 *(Solution on p. 420.)*
Which innate immune system component uses MHC class I molecules directly in its defense strategy?

a. macrophages
b. neutrophils
c. NK cells
d. interferon

19.2.5 Free Response

Exercise 19.2.4 *(Solution on p. 420.)*
Different MHC class I molecules between donor and recipient cells can lead to rejection of a transplanted organ or tissue. Suggest a reason for this.

Exercise 19.2.5 *(Solution on p. 420.)*
If a series of genetic mutations prevented some, but not all, of the complement proteins from binding antibodies or pathogens, would the entire complement system be compromised?

19.3 Adaptive Immunity[4]

The adaptive, or acquired, immune response takes days or even weeks to become established—much longer than the innate response; however, adaptive immunity is more specific to an invading pathogen. **Adaptive immunity** is an immunity that occurs after exposure to an antigen either from a pathogen or a vaccination. An **antigen** is a molecule that stimulates a response in the immune system. This part of the immune system is activated when the innate immune response is insufficient to control an infection. In fact, without information from the innate immune system, the adaptive response could not be mobilized. There are two types of adaptive responses: the **cell-mediated immune response**, which is controlled by activated **T cells**, and the **humoral or antibody- immune response**, which is controlled by activated **B cells** and antibodies. Activated T and B cells whose surface binding sites are specific to the molecules on the pathogen greatly increase in numbers and attack the invading pathogen. Their attack can kill pathogens directly or they can secrete antibodies that enhance the phagocytosis of pathogens and disrupt the infection. Adaptive immunity also involves a memory to give the host long-term protection from reinfection with the same type of pathogen; on reexposure, this host memory will facilitate a rapid and powerful response.

[4]This content is available online at <http://cnx.org/content/m58115/1.3/>.

19.3.1 B and T Cells

Lymphocytes, which are white blood cells, are formed with other blood cells in the red bone marrow found in many flat bones, such as the shoulder or pelvic bones. The two types of lymphocytes of the adaptive immune response are B and T cells (Figure 19.6). Whether an immature lymphocyte becomes a B cell or T cell depends on where in the body it matures. The B cells remain in the bone marrow to mature (hence the name "B" for "bone marrow"), while T cells migrate to the thymus, where they mature (hence the name "T" for "thymus").

Maturation of a B or T cell involves becoming immunocompetent, meaning that it can recognize, by binding, a specific molecule or antigen (discussed below). During the maturation process, B and T cells that bind too strongly to the body's own cells are eliminated in order to minimize an immune response against the body's own tissues. Those cells that react weakly to the body's own cells, but have highly specific receptors on their cell surfaces that allow them to recognize a foreign molecule, or antigen, remain. This process occurs during fetal development and continues throughout life. The specificity of this receptor is determined by the genetics of the individual and is present before a foreign molecule is introduced to the body or encountered. Thus, it is genetics and not experience that initially provides a vast array of cells, each capable of binding to a different specific foreign molecule. Once they are immunocompetent, the T and B cells will migrate to the spleen and lymph nodes where they will remain until they are called on during an infection. B cells are involved in the humoral immune response, which targets pathogens loose in blood and lymph, and T cells are involved in the cell-mediated immune response, which targets infected cells.

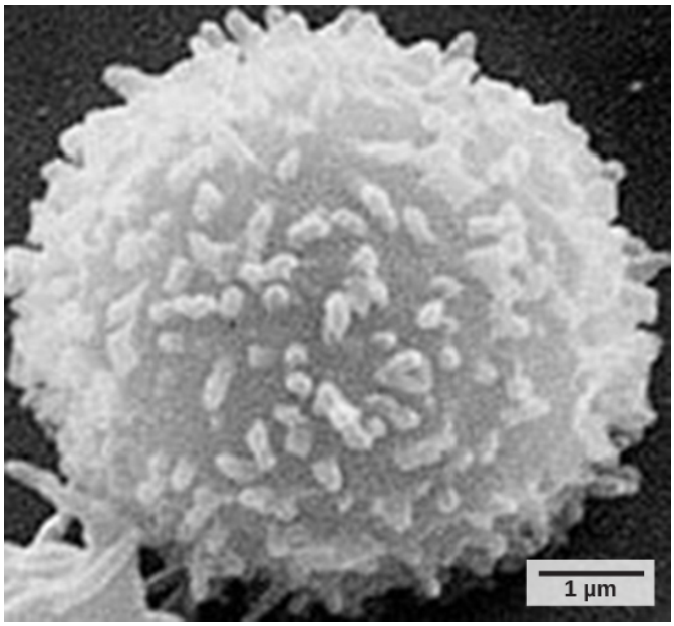

Figure 19.6: This scanning electron micrograph shows a T lymphocyte. T and B cells are indistinguishable by light microscopy but can be differentiated experimentally by probing their surface receptors. (credit: modification of work by NCI; scale-bar data from Matt Russell)

19.3.2 Humoral (or Antibody)-Mediated Immune Response

As mentioned, an antigen is a molecule that stimulates a response in the immune system. Not every molecule is antigenic. B cells participate in a chemical response to antigens present in the body by producing specific antibodies that circulate throughout the body and bind with the antigen whenever it is encountered. This is known as the humoral immune response. As discussed, during maturation of B cells, a set of highly specific B cells are produced that have many antigen receptor molecules in their membrane (Figure 19.7).

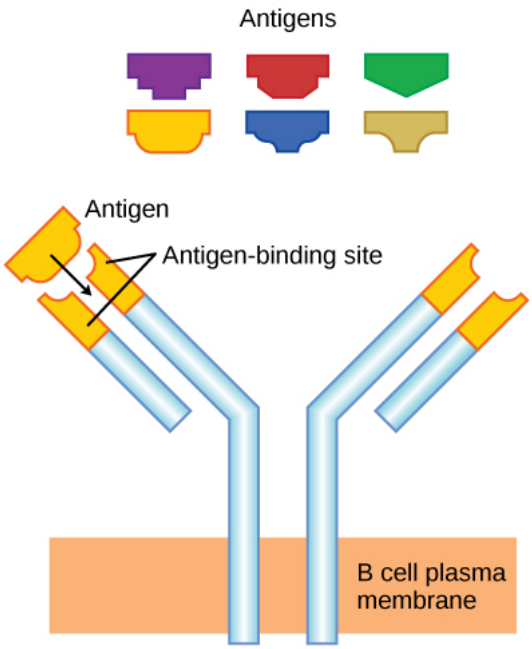

Figure 19.7: B cell receptors are embedded in the membranes of B cells and bind a variety of antigens through their variable regions.

Each B cell has only one kind of antigen receptor, which makes every B cell different. Once the B cells mature in the bone marrow, they migrate to lymph nodes or other lymphatic organs. When a B cell encounters the antigen that binds to its receptor, the antigen molecule is brought into the cell by endocytosis and reappears on the surface of the cell bound to an **MHC class II molecule**. When this process is complete, the B cell is sensitized. In most cases, the sensitized B cell must then encounter a specific kind of T cell, called a helper T cell, before it is activated. The helper T cell must already have been activated through an encounter with the antigen (discussed below).

The helper T cell binds to the antigen-MHC class II complex and is induced to release cytokines that induce the B cell to divide rapidly, which makes thousands of identical (clonal) cells via mitosis. This process is called clonal expansion. These daughter cells become either plasma cells or memory B cells. The memory B cells remain inactive at this point, until another later encounter with the antigen, caused by a reinfection by the same bacteria or virus, results in them dividing into a new population of plasma cells. The plasma cells, on the other hand, produce and secrete large quantities, up to 100 million molecules per hour, of antibody molecules. An **antibody**, also known as an immunoglobulin (Ig), is a protein that is produced by plasma cells after stimulation by an antigen. Antibodies are the agents of humoral immunity. Antibodies

occur in the blood, in gastric and mucus secretions, and in breast milk. Antibodies in these bodily fluids can bind pathogens and mark them for destruction by phagocytes before they can infect cells.

These antibodies circulate in the blood stream and lymphatic system and bind with the antigen whenever it is encountered. The binding can fight infection in several ways. Antibodies can bind to viruses or bacteria and interfere with the chemical interactions required for them to infect or bind to other cells. The antibodies may create bridges between different particles containing antigenic sites clumping them all together and preventing their proper functioning. The antigen-antibody complex stimulates the complement system described previously, destroying the cell bearing the antigen. Phagocytic cells, such as those already described, are attracted by the antigen-antibody complexes, and phagocytosis is enhanced when the complexes are present. Finally, antibodies stimulate inflammation, and their presence in mucus and on the skin prevents pathogen attack.

Antibodies coat extracellular pathogens and neutralize them by blocking key sites on the pathogen that enhance their infectivity (such as receptors that "dock" pathogens on host cells) (Figure 19.8). Antibody neutralization can prevent pathogens from entering and infecting host cells. The neutralized antibody-coated pathogens can then be filtered by the spleen and eliminated in urine or feces.

Antibodies also mark pathogens for destruction by phagocytic cells, such as macrophages or neutrophils, in a process called opsonization. In a process called complement fixation, some antibodies provide a place for complement proteins to bind. The combination of antibodies and complement promotes rapid clearing of pathogens.

The production of antibodies by plasma cells in response to an antigen is called **active immunity** and describes the host's active response of the immune system to an infection or to a vaccination. There is also a **passive immune** response where antibodies come from an outside source, instead of the individual's own plasma cells, and are introduced into the host. For example, antibodies circulating in a pregnant woman's body move across the placenta into the developing fetus. The child benefits from the presence of these antibodies for up to several months after birth. In addition, a passive immune response is possible by injecting antibodies into an individual in the form of an antivenom to a snake-bite toxin or antibodies in blood serum to help fight a hepatitis infection. This gives immediate protection since the body does not need the time required to mount its own response.

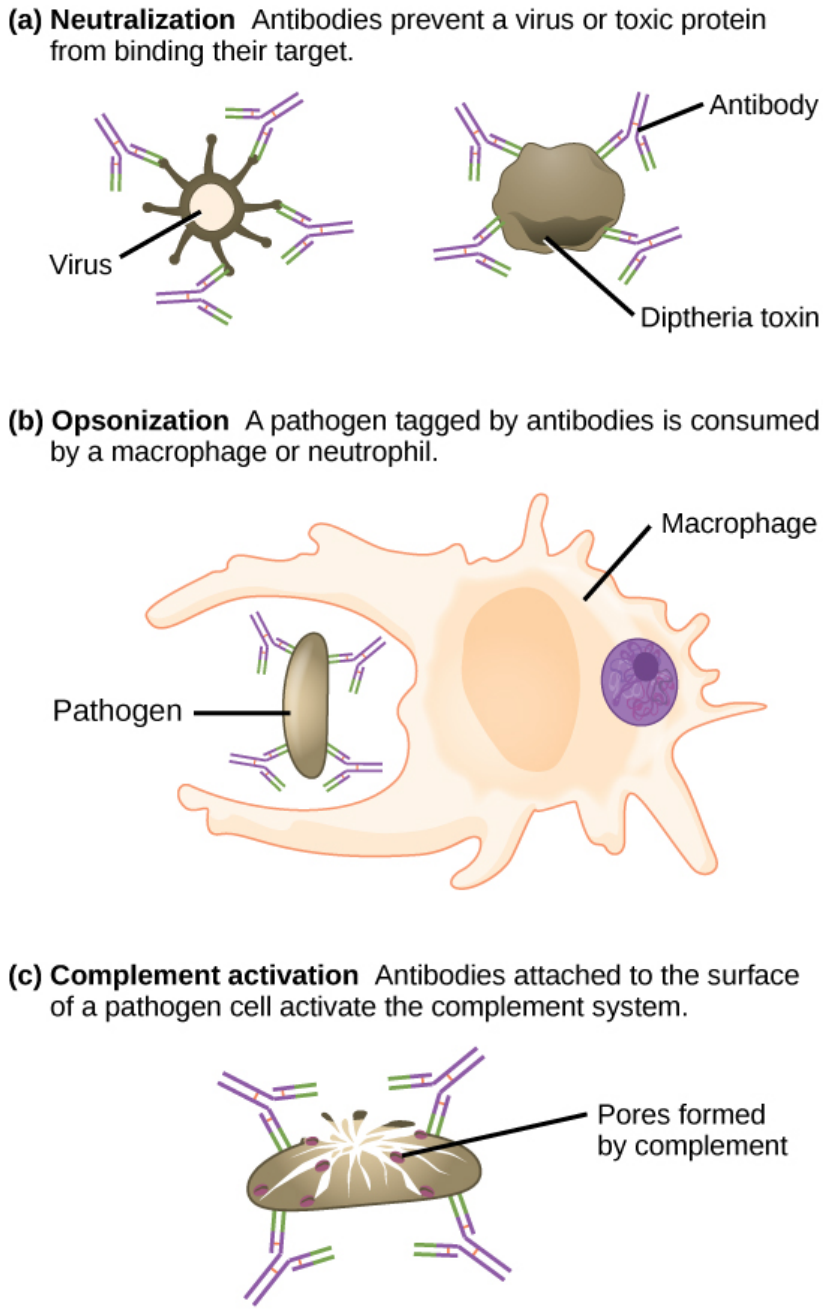

Figure 19.8: Antibodies may inhibit infection by (a) preventing the antigen from binding its target, (b) tagging a pathogen for destruction by macrophages or neutrophils, or (c) activating the complement cascade.

19.3.3 Cell-Mediated Immunity

Unlike B cells, T lymphocytes are unable to recognize pathogens without assistance. Instead, dendritic cells and macrophages first engulf and digest pathogens into hundreds or thousands of antigens. Then, an **antigen-presenting cell (APC)** detects, engulfs, and informs the adaptive immune response about an infection. When a pathogen is detected, these APCs will engulf and break it down through phagocytosis. Antigen fragments will then be transported to the surface of the APC, where they will serve as an indicator to other immune cells. A **dendritic cell** is an immune cell that mops up antigenic materials in its surroundings and presents them on its surface. Dendritic cells are located in the skin, the linings of the nose, lungs, stomach, and intestines. These positions are ideal locations to encounter invading pathogens. Once they are activated by pathogens and mature to become APCs they migrate to the spleen or a lymph node. Macrophages also function as APCs. After phagocytosis by a macrophage, the phagocytic vesicle fuses with an intracellular lysosome. Within the resulting phagolysosome, the components are broken down into fragments; the fragments are then loaded onto MHC class II molecules and are transported to the cell surface for antigen presentation (Figure 19.9). Helper T cells cannot properly respond to an antigen unless it is processed and embedded in an MHC class II molecule. The APCs express MHC class II on their surfaces, and when combined with a foreign antigen, these complexes signal an invader.

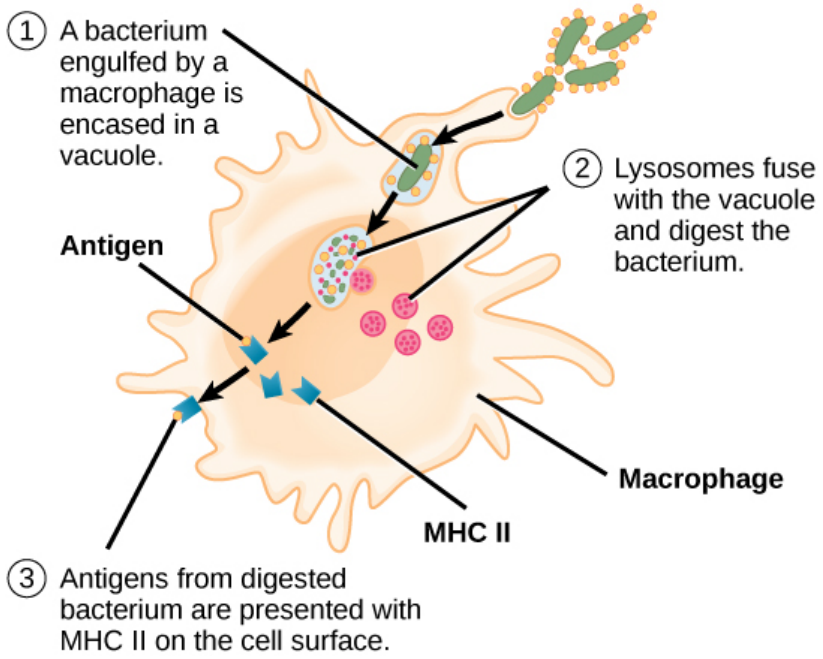

Figure 19.9: An antigen-presenting cell (APC), such as a macrophage, engulfs a foreign antigen, partially digests it in a lysosome, and then embeds it in an MHC class II molecule for presentation at the cell surface. Lymphocytes of the adaptive immune response must interact with antigen-embedded MHC class II molecules to mature into functional immune cells.

: View this animation from Rockefeller University[5] to see how dendritic cells act as sentinels in the body's immune system.

T cells have many functions. Some respond to APCs of the innate immune system and indirectly induce immune responses by releasing cytokines. Others stimulate B cells to start the humoral response as described previously. Another type of T cell detects APC signals and directly kills the infected cells, while some are involved in suppressing inappropriate immune reactions to harmless or "self" antigens.

There are two main types of T cells: helper T lymphocytes (T_H) and the cytotoxic T lymphocytes (T_C). The T_H lymphocytes function indirectly to tell other immune cells about potential pathogens.

Cytotoxic T cells (T_C) are the key component of the cell-mediated part of the adaptive immune system and attack and destroy infected cells. T_C cells are particularly important in protecting against viral infections; this is because viruses replicate within cells where they are shielded from extracellular contact with circulating antibodies. Once activated, the T_C creates a large clone of cells with one specific set of cell-surface receptors, as in the case with clonal expansion of activated B cells. As with B cells, the clone includes active T_C cells and inactive memory T_C cells. The resulting active T_C cells then identify infected host cells. Because of the time required to generate a population of clonal T and B cells, there is a delay in the adaptive immune response compared to the innate immune response.

T_C cells attempt to identify and destroy infected cells before the pathogen can replicate and escape, thereby halting the progression of intracellular infections. T_C cells also support NK lymphocytes to destroy early cancers. Cytokines secreted by the T_H1 response that stimulates macrophages also stimulate T_C cells and enhance their ability to identify and destroy infected cells and tumors. A summary of how the humoral and cell-mediated immune responses are activated appears in Figure 19.10.

B plasma cells and T_C cells are collectively called **effector cells** because they are involved in "effecting" (bringing about) the immune response of killing pathogens and infected host cells.

[5] http://openstaxcollege.org/l/immune_system2

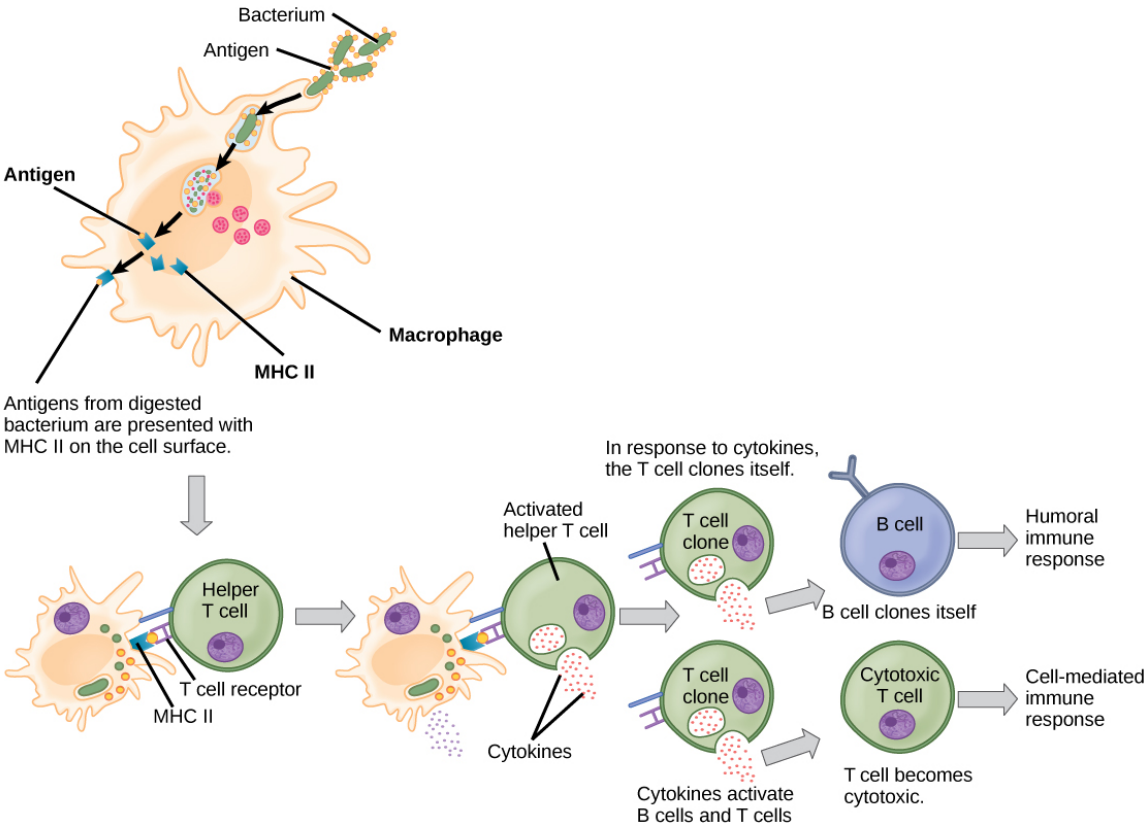

Figure 19.10: A helper T cell becomes activated by binding to an antigen presented by an APC via the MHCII receptor, causing it to release cytokines. Depending on the cytokines released, this activates either the humoral or the cell-mediated immune response.

19.3.4 Immunological Memory

The adaptive immune system has a memory component that allows for a rapid and large response upon reinvasion of the same pathogen. During the adaptive immune response to a pathogen that has not been encountered before, known as the **primary immune response**, plasma cells secreting antibodies and differentiated T cells increase, then plateau over time. As B and T cells mature into effector cells, a subset of the naïve populations differentiates into B and T memory cells with the same antigen specificities (Figure 19.11). A **memory cell** is an antigen-specific B or T lymphocyte that does not differentiate into an effector cell during the primary immune response, but that can immediately become an effector cell on reexposure to the same pathogen. As the infection is cleared and pathogenic stimuli subside, the effectors are no longer needed and they undergo apoptosis. In contrast, the memory cells persist in the circulation.

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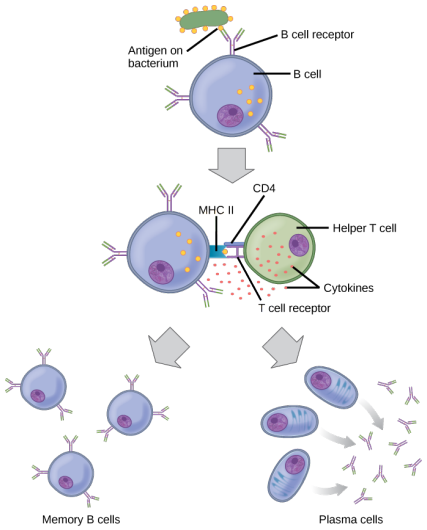

Figure 19.11: After initially binding an antigen to the B cell receptor, a B cell internalizes the antigen and presents it on MHC class II. A helper T cell recognizes the MHC class II- antigen complex and activates the B cell. As a result, memory B cells and plasma cells are made.

If the pathogen is never encountered again during the individual's lifetime, B and T memory cells will circulate for a few years or even several decades and will gradually die off, having never functioned as effector cells. However, if the host is re-exposed to the same pathogen type, circulating memory cells will immediately differentiate into plasma cells and T_C cells without input from APCs or T_H cells. This is known as the **secondary immune response**. One reason why the adaptive immune response is delayed is because it takes time for naïve B and T cells with the appropriate antigen specificities to be identified, activated, and proliferate. On reinfection, this step is skipped, and the result is a more rapid production of immune defenses. Memory B cells that differentiate into plasma cells output tens to hundreds-fold greater antibody amounts than were secreted during the primary response (Figure 19.12). This rapid and dramatic antibody response may stop the infection before it can even become established, and the individual may not realize they had been exposed.

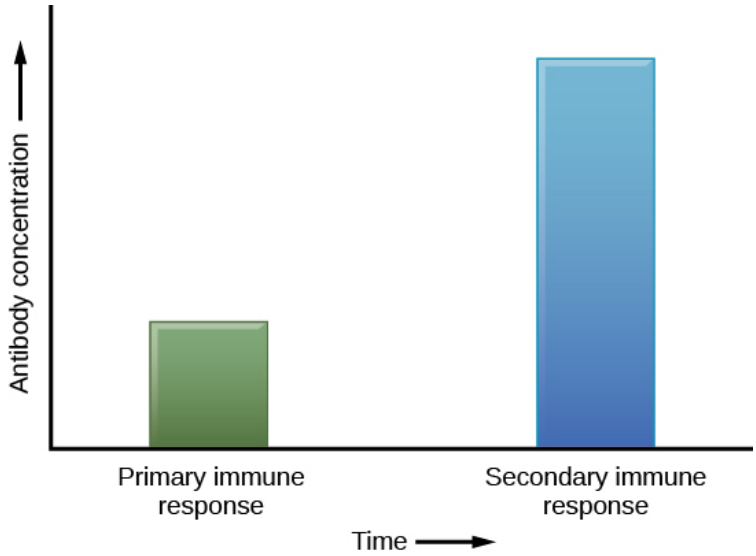

Figure 19.12: In the primary response to infection, antibodies are secreted first from plasma cells. Upon re-exposure to the same pathogen, memory cells differentiate into antibody-secreting plasma cells that output a greater amount of antibody for a longer period of time.

Vaccination is based on the knowledge that exposure to noninfectious antigens, derived from known pathogens, generates a mild primary immune response. The immune response to vaccination may not be perceived by the host as illness but still confers immune memory. When exposed to the corresponding pathogen to which an individual was vaccinated, the reaction is similar to a secondary exposure. Because each reinfection generates more memory cells and increased resistance to the pathogen, some vaccine courses involve one or more booster vaccinations to mimic repeat exposures.

19.3.5 The Lymphatic System

Lymph is the watery fluid that bathes tissues and organs and contains protective white blood cells but does not contain erythrocytes. Lymph moves about the body through the lymphatic system, which is made up of vessels, lymph ducts, lymph glands, and organs, such as tonsils, adenoids, thymus, and spleen.

Although the immune system is characterized by circulating cells throughout the body, the regulation, maturation, and intercommunication of immune factors occur at specific sites. The blood circulates immune cells, proteins, and other factors through the body. Approximately 0.1 percent of all cells in the blood are leukocytes, which include monocytes (the precursor of macrophages) and lymphocytes. Most cells in the blood are red blood cells. Cells of the immune system can travel between the distinct lymphatic and blood circulatory systems, which are separated by interstitial space, by a process called extravasation (passing through to surrounding tissue).

Recall that cells of the immune system originate from stem cells in the bone marrow. B cell maturation occurs in the bone marrow, whereas progenitor cells migrate from the bone marrow and develop and mature into naïve T cells in the organ called the thymus.

On maturation, T and B lymphocytes circulate to various destinations. Lymph nodes scattered throughout the body house large populations of T and B cells, dendritic cells, and macrophages (Figure 19.13). Lymph gathers antigens as it drains from tissues. These antigens then are filtered through lymph nodes

before the lymph is returned to circulation. APCs in the lymph nodes capture and process antigens and inform nearby lymphocytes about potential pathogens.

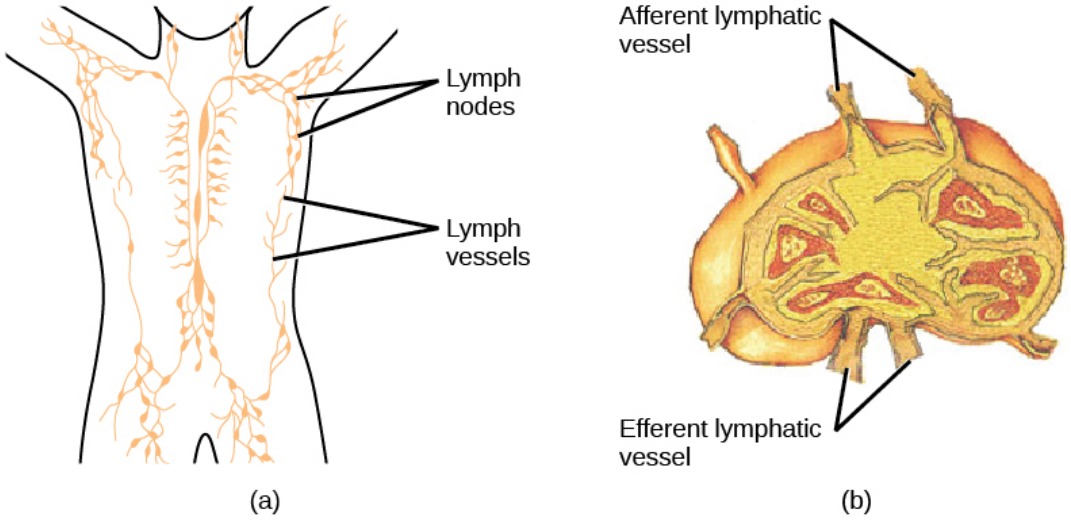

Figure 19.13: (a) Lymphatic vessels carry a clear fluid called lymph throughout the body. The liquid passes through (b) lymph nodes that filter the lymph that enters the node through afferent vessels and leaves through efferent vessels; lymph nodes are filled with lymphocytes that purge infecting cells. (credit a: modification of work by NIH; credit b: modification of work by NCI, NIH)

The spleen houses B and T cells, macrophages, dendritic cells, and NK cells (Figure 19.14). The spleen is the site where APCs that have trapped foreign particles in the blood can communicate with lymphocytes. Antibodies are synthesized and secreted by activated plasma cells in the spleen, and the spleen filters foreign substances and antibody-complexed pathogens from the blood. Functionally, the spleen is to the blood as lymph nodes are to the lymph.

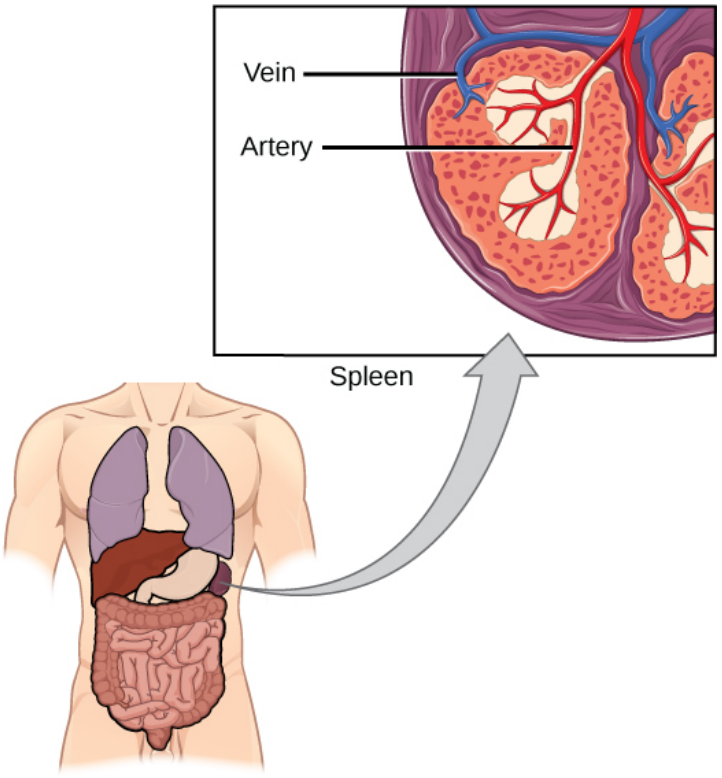

Figure 19.14: The spleen functions to immunologically filter the blood and allow for communication between cells corresponding to the innate and adaptive immune responses. (credit: modification of work by NCI, NIH)

19.3.6 Section Summary

The adaptive immune response is a slower-acting, longer-lasting, and more specific response than the innate response. However, the adaptive response requires information from the innate immune system to function. APCs display antigens on MHC molecules to naïve T cells. T cells with cell-surface receptors that bind a specific antigen will bind to that APC. In response, the T cells differentiate and proliferate, becoming T_H cells or T_C cells. T_H cells stimulate B cells that have engulfed and presented pathogen-derived antigens. B cells differentiate into plasma cells that secrete antibodies, whereas T_C cells destroy infected or cancerous cells. Memory cells are produced by activated and proliferating B and T cells and persist after a primary exposure to a pathogen. If re-exposure occurs, memory cells differentiate into effector cells without input from the innate immune system.

19.3.7 Art Connections

Exercise 19.3.1 ***(Solution on p. 420.)***

Figure 19.11 The Rh antigen is found on Rh-positive red blood cells. An Rh-negative female can usually carry an Rh-positive fetus to term without difficulty. However, if she has a second

Rh-positive fetus, her body may launch an immune attack that causes hemolytic disease of the newborn. Why do you think hemolytic disease is only a problem during the second or subsequent pregnancies?

19.3.8 Review Questions

Exercise 19.3.2 *(Solution on p. 420.)*

The humoral immune response depends on which cells?

a. T_C cells
b. B cells
c. B and T_H cells
d. T_C and T_H cells

Exercise 19.3.3 *(Solution on p. 420.)*

Foreign particles circulating in the blood are filtered by the _____.

a. spleen
b. lymph nodes
c. MALT
d. lymph

19.3.9 Free Response

Exercise 19.3.4 *(Solution on p. 420.)*

How do B and T cells differ with respect to antigens that they bind?

Exercise 19.3.5 *(Solution on p. 420.)*

Why is the immune response after reinfection much faster than the adaptive immune response after the initial infection?

Solutions to Exercises in Chapter 19

to Exercise 19.2.1 (p. 406)
A
to Exercise 19.2.2 (p. 407)
B
to Exercise 19.2.3 (p. 407)
C
to Exercise 19.2.4 (p. 407)
If the MHC class I molecules expressed on donor cells differ from the MHC class I molecules expressed on recipient cells, NK cells may identify the donor cells as not normal and produce enzymes to induce the donor cells to undergo apoptosis, which would destroy the transplanted organ.
to Exercise 19.2.5 (p. 407)
The entire complement system would probably be affected even when only a few members were mutated such that they could no longer bind. Because the complement involves the binding of activated proteins in a specific sequence, when one or more proteins in the sequence is absent, the subsequent proteins would be incapable of binding to elicit the complement's pathogen-destructive effects.
to Exercise 19.3.1 (p. 418)
Figure 19.11 If the blood of the mother and fetus mixes, memory cells that recognize the Rh antigen of the fetus can form in the mother late in the first pregnancy. During subsequent pregnancies, these memory cells launch an immune attack on the fetal blood cells of an Rh-positive fetus. Injection of anti-Rh antibody during the first pregnancy prevents the immune response from occurring.
to Exercise 19.3.2 (p. 419)
C
to Exercise 19.3.3 (p. 419)
A
to Exercise 19.3.4 (p. 419)
T cells bind antigens that have been digested and embedded in MHC molecules by APCs. In contrast, B cells function as APCs to bind intact, unprocessed antigens.
to Exercise 19.3.5 (p. 419)
Upon reinfection, the memory cells will immediately differentiate into plasma cells and CTLs without input from APCs or T_H cells. In contrast, the adaptive immune response to the initial infection requires time for naïve B and T cells with the appropriate antigen specificities to be identified and activated.

Glossary

A

ABO blood group
: blood-type classification based on the presence or absence of A and B glycoproteins on the erythrocyte membrane surface

acetyl CoA
: the combination of an acetyl group derived from pyruvic acid and coenzyme A which is made from pantothenic acid (a B-group vitamin)

acetylcholinesterase
: (AChE) enzyme that breaks down ACh into acetyl and choline

acid
: a substance that donates hydrogen ions and therefore lowers pH

actin
: globular contractile protein that interacts with myosin for muscle contraction

action potential
: a momentary change in the electrical potential of a neuron (or muscle) membrane

action potential
: self-propagating momentary change in the electrical potential of a neuron (or muscle) membrane

activation energy
: the amount of initial energy necessary for reactions to occur

active immunity
: an immunity that occurs as a result of the activity of the body's own cells rather than from antibodies acquired from an external source

active site
: a specific region on the enzyme where the substrate binds

active transport
: the method of transporting material that requires energy

adaptive immunity
: a specific immune response that occurs after exposure to an antigen either from a pathogen or a vaccination

adhesion
: the attraction between water molecules and molecules of a different substance

adrenal gland
: the endocrine gland associated with the kidneys

afferent arteriole
: arteriole that branches from the cortical radiate artery and enters the glomerulus

agglutination
: clustering of cells into masses linked by antibodies

ala
: (plural = alae) small, flaring structure of a nostril that forms the lateral side of the nares

alar cartilage
: cartilage that supports the apex of the nose and helps shape the nares; it is connected to the septal cartilage and connective tissue of the alae

albumin
: most abundant plasma protein, accounting for most of the osmotic pressure of plasma

allosteric inhibition
: the mechanism for inhibiting enzyme action in which a regulatory molecule binds to a second site (not the active site) and initiates a conformation change in the active site, preventing binding with the substrate

alveolar dead space

air space within alveoli that are unable to participate in gas exchange

alveolar duct

small tube that leads from the terminal bronchiole to the respiratory bronchiole and is the point of attachment for alveoli

alveolar macrophage

immune system cell of the alveolus that removes debris and pathogens

alveolar pore

opening that allows airflow between neighboring alveoli

alveolar sac

cluster of alveoli

alveolus

small, grape-like sac that performs gas exchange in the lungs

amino acid

a monomer of a protein

amygdala

a structure within the limbic system that processes fear

amylase

an enzyme found in saliva and secreted by the pancreas that converts carbohydrates to maltose

anabolic

describes the pathway that requires a net energy input to synthesize complex molecules from simpler ones

anabolism

assembly of more complex molecules from simpler molecules

anaerobic cellular respiration

the use of an electron acceptor other than oxygen to complete metabolism using electron transport-based chemiosmosis

anaphase

the stage of mitosis during which sister chromatids are separated from each other

anastomosis

(plural = anastomoses) area where vessels unite to allow blood to circulate even if there may be partial blockage in another branch

anatomical dead space

air space present in the airway that never reaches the alveoli and therefore never participates in gas exchange

anemia

deficiency of red blood cells or hemoglobin

angiotensin converting enzyme (ACE)

enzyme that converts angiotensin I to angiotensin II

angiotensin I

product in the renin-angiotensin-aldosterone pathway

angiotensin II

molecule that affects different organs to increase blood pressure

anion

a negative ion formed by gaining electrons

anterior cardiac veins

vessels that parallel the small cardiac arteries and drain the anterior surface of the right ventricle; bypass the coronary sinus and drain directly into the right atrium

anterior interventricular artery

(also, left anterior descending artery or LAD) major branch of the left coronary artery that follows the anterior interventricular sulcus

anterior interventricular sulcus

sulcus located between the left and right ventricles on the anterior surface of the heart

anti-diuretic hormone (ADH)

hormone that prevents the loss of water

antibodies

(also, immunoglobulins or gamma globulins) antigen-specific proteins produced by specialized B lymphocytes that protect the body by binding to foreign objects such as bacteria and viruses

antibody
a protein that is produced by plasma cells after stimulation by an antigen; also known as an immunoglobulin

antigen
a macromolecule that reacts with cells of the immune system and which may or may not have a stimulatory effect

antigen-presenting cell (APC)
an immune cell that detects, engulfs, and informs the adaptive immune response about an infection by presenting the processed antigen on its cell surface

anus
the exit point of the digestive system for waste material

aortic valve
(also, aortic semilunar valve) valve located at the base of the aorta

apex
tip of the external nose

apneustic center
network of neurons within the pons that stimulate the neurons in the dorsal respiratory group; controls the depth of inspiration

applied science
a form of science that solves real-world problems

arcuate artery
artery that branches from the interlobar artery and arches over the base of the renal pyramids

arteriole
(also, resistance vessel) very small artery that leads to a capillary

arteriovenous anastomosis
short vessel connecting an arteriole directly to a venule and bypassing the capillary beds

artery
blood vessel that conducts blood away from the heart; may be a conducting or distributing vessel

artificial pacemaker
medical device that transmits electrical signals to the heart to ensure that it contracts and pumps blood to the body

ascending limb
part of the loop of Henle that ascends from the renal medulla to the renal cortex

atmospheric pressure
amount of force that is exerted by gases in the air surrounding any given surface

atom
a basic unit of matter that cannot be broken down by normal chemical reactions

atomic number
the number of protons in an atom

ATP
(also, adenosine triphosphate) the cell's energy currency

ATP synthase
a membrane-embedded protein complex that regenerates ATP from ADP with energy from protons diffusing through it

atrioventricular (AV) node
clump of myocardial cells located in the inferior portion of the right atrium within the atrioventricular septum; receives the impulse from the SA node, pauses, and then transmits it into specialized conducting cells within the interventricular septum

atrioventricular bundle
(also, bundle of His) group of specialized myocardial conductile cells that transmit the impulse from the AV node through the interventricular septum; form the left and right atrioventricular bundle branches

atrioventricular bundle branches
(also, left or right bundle branches) specialized myocardial conductile cells that arise from the bifurcation of the atrioventricular bundle and pass through the interventricular septum; lead to the Purkinje fibers and also to the right papillary muscle via the moderator band

atrioventricular septum

cardiac septum located between the atria and ventricles; atrioventricular valves are located here

atrioventricular valves

one-way valves located between the atria and ventricles; the valve on the right is called the tricuspid valve, and the one on the left is the mitral or bicuspid valve

atrium

(plural = atria) upper or receiving chamber of the heart that pumps blood into the lower chambers just prior to their contraction; the right atrium receives blood from the systemic circuit that flows into the right ventricle; the left atrium receives blood from the pulmonary circuit that flows into the left ventricle

audition

sense of hearing

auricle

extension of an atrium visible on the superior surface of the heart

autonomic nervous system

the part of the peripheral nervous system that controls bodily functions

autorhythmicity

ability of cardiac muscle to initiate its own electrical impulse that triggers the mechanical contraction that pumps blood at a fixed pace without nervous or endocrine control

axon

a tube-like structure that propagates a signal from a neuron's cell body to axon terminals

axon hillock

electrically sensitive structure on the cell body of a neuron that integrates signals from multiple neuronal connections

axon terminal

structure on the end of an axon that can form a synapse with another neuron

axon

tube-like structure that propagates a signal from a neuron's cell body to axon terminals

B

B cell

a lymphocyte that matures in the bone marrow

Bachmann's bundle

(also, interatrial band) group of specialized conducting cells that transmit the impulse directly from the SA node in the right atrium to the left atrium

basal ganglia

an interconnected collections of cells in the brain that are involved in movement and motivation

base

a substance that absorbs hydrogen ions and therefore raises pH

basic science

science that seeks to expand knowledge regardless of the short-term application of that knowledge

basilar membrane

stiff structure in the cochlea that indirectly anchors auditory receptors

bicuspid valve

(also, mitral valve or left atrioventricular valve) valve located between the left atrium and ventricle; consists of two flaps of tissue

bile

a digestive juice produced by the liver; important for digestion of lipids

bilirubin

yellowish bile pigment produced when iron is removed from heme and is further broken down into waste products

biliverdin

green bile pigment produced when the non-iron portion of heme is degraded into a waste product; converted to bilirubin in the liver

bioenergetics

the concept of energy flow through living systems

biology

the study of living organisms and their interactions with one another and their environments

biosphere

a collection of all ecosystems on Earth

bipolar neuron

neuron with two processes from the cell body, typically in opposite directions

blood

liquid connective tissue composed of formed elements—erythrocytes, leukocytes, and platelets—and a fluid extracellular matrix called plasma; component of the cardiovascular system

Bohr effect

relationship between blood pH and oxygen dissociation from hemoglobin

bolus

a mass of food resulting from chewing action and wetting by saliva

bone

hard, dense connective tissue that forms the structural elements of the skeleton

Bowman's capsule

structure that encloses the glomerulus

Boyle's law

relationship between volume and pressure as described by the formula: $P_1V_1 = P_2V_2$

brainstem

a portion of brain that connects with the spinal cord; controls basic nervous system functions like breathing and swallowing

bridge

portion of the external nose that lies in the area of the nasal bones

bronchial tree

collective name for the multiple branches of the bronchi and bronchioles of the respiratory system

bronchiole

branch of bronchi that are 1 mm or less in diameter and terminate at alveolar sacs

bronchus

tube connected to the trachea that branches into many subsidiaries and provides a passageway for air to enter and leave the lungs

buffer

a solution that resists a change in pH by absorbing or releasing hydrogen or hydroxide ions

buffy coat

thin, pale layer of leukocytes and platelets that separates the erythrocytes from the plasma in a sample of centrifuged blood

bulbourethral gland

the paired glands in the human male that produce a secretion that cleanses the urethra prior to ejaculation

bundle of His

(also, atrioventricular bundle) group of specialized myocardial conductile cells that transmit the impulse from the AV node through the interventricular septum; form the left and right atrioventricular bundle branches

C

calyx

structure that connects the renal pelvis to the renal medulla

canaliculi

(singular = canaliculus) channels within the bone matrix that house one of an osteocyte's many cytoplasmic extensions that it uses to communicate and receive nutrients

candela

(cd) unit of measurement of luminous intensity (brightness)

capacitance

ability of a vein to distend and store blood

capacitance vessels

veins

capillary bed

network of 10–100 capillaries connecting arterioles to venules

capillary

smallest of blood vessels where physical exchange occurs between the blood and tissue cells surrounded by interstitial fluid

carbaminohemoglobin

bound form of hemoglobin and carbon dioxide

carbaminohemoglobin

compound of carbon dioxide and hemoglobin, and one of the ways in which carbon dioxide is carried in the blood

carbohydrate

a biological macromolecule in which the ratio of carbon to hydrogen to oxygen is 1:2:1; carbohydrates serve as energy sources and structural support in cells

carbonic anhydrase (CA)

enzyme that catalyzes the reaction that causes carbon dioxide and water to form carbonic acid

cardiac cycle

period of time between the onset of atrial contraction (atrial systole) and ventricular relaxation (ventricular diastole)

cardiac muscle

tissue muscle tissue found only in the heart; cardiac contractions pump blood throughout the body and maintain blood pressure

cardiac notch

depression in the medial surface of the inferior lobe of the left lung where the apex of the heart is located

cardiac skeleton

(also, skeleton of the heart) reinforced connective tissue located within the atrioventricular septum; includes four rings that surround the openings between the atria and ventricles, and the openings to the pulmonary trunk and aorta; the point of attachment for the heart valves

cardiomyocyte

muscle cell of the heart

cartilage

semi-rigid connective tissue found on the skeleton in areas where flexibility and smooth surfaces support movement

catabolic

describes the pathway in which complex molecules are broken down into simpler ones, yielding energy as an additional product of the reaction

catabolism

breaking down of more complex molecules into simpler molecules

cation

a positive ion formed by losing electrons

cell cycle checkpoints

mechanisms that monitor the preparedness of a eukaryotic cell to advance through the various cell cycle stages

cell cycle

the ordered sequence of events that a cell passes through between one cell division and the next

cell plate

a structure formed during plant-cell cytokinesis by Golgi vesicles fusing at the metaphase plate; will ultimately lead to formation of a cell wall to separate the two daughter cells

cell

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

cell

the smallest fundamental unit of structure and function in living things

cell wall

a rigid cell covering made of cellulose in plants, peptidoglycan in bacteria, non-peptidoglycan compounds in Archaea, and chitin in fungi that protects the cell, provides structural support, and gives shape to the cell

cell-mediated immune response

an adaptive immune response that is controlled by T cells

cellulose

a polysaccharide that makes up the cell walls of plants and provides structural support to the cell

central canal

longitudinal channel in the center of each osteon; contains blood vessels, nerves, and lymphatic vessels; also known as the Haversian canal

central chemoreceptor

one of the specialized receptors that are located in the brain that sense changes in hydrogen ion, oxygen, or carbon dioxide concentrations in the brain

central nervous system (CNS)

the nervous system made up of the brain and spinal cord; covered with three layers of protective meninges

central vacuole

a large plant cell organelle that acts as a storage compartment, water reservoir, and site of macromolecule degradation

centriole

a paired rod-like structure constructed of microtubules at the center of each animal cell centrosome

cerebellum

the brain structure involved in posture, motor coordination, and learning new motor actions

cerebral cortex

the outermost sheet of brain tissue; involved in many higher-order functions

cerebrospinal fluid (CSF)

a clear liquid that surrounds the brain and fills its ventricles and acts as a shock absorber

chemical bond

an interaction between two or more of the same or different elements that results in the formation of molecules

chemiosmosis

the movement of hydrogen ions down their electrochemical gradient across a membrane through ATP synthase to generate ATP

chiasmata

(singular = *chiasma*) the structure that forms at the crossover points after genetic material is exchanged

chitin

a type of carbohydrate that forms the outer skeleton of arthropods, such as insects and crustaceans, and the cell walls of fungi

chloride shift

facilitated diffusion that exchanges bicarbonate (HCO_3^-) with chloride (Cl^-) ions

chloroplast

a plant cell organelle that carries out photosynthesis

chordae tendineae

string-like extensions of tough connective tissue that extend from the flaps of the atrioventricular valves to the papillary muscles

chyme

a mixture of partially digested food and stomach juices

cilium

(plural: cilia) a short, hair-like structure that extends from the plasma membrane in large numbers and is used to move an entire cell or move substances along the outer surface of the cell

circadian

describes a time cycle about one day in length

circumflex artery

branch of the left coronary artery that follows coronary sulcus

citric acid cycle

a series of enzyme-catalyzed chemical reactions of central importance in all living cells that harvests the energy in carbon-carbon bonds of sugar molecules to generate ATP; the citric acid cycle is an aerobic metabolic pathway because it requires oxygen in later reactions to proceed

cleavage furrow

a constriction formed by the actin ring during animal-cell cytokinesis that leads to cytoplasmic division

clitoris

a sensory and erectile structure in female mammals, homologous to the male penis, stimulated during sexual arousal

cochlea

whorled structure that contains receptors for transduction of the mechanical wave into an electrical signal

codon

three consecutive nucleotides in mRNA that specify the addition of a specific amino acid or the release of a polypeptide chain during translation

cohesion

the intermolecular forces between water molecules caused by the polar nature of water; creates surface tension

colon

the largest portion of the large intestine consisting of the ascending colon, transverse colon, and descending colon

community

a set of populations inhabiting a particular area

compact bone

dense osseous tissue that can withstand compressive forces

competitive inhibition

a general mechanism of enzyme activity regulation in which a molecule other than the enzyme's substrate is able to bind the active site and prevent the substrate itself from binding, thus inhibiting the overall rate of reaction for the enzyme

complement system

an array of approximately 20 soluble proteins of the innate immune system that enhance phagocytosis, bore holes in pathogens, and recruit lymphocytes

concentration gradient

an area of high concentration across from an area of low concentration

conducting zone

region of the respiratory system that includes the organs and structures that provide passageways for air and are not directly involved in gas exchange

cone

weakly photosensitive, chromatic, cone-shaped neuron in the fovea of the retina that detects bright light and is used in daytime color vision

continuous capillary

most common type of capillary, found in virtually all tissues except epithelia and cartilage; contains very small gaps in the endothelial lining that permit exchange

control

a part of an experiment that does not change during the experiment

cornea

transparent layer over the front of the eye that helps focus light waves

coronary arteries

branches of the ascending aorta that supply blood to the heart; the left coronary artery feeds the left side of the heart, the left atrium and ventricle, and the interventricular septum; the right coronary artery feeds the right atrium, portions of both ventricles, and the heart conduction system

coronary sinus

large, thin-walled vein on the posterior surface of the heart that lies within the atrioventricular sulcus and drains the heart myocardium directly into the right atrium

coronary sulcus

sulcus that marks the boundary between the atria and ventricles

coronary veins

vessels that drain the heart and generally parallel the large surface arteries

corpus callosum

a thick nerve bundle that connects the cerebral hemispheres

corpus luteum

the endocrine tissue that develops from an ovarian follicle after ovulation; secretes progesterone and estrogen during pregnancy

cortex (animal)

outer layer of an organ like the kidney or adrenal gland

cortical nephron

nephron that lies in the renal cortex

cortical radiate artery

artery that radiates from the arcuate arteries into the renal cortex

countercurrent exchanger

peritubular capillary network that allows exchange of solutes and water from the renal tubules

countercurrent multiplier

osmotic gradient in the renal medulla that is responsible for concentration of urine

covalent bond

a type of strong bond between two or more of the same or different elements; forms when electrons are shared between elements

cricoid cartilage

portion of the larynx composed of a ring of cartilage with a wide posterior region and a thinner anterior region; attached to the esophagus

cross matching

blood test for identification of blood type using antibodies and small samples of blood

crossing over

(also, recombination) the exchange of genetic material between homologous chromosomes resulting in chromosomes that incorporate genes from both parents of the organism forming reproductive cells

cytokine

a chemical messenger that regulates cell differentiation, proliferation, and gene expression to effect immune responses

cytokinesis

the division of the cytoplasm following mitosis to form two daughter cells

cytoplasm

the entire region between the plasma membrane and the nuclear envelope, consisting of organelles suspended in the gel-like cytosol, the cytoskeleton, and various chemicals

cytoskeleton

the network of protein fibers that collectively maintains the shape of the cell, secures some organelles in specific positions, allows cytoplasm and vesicles to move within the cell, and enables unicellular organisms to move

cytosol

the gel-like material of the cytoplasm in which cell structures are suspended

cytotoxic T lymphocyte (TC)

an adaptive immune cell that directly kills infected cells via enzymes, and that releases cytokines to enhance the immune response

D

Dalton's law

statement of the principle that a specific gas type in a mixture exerts its own pressure, as if that specific gas type was not part of a mixture of gases

deductive reasoning

a form of logical thinking that uses a general statement to forecast specific results

denaturation

the loss of shape in a protein as a result of changes in temperature, pH, or exposure to chemicals

dendrite

a structure that extends away from the cell body to receive messages from other neurons

dendrite

structure that extends away from the cell body to receive messages from other neurons

dendritic cell

an immune cell that processes antigen material and presents it on the surface of its cell in MHC class II molecules and induces an immune response in other cells

deoxyhemoglobin

molecule of hemoglobin without an oxygen molecule bound to it

deoxyribonucleic acid (DNA)

a double-stranded polymer of nucleotides that carries the hereditary information of the cell

deoxyribose

a five-carbon sugar molecule with a hydrogen atom rather than a hydroxyl group in the 2' position; the sugar component of DNA nucleotides

depolarization

a change in the membrane potential to a less negative value

depolarization

change in the membrane potential to a less negative value

descending limb

part of the loop of Henle that descends from the renal cortex into the renal medulla

descriptive science

a form of science that aims to observe, explore, and find things out

desmosome

a linkage between adjacent epithelial cells that forms when cadherins in the plasma membrane attach to intermediate filaments

development

changes an organism goes through during its life

diaphysis

tubular shaft that runs between the proximal and distal ends of a long bone

diastole

period of time when the heart muscle is relaxed and the chambers fill with blood

differentiation

process by which unspecialized cells become specialized in structure and function

diffusion

a passive process of transport of low-molecular weight material down its concentration gradient

diploid

describes a cell, nucleus, or organism containing two sets of chromosomes ($2n$)

diploë

layer of spongy bone, that is sandwiched between two the layers of compact bone found in flat bones

disaccharide

two sugar monomers that are linked together by a peptide bond

distal convoluted tubule (DCT)

part of the renal tubule that is the most distant from the glomerulus

DNA ligase

the enzyme that catalyzes the joining of DNA fragments together

DNA polymerase

an enzyme that synthesizes a new strand of DNA complementary to a template strand

dorsal respiratory group (DRG)

region of the medulla oblongata that stimulates the contraction of the diaphragm and intercostal muscles to induce inspiration

dorsum nasi

intermediate portion of the external nose that connects the bridge to the apex and is supported by the nasal bone

double helix

the molecular shape of DNA in which two strands of nucleotides wind around each other in a spiral shape

down-regulation

a decrease in the number of hormone receptors in response to increased hormone levels

E

ecosystem

all living things in a particular area together with the abiotic, nonliving parts of that environment

ectotherm

an organism that relies primarily on environmental heat sources to maintain its body temperature

effector cell

a lymphocyte that has differentiated, such as a B cell, plasma cell, or cytotoxic T cell

efferent arteriole

arteriole that exits from the glomerulus

elastic artery

(also, conducting artery) artery with abundant elastic fibers located closer to the heart, which maintains the pressure gradient and conducts blood to smaller branches

electrocardiogram (ECG)

surface recording of the electrical activity of the heart that can be used for diagnosis of irregular heart function; also abbreviated as EKG

electrochemical gradient

a gradient produced by the combined forces of the electrical gradient and the chemical gradient

electron

a negatively charged particle that resides outside of the nucleus in the electron orbital; lacks functional mass and has a charge of –1

electron transfer

the movement of electrons from one element to another

electron transport chain

a series of four large, multi-protein complexes embedded in the inner mitochondrial membrane that accepts electrons from donor compounds and harvests energy from a series of chemical reactions to generate a hydrogen ion gradient across the membrane

element

one of 118 unique substances that cannot be broken down into smaller substances and retain the characteristic of that substance; each element has a specified number of protons and unique properties

end diastolic volume (EDV)

(also, preload) the amount of blood in the ventricles at the end of atrial systole just prior to ventricular contraction

end systolic volume (ESV)

amount of blood remaining in each ventricle following systole

endergonic

describes a chemical reaction that results in products that store more chemical potential energy than the reactants

endocardium

innermost layer of the heart lining the heart chambers and heart valves; composed of endothelium reinforced with a thin layer of connective tissue that binds to the myocardium

endochondral ossification

process in which bone forms by replacing hyaline cartilage

endocrine gland

the gland that secretes hormones into the surrounding interstitial fluid, which then diffuse into blood and are carried to various organs and tissues within the body

endocytosis

a type of active transport that moves substances, including fluids and particles, into a cell

endomembrane system

the group of organelles and membranes in eukaryotic cells that work together to modify, package, and transport lipids and proteins

endoplasmic reticulum (ER)

a series of interconnected membranous structures within eukaryotic cells that collectively modify proteins and synthesize lipids

endothelium

layer of smooth, simple squamous epithelium that lines the endocardium and blood vessels

endotherm

an organism that relies primarily on internal heat sources to maintain its body temperature

enzyme

a catalyst in a biochemical reaction that is usually a complex or conjugated protein

enzyme

a molecule that catalyzes a biochemical reaction

epicardial coronary arteries

surface arteries of the heart that generally follow the sulci

epicardium

innermost layer of the serous pericardium and the outermost layer of the heart wall

epiglottis

leaf-shaped piece of elastic cartilage that is a portion of the larynx that swings to close the trachea during swallowing

epiphyseal line

completely ossified remnant of the epiphyseal plate

epiphyseal plate

(also, growth plate) sheet of hyaline cartilage in the metaphysis of an immature bone; replaced by bone tissue as the organ grows in length

epiphysis

wide section at each end of a long bone; filled with spongy bone and red marrow

erythrocyte

(also, red blood cell) mature myeloid blood cell that is composed mostly of hemoglobin and functions primarily in the transportation of oxygen and carbon dioxide

esophagus

a tubular organ that connects the mouth to the stomach

essential nutrient

a nutrient that cannot be synthesized by the body; it must be obtained from food

estrogen

a reproductive hormone in females that assists in endometrial regrowth, ovulation, and calcium absorption

eukaryote

an organism with cells that have nuclei and membrane-bound organelles

eukaryotic cell

a cell that has a membrane-bound nucleus and several other membrane-bound compartments or sacs

evaporation

the release of water molecules from liquid water to form water vapor

evolution

the process of gradual change in a population that can also lead to new species arising from older species

excitatory postsynaptic potential (EPSP)

depolarization of a postsynaptic membrane caused by neurotransmitter molecules released from a presynaptic cell

exergonic

describes a chemical reaction that results in products with less chemical potential energy than the reactants, plus the release of free energy

exocrine gland

the gland that secretes chemicals through ducts that lead to skin surfaces, body cavities, and organ cavities.

exocytosis

a process of passing material out of a cell

exon

a sequence present in protein-coding mRNA after completion of pre-mRNA splicing

expiration

(also, exhalation) process that causes the air to leave the lungs

expiratory reserve volume (ERV)

amount of air that can be forcefully exhaled after a normal tidal exhalation

external elastic membrane

membrane composed of elastic fibers that separates the tunica media from the tunica externa; seen in larger arteries

external nose

region of the nose that is easily visible to others

external respiration

gas exchange that occurs in the alveoli

extracellular matrix

the material, primarily collagen, glycoproteins, and proteoglycans, secreted from animal cells that holds cells together as a tissue, allows cells to communicate with each other, and provides mechanical protection and anchoring for cells in the tissue

F

facilitated transport

a process by which material moves down a concentration gradient (from high to low concentration) using integral membrane proteins

falsifiable

able to be disproven by experimental results

fat

a lipid molecule composed of three fatty acids and a glycerol (triglyceride) that typically exists in a solid form at room temperature

fauces

portion of the posterior oral cavity that connects the oral cavity to the oropharynx

feedback inhibition

a mechanism of enzyme activity regulation in which the product of a reaction or the final product of a series of sequential reactions inhibits an enzyme for an earlier step in the reaction series

fenestrated capillary

type of capillary with pores or fenestrations in the endothelium that allow for rapid passage of certain small materials

fermentation

the steps that follow the partial oxidation of glucose via glycolysis to regenerate NAD^+; occurs in the absence of oxygen and uses an organic compound as the final electron acceptor

ferritin

protein-containing storage form of iron found in the bone marrow, liver, and spleen

fertilization

the union of two haploid cells typically from two individual organisms

fibrinogen

plasma protein produced in the liver and involved in blood clotting

fibroelastic membrane

specialized membrane that connects the ends of the C-shape cartilage in the trachea; contains smooth muscle fibers

flagellum

(plural: flagella) the long, hair-like structure that extends from the plasma membrane and is used to move the cell

fluid mosaic model

a model of the structure of the plasma membrane as a mosaic of components, including phospholipids, cholesterol, proteins, and glycolipids, resulting in a fluid rather than static character

follicle stimulating hormone (FSH)

a reproductive hormone that causes sperm production in men and follicle development in women

foramen ovale

opening in the fetal heart that allows blood to flow directly from the right atrium to the left atrium, bypassing the fetal pulmonary circuit

forced breathing

(also, hyperpnea) mode of breathing that occurs during exercise or by active thought that requires muscle contraction for both inspiration and expiration

formed elements

cellular components of blood; that is, erythrocytes, leukocytes, and platelets

fossa ovalis

oval-shaped depression in the interatrial septum that marks the former location of the foramen ovale

fovea

region in the center of the retina with a high density of photoreceptors and which is responsible for acute vision

frontal lobe

the part of the cerebral cortex that contains the motor cortex and areas involved in planning, attention, and language

functional residual capacity (FRC)

sum of ERV and RV, which is the amount of air that remains in the lungs after a tidal expiration

G

G0 phase

a cell-cycle phase distinct from the G_1 phase of interphase; a cell in G_0 is not preparing to divide

G1 phase

(also, first gap) a cell-cycle phase; first phase of interphase centered on cell growth during mitosis

G2 phase

(also, second gap) a cell-cycle phase; third phase of interphase where the cell undergoes the final preparations for mitosis

gallbladder

the organ that stores and concentrates bile

gamete

a haploid reproductive cell or sex cell (sperm or egg)

gap junction

a channel between two adjacent animal cells that allows ions, nutrients, and other low-molecular weight substances to pass between the cells, enabling the cells to communicate

gene

the physical and functional unit of heredity; a sequence of DNA that codes for a specific peptide or RNA molecule

genetic code

the amino acids that correspond to three-nucleotide codons of mRNA

genome

the entire genetic complement (DNA) of an organism

gestation period

the length of time of development, from conception to birth, of the young of a viviparous animal

gestation

the development before birth of a viviparous animal

glia

(also, glial cells) cells that provide support functions for neurons

glia

(also, glial cells) the cells that provide support functions for neurons

globin

heme-containing globular protein that is a constituent of hemoglobin

globulins

heterogeneous group of plasma proteins that includes transport proteins, clotting factors, immune proteins, and others

glomerular filtration

filtration of blood in the glomerular capillary network into the glomerulus

glomerular filtration rate (GFR)

amount of filtrate formed by the glomerulus per minute

glomerulus (renal)

part of the renal corpuscle that contains the capillary network

glomerulus

in the olfactory bulb, one of the two neural clusters that receives signals from one type of olfactory receptor

glottis

opening between the vocal folds through which air passes when producing speech

glycogen

a storage carbohydrate in animals

glycolysis

the process of breaking glucose into two three-carbon molecules with the production of ATP and NADH

Golgi apparatus

a eukaryotic organelle made up of a series of stacked membranes that sorts, tags, and packages lipids and proteins for distribution

gonadotropin-releasing hormone (GnRH)

a hormone from the hypothalamus that causes the release of FSH and LH from the anterior pituitary

great cardiac vein

vessel that follows the interventricular sulcus on the anterior surface of the heart and flows along the coronary sulcus into the coronary sinus on the posterior surface; parallels the anterior interventricular artery and drains the areas supplied by this vessel

growth

process of increasing in size

gustation

sense of taste

H

Haldane effect

relationship between the partial pressure of oxygen and the affinity of hemoglobin for carbon dioxide

haploid

describes a cell, nucleus, or organism containing one set of chromosomes (n)

heart block

interruption in the normal conduction pathway

heart sounds

sounds heard via auscultation with a stethoscope of the closing of the atrioventricular valves ("lub") and semilunar valves ("dub")

heat energy

the energy transferred from one system to another that is not work

helicase

an enzyme that helps to open up the DNA helix during DNA replication by breaking the hydrogen bonds

helper T lymphocyte (TH)

a cell of the adaptive immune system that binds APCs via MHC class II molecules and stimulates B cells or secretes cytokines to initiate the immune response

hematocrit

(also, packed cell volume) volume percentage of erythrocytes in a sample of centrifuged blood

hematopoiesis

production of blood cells, which occurs in the red marrow of the bones

heme

red, iron-containing pigment to which oxygen binds in hemoglobin

hemoglobin

oxygen-carrying compound in erythrocytes

hemolysis

destruction (lysis) of erythrocytes and the release of their hemoglobin into circulation

hemolytic disease of the newborn (HDN)

(also, erythroblastosis fetalis) disorder causing agglutination and hemolysis in an Rh^+ fetus or newborn of an Rh^- mother

hemosiderin

protein-containing storage form of iron found in the bone marrow, liver, and spleen

Henry's law

statement of the principle that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas

hilum

region in the renal pelvis where blood vessels, nerves, and ureters bunch before entering or exiting the kidney

hippocampus

the brain structure in the temporal lobe involved in processing memories

hole

opening or depression in a bone

homeostasis

the ability of an organism to maintain constant internal conditions

homologous chromosomes

chromosomes of the same length with genes in the same location; diploid organisms have pairs of homologous chromosomes, and the members of each pair come from different parents

hormone

a chemical released by cells in one area of the body that affects cells in other parts of the body

hormone

a chemical signaling molecule, usually a protein or steroid, secreted by an endocrine gland or group of endocrine cells; acts to control or regulate specific physiological processes

host

an organism that is invaded by a pathogen or parasite

human beta chorionic gonadotropin (β-HCG)

a hormone produced by the chorion of the zygote that helps to maintain the corpus luteum and elevated levels of progesterone

humoral immune response

the adaptive immune response that is controlled by activated B cells and antibodies

hydrogen bond

a weak bond between partially positively charged hydrogen atoms and partially negatively charged elements or molecules

hydrophilic

describes a substance that dissolves in water; water-loving

hydrophobic

describes a substance that does not dissolve in water; water-fearing

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

hyperpolarization

change in the membrane potential to a more negative value

hypertonic

describes a solution in which extracellular fluid has higher osmolarity than the fluid inside the cell

hypertrophic cardiomyopathy

pathological enlargement of the heart, generally for no known reason

hypothalamus

the brain structure that controls hormone release and body homeostasis

hypothesis

a suggested explanation for an event, which can be tested

hypothesis-based science

a form of science that begins with a specific explanation that is then tested

hypotonic

describes a solution in which extracellular fluid has lower osmolarity than the fluid inside the cell

hypoxemia

below-normal level of oxygen saturation of blood (typically <95 percent)

I

immune tolerance

an acquired ability to prevent an unnecessary or harmful immune response to a detected foreign body known not to cause disease

immunoglobulins

(also, antibodies or gamma globulins) antigen-specific proteins produced by specialized B lymphocytes that protect the body by binding to foreign objects such as bacteria and viruses

incus

(also, anvil) second of the three bones of the middle ear

inductive reasoning

a form of logical thinking that uses related observations to arrive at a general conclusion

inferior vena cava

large systemic vein that returns blood to the heart from the inferior portion of the body

inferior vena cava

one of the main veins in the human body

inflammation

the localized redness, swelling, heat, and pain that results from the movement of leukocytes through opened capillaries to a site of infection

inhibin

a hormone made by Sertoli cells, provides negative feedback to hypothalamus in control of FSH and GnRH release

inhibitory postsynaptic potential (IPSP)

hyperpolarization of a postsynaptic membrane caused by neurotransmitter molecules released from a presynaptic cell

innate immunity

an immunity that occurs naturally because of genetic factors or physiology, and is not caused by infection or vaccination

inner ear

innermost part of the ear; consists of the cochlea and the vestibular system

inspiration

(also, inhalation) process that causes air to enter the lungs

inspiratory capacity (IC)

sum of the TV and IRV, which is the amount of air that can maximally be inhaled past a tidal expiration

inspiratory reserve volume (IRV)

amount of air that enters the lungs due to deep inhalation past the tidal volume

interatrial band

(also, Bachmann's bundle) group of specialized conducting cells that transmit the impulse directly from the SA node in the right atrium to the left atrium

interatrial septum

cardiac septum located between the two atria; contains the fossa ovalis after birth

intercalated disc

physical junction between adjacent cardiac muscle cells; consisting of desmosomes, specialized linking proteoglycans, and gap junctions that allow passage of ions between the two cells

interferon

a cytokine that inhibits viral replication

interkinesis

a period of rest that may occur between meiosis I and meiosis II; there is no replication of DNA during interkinesis

interlobar artery

artery that branches from the segmental artery and travels in between the renal lobes

internal elastic membrane

membrane composed of elastic fibers that separates the tunica intima from the tunica media; seen in larger arteries

internal respiration

gas exchange that occurs at the level of body tissues

internodal pathways

specialized conductile cells within the atria that transmit the impulse from the SA node throughout the myocardial cells of the atrium and to the AV node

interphase

the period of the cell cycle leading up to mitosis; includes G_1, S, and G_2 phases; the interim between two consecutive cell divisions

interstitial cell of Leydig

a cell type found next to the seminiferous tubules that makes testosterone

interstitial fluid

the fluid found between cells in the body, similar in constitution to the fluid component of blood, but without the high concentrations of proteins

interstitial/Leydig cell

a cell type found next to the seminiferous tubules that makes testosterone

interventricular septum

cardiac septum located between the two ventricles

intra-alveolar pressure

(intrapulmonary pressure) pressure of the air within the alveoli

intracellular hormone receptor

a hormone receptor in the cytoplasm or nucleus of a cell

intrapleural pressure

pressure of the air within the pleural cavity

intron

non–protein-coding intervening sequences that are spliced from mRNA during processing

ion

an atom or compound that does not contain equal numbers of protons and electrons, and therefore has a net charge

ionic bond

a chemical bond that forms between ions of opposite charges

iris

pigmented, circular muscle at the front of the eye that regulates the amount of light entering the eye

isotonic

describes a solution in which the extracellular fluid has the same osmolarity as the fluid inside the cell

isotope

one or more forms of an element that have different numbers of neutrons

isovolumic contraction

(also, isovolumetric contraction) initial phase of ventricular contraction in which tension and pressure in the ventricle increase, but no blood is pumped or ejected from the heart

isovolumic ventricular relaxation phase

initial phase of the ventricular diastole when pressure in the ventricles drops below pressure in the two major arteries, the pulmonary trunk, and the aorta, and blood attempts to flow back into the ventricles, producing the dicrotic notch of the ECG and closing the two semilunar valves

J

juxtaglomerular cell

cell in the afferent and efferent arterioles that responds to stimuli from the macula densa

juxtamedullary nephron

nephron that lies in the cortex but close to the renal medulla

K

kidney

organ that performs excretory and osmoregulatory functions

kidney

the organ that performs excretory and osmoregulatory functions

kinetic energy

the type of energy associated with objects in motion

kinetochore

a protein structure in the centromere of each sister chromatid that attracts and binds spindle microtubules during prometaphase

L

labia majora

the large folds of tissue covering inguinal area

labia minora

the smaller folds of tissue within labia majora

labyrinth

bony, hollow structure that is the most internal part of the ear; contains the sites of transduction of auditory and vestibular information

lacunae

(singular = lacuna) spaces in a bone that house an osteocyte

lagging strand

during replication of the 3' to 5' strand, the strand that is replicated in short fragments and away from the replication fork

large intestine

a digestive system organ that reabsorbs water from undigested material and processes waste matter

laryngeal prominence

region where the two lamina of the thyroid cartilage join, forming a protrusion known as "Adam's apple"

laryngopharynx

portion of the pharynx bordered by the oropharynx superiorly and esophagus and trachea inferiorly; serves as a route for both air and food

larynx

cartilaginous structure that produces the voice, prevents food and beverages from entering the trachea, and regulates the volume of air that enters and leaves the lungs

leading strand

the strand that is synthesized continuously in the 5' to 3' direction that is synthesized in the direction of the replication fork

left atrioventricular valve

(also, mitral valve or bicuspid valve) valve located between the left atrium and ventricle; consists of two flaps of tissue

lens

transparent, convex structure behind the cornea that helps focus light waves on the retina

life science

a field of science, such as biology, that studies living things

limbic system

a connected brain area that processes emotion and motivation

lingual tonsil

lymphoid tissue located at the base of the tongue

lipids

a class of macromolecules that are nonpolar and insoluble in water

litmus paper

filter paper that has been treated with a natural water-soluble dye so it can be used as a pH indicator

liver

an organ that produces bile for digestion and processes vitamins and lipids

lobes of the kidney

renal pyramid along with the adjoining cortical region

locus

the position of a gene on a chromosome

loop of Henle

part of the renal tubule that loops into the renal medulla

lumen

interior of a tubular structure such as a blood vessel or a portion of the alimentary canal through which blood, chyme, or other substances travel

luteinizing hormone (LH)

a reproductive hormone in both men and women, causes testosterone production in men and ovulation and lactation in women

lymph

the watery fluid present in the lymphatic circulatory system that bathes tissues and organs with protective white blood cells and does not contain erythrocytes

lymphocyte

a type of white blood cell that includes natural killer cells of the innate immune system and B and T cells of the adaptive immune system

lysosome

an 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

M

macromolecule

a large molecule typically formed by the joining of smaller molecules

macromolecule

a large molecule, often formed by polymerization of smaller monomers

macrophage

a large phagocytic cell that engulfs foreign particles and pathogens

macrophage

phagocytic cell of the myeloid lineage; a matured monocyte

macula densa

group of cells that senses changes in sodium ion concentration; present in parts of the renal tubule and collecting ducts

major histocompatibility class (MHC) I

a group of proteins found on the surface of all nucleated cells that signals to immune cells whether the cell is normal or is infected or cancerous; it also provides the appropriate sites into which antigens can be loaded for recognition by lymphocytes

major histocompatibility class (MHC) II molecule

a protein found on the surface of antigen-presenting cells that signals to immune cells whether the cell is normal or is infected or cancerous; it provides the appropriate template into which antigens can be loaded for recognition by lymphocytes

malleus

(also, hammer) first of the three bones of the middle ear

marginal arteries

branches of the right coronary artery that supply blood to the superficial portions of the right ventricle

mass number

the number of protons plus neutrons in an atom

mast cell

a leukocyte that produces inflammatory molecules, such as histamine, in response to large pathogens

matter

anything that has mass and occupies space

meatus

one of three recesses (superior, middle, and inferior) in the nasal cavity attached to the conchae that increase the surface area of the nasal cavity

medulla

middle layer of an organ like the kidney or adrenal gland

medullary cavity

hollow region of the diaphysis; filled with yellow marrow

meiosis I

the first round of meiotic cell division; referred to as reduction division because the resulting cells are haploid

meiosis II

the second round of meiotic cell division following meiosis I; sister chromatids are separated from each other, and the result is four unique haploid cells

membrane potential

a difference in electrical potential between the inside and outside of a cell

membrane potential

difference in electrical potential between the inside and outside of a cell

memory cell

an antigen-specific B or T lymphocyte that does not differentiate into an effector cell during the primary immune response but that can immediately become an effector cell on reexposure to the same pathogen

meninges

(singular: meninx) the membranes that cover and protect the central nervous system

menstrual cycle

the cycle of the degradation and re-growth of the endometrium

mesothelium

simple squamous epithelial portion of serous membranes, such as the superficial portion of the epicardium (the visceral pericardium) and the deepest portion of the pericardium (the parietal pericardium)

metabolism

all the chemical reactions that take place inside cells, including those that use energy and those that release energy

metabolism

sum of all of the body's chemical reactions

metaphase plate

the equatorial plane midway between two poles of a cell where the chromosomes align during metaphase

metaphase

the stage of mitosis during which chromosomes are lined up at the metaphase plate

metarteriole

short vessel arising from a terminal arteriole that branches to supply a capillary bed

microcirculation

blood flow through the capillaries

middle cardiac vein

vessel that parallels and drains the areas supplied by the posterior interventricular artery; drains into the great cardiac vein

middle ear

part of the hearing apparatus that functions to transfer energy from the tympanum to the oval window of the inner ear

mineral

an inorganic, elemental molecule that carries out important roles in the body

mismatch repair

a form of DNA repair in which non-complementary nucleotides are recognized, excised, and replaced with correct nucleotides

mitochondria

(singular: mitochondrion) the cellular organelles responsible for carrying out cellular respiration, resulting in the production of ATP, the cell's main energy-carrying molecule

mitosis

the period of the cell cycle at which the duplicated chromosomes are separated into identical nuclei; includes prophase, prometaphase, metaphase, anaphase, and telophase

mitotic phase

the period of the cell cycle when duplicated chromosomes are distributed into two nuclei and the cytoplasmic contents are divided; includes mitosis and cytokinesis

mitotic spindle

the microtubule apparatus that orchestrates the movement of chromosomes during mitosis

mitral valve

(also, left atrioventricular valve or bicuspid valve) valve located between the left atrium and ventricle; consists of two flaps of tissue

modeling

process, during bone growth, by which bone is resorbed on one surface of a bone and deposited on another

moderator band

band of myocardium covered by endocardium that arises from the inferior portion of the interventricular septum in the right ventricle and crosses to the anterior papillary muscle; contains conductile fibers that carry electrical signals followed by contraction of the heart

molecule

a chemical structure consisting of at least two atoms held together by a chemical bond

monocyte

a type of white blood cell that circulates in the blood and lymph and differentiates into a macrophage after it moves into infected tissue

monosaccharide

a single unit or monomer of carbohydrates

motor end plate

sarcolemma of the muscle fiber that interacts with the neuron

mRNA

messenger RNA; a form of RNA that carries the nucleotide sequence code for a protein sequence that is translated into a polypeptide sequence

murmur

unusual heart sound detected by auscultation; typically related to septal or valve defects

muscular artery

(also, distributing artery) artery with abundant smooth muscle in the tunica media that branches to distribute blood to the arteriole network

mutation

a permanent variation in the nucleotide sequence of a genome

myelin

fatty substance produced by glia that insulates axons

myelin sheath

a cellular extension containing a fatty substance produced by glia that surrounds and insulates axons

myocardial conducting cells

specialized cells that transmit electrical impulses throughout the heart and trigger contraction by the myocardial contractile cells

myocardial contractile cells

bulk of the cardiac muscle cells in the atria and ventricles that conduct impulses and contract to propel blood

myocardium

thickest layer of the heart composed of cardiac muscle cells built upon a framework of primarily collagenous fibers and blood vessels that supply it and the nervous fibers that help to regulate it

myofibril

long cylindrical structures that lie parallel to the muscle fiber

myofilament

small structures that make up myofibrils

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

myosin

contractile protein that interacts with actin for muscle contraction

N

naris

(plural = nares) opening of the nostrils

nasal bone

bone of the skull that lies under the root and bridge of the nose and is connected to the frontal and maxillary bones

nasal septum

wall composed of bone and cartilage that separates the left and right nasal cavities

nasopharynx

portion of the pharynx flanked by the conchae and oropharynx that serves as an airway

natural killer (NK) cell

a lymphocyte that can kill cells infected with viruses or tumor cells

natural science

a field of science that studies the physical world, its phenomena, and processes

nephron

functional unit of the kidney

nephron

the functional unit of the kidney

nervi vasorum

small nerve fibers found in arteries and veins that trigger contraction of the smooth muscle in their walls

neuron

a specialized cell that can receive and transmit electrical and chemical signals

neuron

specialized cell that can receive and transmit electrical and chemical signals

neutron

a particle with no charge that resides in the nucleus of an atom; has a mass of 1

neutrophil

a phagocytic leukocyte that engulfs and digests pathogens

nitrogenous base

a nitrogen-containing molecule that acts as a base; often referring to one of the purine or pyrimidine components of nucleic acids

nodes of Ranvier

gaps in the myelin sheath where the signal is recharged

noncompetitive inhibition

a general mechanism of enzyme activity regulation in which a regulatory molecule binds to a site other than the active site and prevents the active site from binding the substrate; thus, the inhibitor molecule does not compete with the substrate for the active site; allosteric inhibition is a form of noncompetitive inhibition

nonpolar covalent bond

a type of covalent bond that forms between atoms when electrons are shared equally between atoms, resulting in no regions with partial charges as in polar covalent bonds

nontemplate strand

the strand of DNA that is not used to transcribe mRNA; this strand is identical to the mRNA except that T nucleotides in the DNA are replaced by U nucleotides in the mRNA

nuclear envelope

the double-membrane structure that constitutes the outermost portion of the nucleus

nucleic acid

a biological macromolecule that carries the genetic information of a cell and carries instructions for the functioning of the cell

nucleolus

the darkly staining body within the nucleus that is responsible for assembling ribosomal subunits

nucleotide

a monomer of nucleic acids; contains a pentose sugar, a phosphate group, and a nitrogenous base

nucleotide excision repair

a form of DNA repair in which the DNA molecule is unwound and separated in the region of the nucleotide damage, the damaged nucleotides are removed and replaced with new nucleotides using the complementary strand, and the DNA strand is resealed and allowed to rejoin its complement

nucleus

(chemistry) the dense center of an atom made up of protons and (except in the case of a hydrogen atom) neutrons

nucleus

the cell organelle that houses the cell's DNA and directs the synthesis of ribosomes and proteins

nutrient foramen

small opening in the middle of the external surface of the diaphysis, through which an artery enters the bone to provide nourishment

O

occipital lobe

the part of the cerebral cortex that contains visual cortex and processes visual stimuli

octet rule

states that the outermost shell of an element with a low atomic number can hold eight electrons

odorant

airborne molecule that stimulates an olfactory receptor

oil

an unsaturated fat that is a liquid at room temperature

Okazaki fragments

the DNA fragments that are synthesized in short stretches on the lagging strand

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

oogenesis

the process of producing haploid eggs

oral cavity

the point of entry of food into the digestive system

organ

a structure formed of tissues operating together to perform a common function

organ

functionally distinct structure composed of two or more types of tissues

organ of Corti

in the basilar membrane, the site of the transduction of sound, a mechanical wave, to a neural signal

organ system

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

organ system

the higher level of organization that consists of functionally related organs

organelle

a membrane-bound compartment or sac within a cell

organism

an individual living entity

organism

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

oropharynx

portion of the pharynx flanked by the nasopharynx, oral cavity, and laryngopharynx that is a passageway for both air and food

orthopedist

doctor who specializes in diagnosing and treating musculoskeletal disorders and injuries

osmolarity

the total amount of substances dissolved in a specific amount of solution

osmoregulation

the mechanism by which water and solute concentrations are maintained at desired levels

osmosis

the transport of water through a semipermeable membrane from an area of high water concentration to an area of low water concentration across a membrane

osmotic balance

the appropriate values of water and solute concentrations for a healthy organism

osseous tissue

bone tissue; a hard, dense connective tissue that forms the structural elements of the skeleton

ossicle

one of the three bones of the middle ear

ossification

(also, osteogenesis) bone formation

osteoblast

cell responsible for forming new bone

osteoclast

cell responsible for resorbing bone

osteocyte

primary cell in mature bone; responsible for maintaining the matrix

osteogenic cell

undifferentiated cell with high mitotic activity; the only bone cells that divide; they differentiate and develop into osteoblasts

osteon

(also, Haversian system) basic structural unit of compact bone; made of concentric layers of calcified matrix

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

ovarian cycle

the cycle of preparation of egg for ovulation and the conversion of the follicle to the corpus luteum

oviduct

(also, fallopian tube) the muscular tube connecting uterus with ovary area

ovulation

the release of an oocyte from a mature follicle in the ovary of a vertebrate

oxidative phosphorylation

the production of ATP by the transfer of electrons down the electron transport chain to create a proton gradient that is used by ATP synthase to add phosphate groups to ADP molecules

oxygen–hemoglobin dissociation curve

graph that describes the relationship of partial pressure to the binding and disassociation of oxygen to and from heme

oxyhemoglobin

($Hb–O_2$) bound form of hemoglobin and oxygen

oxyhemoglobin

molecule of hemoglobin to which oxygen is bound

P

P wave

component of the electrocardiogram that represents the depolarization of the atria

pacemaker

cluster of specialized myocardial cells known as the SA node that initiates the sinus rhythm

packed cell volume (PCV)

(also, hematocrit) volume percentage of erythrocytes present in a sample of centrifuged blood

palatine tonsil

one of the paired structures composed of lymphoid tissue located anterior to the uvula at the roof of isthmus of the fauces

pancreas

a gland that secretes digestive juices

pancreas
the organ located between the stomach and the small intestine that contains exocrine and endocrine cells

papilla
one of the small bump-like projections from the tongue

papillary muscle
extension of the myocardium in the ventricles to which the chordae tendineae attach

paranasal sinus
one of the cavities within the skull that is connected to the conchae that serve to warm and humidify incoming air, produce mucus, and lighten the weight of the skull; consists of frontal, maxillary, sphenoidal, and ethmoidal sinuses

parasympathetic nervous system
the division of autonomic nervous system that regulates visceral functions during relaxation

parathyroid gland
the gland located on the surface of the thyroid that produces parathyroid hormone

parietal lobe
the part of the cerebral cortex involved in processing touch and the sense of the body in space

partial pressure
force exerted by each gas in a mixture of gases

passive immunity
an immunity that does not result from the activity of the body's own immune cells but by transfer of antibodies from one individual to another

passive transport
a method of transporting material that does not require energy

pathogen
an agent, usually a microorganism, that causes disease in the organisms that they invade

pectinate muscles
muscular ridges seen on the anterior surface of the right atrium

peer-reviewed article
a scientific report that is reviewed by a scientist's colleagues before publication

penis
the male reproductive structure for urine elimination and copulation

pepsin
an enzyme found in the stomach whose main role is protein digestion

perfusion
distribution of blood into the capillaries so the tissues can be supplied

pericardial cavity
cavity surrounding the heart filled with a lubricating serous fluid that reduces friction as the heart contracts

pericardial sac
(also, pericardium) membrane that separates the heart from other mediastinal structures; consists of two distinct, fused sublayers: the fibrous pericardium and the parietal pericardium

pericardium
(also, pericardial sac) membrane that separates the heart from other mediastinal structures; consists of two distinct, fused sublayers: the fibrous pericardium and the parietal pericardium

periodic table of elements
an organizational chart of elements, indicating the atomic number and mass number of each element; also provides key information about the properties of elements

peripheral chemoreceptor
one of the specialized receptors located in the aortic arch and carotid arteries that sense changes in pH, carbon dioxide, or oxygen blood levels

peripheral nervous system (PNS)

the nervous system that serves as the connection between the central nervous system and the rest of the body; consists of the autonomic nervous system and the sensory-somatic nervous system

perirenal fat capsule

fat layer that suspends the kidneys

peristalsis

wave-like movements of muscle tissue

peritubular capillary network

capillary network that surrounds the renal tubule after the efferent artery exits the glomerulus

peroxisome

a small, round organelle that contains hydrogen peroxide, oxidizes fatty acids and amino acids, and detoxifies many poisons

pH scale

a scale ranging from 0 to 14 that measures the approximate concentration of hydrogen ions of a substance

phagocytosis

a process that takes macromolecules that the cell needs from the extracellular fluid; a variation of endocytosis

pharyngeal tonsil

structure composed of lymphoid tissue located in the nasopharynx

pharynx

region of the conducting zone that forms a tube of skeletal muscle lined with respiratory epithelium; located between the nasal conchae and the esophagus and trachea

pheromone

substance released by an animal that can affect the physiology or behavior of other animals

philtrum

concave surface of the face that connects the apex of the nose to the top lip

phosphate group

a molecular group consisting of a central phosphorus atom bound to four oxygen atoms

phospholipid

a major constituent of the membranes of cells; composed of two fatty acids and a phosphate group attached to the glycerol backbone

phylogenetic tree

a diagram showing the evolutionary relationships among biological species based on similarities and differences in genetic or physical traits or both

physical science

a field of science, such as astronomy, physics, and chemistry, that studies nonliving matter

pinna

cartilaginous outer ear

pinocytosis

a process that takes solutes that the cell needs from the extracellular fluid; a variation of endocytosis

pituitary gland

the endocrine gland located at the base of the brain composed of an anterior and posterior region; also called hypophysis

placenta

the organ that supports the transport of nutrients and waste between the mothers and fetus' blood in eutherian mammals

plasma

in blood, the liquid extracellular matrix composed mostly of water that circulates the formed elements and dissolved materials throughout the cardiovascular system

plasma membrane

a phospholipid bilayer with embedded (integral) or attached (peripheral) proteins that separates the internal contents of the cell from its surrounding environment

plasmodesma

(plural: plasmodesmata) a channel that passes between the cell walls of adjacent plant cells, connects their cytoplasm, and allows materials to be transported from cell to cell

platelets

(also, thrombocytes) one of the formed elements of blood that consists of cell fragments broken off from megakaryocytes

pneumotaxic center

network of neurons within the pons that inhibit the activity of the neurons in the dorsal respiratory group; controls rate of breathing

polar covalent bond

a type of covalent bond in which electrons are pulled toward one atom and away from another, resulting in slightly positive and slightly negative charged regions of the molecule

polycythemia

elevated level of hemoglobin, whether adaptive or pathological

polypeptide

a long chain of amino acids linked by peptide bonds

polysaccharide

a long chain of monosaccharides; may be branched or unbranched

population

all individuals within a species living within a specific area

posterior cardiac vein

vessel that parallels and drains the areas supplied by the marginal artery branch of the circumflex artery; drains into the great cardiac vein

posterior interventricular artery

(also, posterior descending artery) branch of the right coronary artery that runs along the posterior portion of the interventricular sulcus toward the apex of the heart and gives rise to branches that supply the interventricular septum and portions of both ventricles

posterior interventricular sulcus

sulcus located between the left and right ventricles on the anterior surface of the heart

potential energy

the type of energy that refers to the potential to do work

precapillary sphincters

circular rings of smooth muscle that surround the entrance to a capillary and regulate blood flow into that capillary

preload

(also, end diastolic volume) amount of blood in the ventricles at the end of atrial systole just prior to ventricular contraction

prepotential depolarization

(also, spontaneous depolarization) mechanism that accounts for the autorhythmic property of cardiac muscle; the membrane potential increases as sodium ions diffuse through the always-open sodium ion channels and causes the electrical potential to rise

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

primary immune response

the response of the adaptive immune system to the first exposure to an antigen

primer

a short stretch of RNA nucleotides that is required to initiate replication and allow DNA polymerase to bind and begin replication

progesterone

a reproductive hormone in women; assists in endometrial regrowth and inhibition of FSH and LH release

prokaryote

a unicellular organism that lacks a nucleus or any other membrane-bound organelle

prokaryotic cell

prometaphase
the stage of mitosis during which mitotic spindle fibers attach to kinetochores

promoter
a sequence on DNA to which RNA polymerase and associated factors bind and initiate transcription

prophase
the stage of mitosis during which chromosomes condense and the mitotic spindle begins to form

prostate gland
a structure that is a mixture of smooth muscle and glandular material and that contributes to semen

protein
a biological macromolecule composed of one or more chains of amino acids

proton
a positively charged particle that resides in the nucleus of an atom; has a mass of 1 and a charge of +1

proximal convoluted tubule (PCT)
part of the renal tubule that lies close to the glomerulus

pulmonary arteries
left and right branches of the pulmonary trunk that carry deoxygenated blood from the heart to each of the lungs

pulmonary capillaries
capillaries surrounding the alveoli of the lungs where gas exchange occurs: carbon dioxide exits the blood and oxygen enters

pulmonary circuit
blood flow to and from the lungs

pulmonary surfactant
substance composed of phospholipids and proteins that reduces the surface tension of the alveoli; made by type II alveolar cells

pulmonary trunk
large arterial vessel that carries blood ejected from the right ventricle; divides into the left and right pulmonary arteries

pulmonary valve
(also, pulmonary semilunar valve, the pulmonic valve, or the right semilunar valve) valve at the base of the pulmonary trunk that prevents backflow of blood into the right ventricle; consists of three flaps

pulmonary veins
veins that carry highly oxygenated blood into the left atrium, which pumps the blood into the left ventricle, which in turn pumps oxygenated blood into the aorta and to the many branches of the systemic circuit

pulmonary ventilation
exchange of gases between the lungs and the atmosphere; breathing

pupil
small opening though which light enters

Purkinje fibers
specialized myocardial conduction fibers that arise from the bundle branches and spread the impulse to the myocardial contraction fibers of the ventricles

Q

QRS complex
component of the electrocardiogram that represents the depolarization of the ventricles and includes, as a component, the repolarization of the atria

quiescent
describes a cell that is performing normal cell functions and has not initiated preparations for cell division

quiet breathing
(also, eupnea) mode of breathing that occurs at rest and does not require the cognitive thought of the individual

R

radioactive isotope
an isotope that spontaneously emits particles or energy to form a more stable element

receptor-mediated endocytosis

a variant of endocytosis that involves the use of specific binding proteins in the plasma membrane for specific molecules or particles

recombinant

describing something composed of genetic material from two sources, such as a chromosome with both maternal and paternal segments of DNA

rectum

the area of the body where feces is stored until elimination

red blood cells (RBCs)

(also, erythrocytes) one of the formed elements of blood that transports oxygen

red marrow

connective tissue in the interior cavity of a bone where hematopoiesis takes place

reduction division

a nuclear division that produces daughter nuclei each having one-half as many chromosome sets as the parental nucleus; meiosis I is a reduction division

refractory period

period after an action potential when it is more difficult or impossible for an action potential to be fired; caused by inactivation of sodium channels and activation of additional potassium channels of the membrane

remodeling

process by which osteoclasts resorb old or damaged bone at the same time as and on the same surface where osteoblasts form new bone to replace that which is resorbed

renal artery

branch of the artery that enters the kidney

renal artery

the artery that delivers blood to the kidney

renal capsule

layer that encapsulates the kidneys

renal column

area of the kidney through which the interlobar arteries travel in the process of supplying blood to the renal lobes

renal corpuscle

glomerulus and the Bowman's capsule together

renal fascia

connective tissue that supports the kidneys

renal pelvis

region in the kidney where the calyces join the ureters

renal pyramid

conical structure in the renal medulla

renal tubule

tubule of the nephron that arises from the glomerulus

renal vein

branch of a vein that exits the kidney and joins the inferior vena cava

renal vein

the vein that drains blood from the kidney

renewal

process by which worn-out cells are replaced

renin-angiotensin-aldosterone

biochemical pathway that activates angiotensin II, which increases blood pressure

replication fork

the Y-shaped structure formed during the initiation of replication

reproduction

process by which new organisms are generated

residual volume (RV)

amount of air that remains in the lungs after maximum exhalation

respiratory bronchiole

specific type of bronchiole that leads to alveolar sacs

respiratory cycle

one sequence of inspiration and expiration

respiratory epithelium

ciliated lining of much of the conducting zone that is specialized to remove debris and pathogens, and produce mucus

respiratory membrane

alveolar and capillary wall together, which form an air-blood barrier that facilitates the simple diffusion of gases

respiratory rate

total number of breaths taken each minute

respiratory volume

varying amounts of air within the lung at a given time

respiratory zone

includes structures of the respiratory system that are directly involved in gas exchange

responsiveness

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

reticulocyte

immature erythrocyte that may still contain fragments of organelles

retina

layer of photoreceptive and supporting cells on the inner surface of the back of the eye

Rh blood group

blood-type classification based on the presence or absence of the antigen Rh on the erythrocyte membrane surface

rhodopsin

main photopigment in vertebrates

ribonucleic acid (RNA)

a single-stranded polymer of nucleotides that is involved in protein synthesis

ribosome

a cellular structure that carries out protein synthesis

right atrioventricular valve

(also, tricuspid valve) valve located between the right atrium and ventricle; consists of three flaps of tissue

RNA polymerase

an enzyme that synthesizes an RNA strand from a DNA template strand

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

root

region of the external nose between the eyebrows

rough endoplasmic reticulum (RER)

the region of the endoplasmic reticulum that is studded with ribosomes and engages in protein modification

rRNA

ribosomal RNA; molecules of RNA that combine to form part of the ribosome

S

S phase

the second, or synthesis phase, of interphase during which DNA replication occurs

salivary gland

one of three pairs of exocrine glands in the mammalian mouth that secretes saliva, a mix of watery mucus and enzymes

saltatory conduction

"jumping" of an action potential along an axon from one node of Ranvier to the next

sarcolemma

plasma membrane of a skeletal muscle fiber

sarcomere

functional unit of skeletal muscle

saturated fatty acid

a long-chain hydrocarbon with single covalent bonds in the carbon chain; the number of hydrogen atoms attached to the carbon skeleton is maximized

science

knowledge that covers general truths or the operation of general laws, especially when acquired and tested by the scientific method

scientific law

a description, often in the form of a mathematical formula, for the behavior of some aspect of nature under certain specific conditions

scientific method

a method of research with defined steps that include experiments and careful observation

scientific theory

a thoroughly tested and confirmed explanation for observations or phenomena

scrotum

a sac containing testes, exterior to body

secondary immune response

the response of the adaptive immune system to a second or later exposure to an antigen mediated by memory cells

segmental artery

artery that branches from the renal artery

selectively permeable

the characteristic of a membrane that allows some substances through but not others

semen

a fluid mixture of sperm and supporting materials

semicircular canal

one of three half-circular, fluid-filled tubes in the vestibular labyrinth that monitors angular acceleration and deceleration

semiconservative replication

the method used to replicate DNA in which the double-stranded molecule is separated and each strand acts as a template for a new strand to be synthesized, so the resulting DNA molecules are composed of one new strand of nucleotides and one old strand of nucleotides

semilunar valves

valves located at the base of the pulmonary trunk and at the base of the aorta

seminal vesicle

a secretory accessory gland in male; contributes to semen

seminiferous tubule

the structures within which sperm production occurs in the testes

sensory-somatic nervous system

the system of sensory and motor nerves

septum

(plural = septa) walls or partitions that divide the heart into chambers

septum primum

flap of tissue in the fetus that covers the foramen ovale within a few seconds after birth

Sertoli cell

a cell in the walls of the seminiferous tubules that assists developing sperm and secretes inhibin

set point

the target value of a physiological state in homeostasis

sickle cell disease

(also, sickle cell anemia) inherited blood disorder in which hemoglobin molecules are malformed, leading to the breakdown of RBCs that take on a characteristic sickle shape

sinoatrial (SA) node

known as the pacemaker, a specialized clump of myocardial conducting cells located in the superior portion of the right atrium that has the highest inherent rate of depolarization that then spreads throughout the heart

sinus rhythm

normal contractile pattern of the heart

sinusoid capillary

rarest type of capillary, which has extremely large intercellular gaps in the basement membrane in addition to clefts and fenestrations; found in areas such as the bone marrow and liver where passage of large molecules occurs

skeletal muscle tissue

forms skeletal muscles, which attach to bones and control locomotion and any movement that can be consciously controlled

skeletal system

organ system composed of bones and cartilage that provides for movement, support, and protection

small cardiac vein

parallels the right coronary artery and drains blood from the posterior surfaces of the right atrium and ventricle; drains into the great cardiac vein

small intestine

the organ where digestion of protein, fats, and carbohydrates is completed

smooth endoplasmic reticulum (SER)

the region of the endoplasmic reticulum that has few or no ribosomes on its cytoplasmic surface and synthesizes carbohydrates, lipids, and steroid hormones; detoxifies chemicals like pesticides, preservatives, medications, and environmental pollutants, and stores calcium ions

smooth muscle

tissue occurs in the walls of hollow organs such as the intestines, stomach, and urinary bladder, and around passages such as the respiratory tract and blood vessels

solute

a substance dissolved in another to form a solution

solvent

a substance capable of dissolving another substance

somatic cell

all the cells of a multicellular organism except the gamete-forming cells

spermatogenesis

the process of producing haploid sperm

spinal cord

a thick fiber bundle that connects the brain with peripheral nerves; transmits sensory and motor information; contains neurons that control motor reflexes

splicing

the process of removing introns and reconnecting exons in a pre-mRNA

spongy bone

(also, cancellous bone) trabeculated osseous tissue that supports shifts in weight distribution

spontaneous depolarization

(also, prepotential depolarization) the mechanism that accounts for the autorhythmic property of cardiac muscle; the membrane potential increases as sodium ions diffuse through the always-open sodium ion channels and causes the electrical potential to rise

stapes

(also, stirrup) third of the three bones of the middle ear

starch

a storage carbohydrate in plants

start codon

the AUG (or, rarely GUG) on an mRNA from which translation begins; always specifies methionine

stereocilia

in the auditory system, hair-like projections from hair cells that help detect sound waves

steroid

a type of lipid composed of four fused hydrocarbon rings

stomach

a saclike organ containing acidic digestive juices

stop codon

one of the three mRNA codons that specifies termination of translation

substrate

a molecule on which the enzyme acts

sulcus

(plural = sulci) fat-filled groove visible on the surface of the heart; coronary vessels are also located in these areas

summation

process of multiple presynaptic inputs creating EPSPs around the same time for the postsynaptic neuron to be sufficiently depolarized to fire an action potential

superior colliculus

paired structure in the top of the midbrain, which manages eye movements and auditory integration

superior vena cava

large systemic vein that returns blood to the heart from the superior portion of the body

suprachiasmatic nucleus

cluster of cells in the hypothalamus that plays a role in the circadian cycle

surface tension

the cohesive force at the surface of a body of liquid that prevents the molecules from separating

sympathetic nervous system

the division of autonomic nervous system activated during stressful "fight-or-flight" situations

synapse

a junction between two neurons where neuronal signals are communicated

synapse

junction between two neurons where neuronal signals are communicated

synapsis

the formation of a close association between homologous chromosomes during prophase I

synaptic cleft

a space between the presynaptic and postsynaptic membranes

synaptic cleft

space between the presynaptic and postsynaptic membranes

synaptic vesicle

spherical structure that contains a neurotransmitter

systemic circuit

blood flow to and from virtually all of the tissues of the body

systole

period of time when the heart muscle is contracting

T

T cell

a lymphocyte that matures in the thymus gland

T wave

component of the electrocardiogram that represents the repolarization of the ventricles

tastant

food molecule that stimulates gustatory receptors

taste bud

clusters of taste cells

tectorial membrane

cochlear structure that lies above the hair cells and participates in the transduction of sound at the hair cells

telomerase

an enzyme that contains a catalytic part and an inbuilt RNA template; it functions to maintain telomeres at chromosome ends

telomere

the DNA at the end of linear chromosomes

telophase

the stage of mitosis during which chromosomes arrive at opposite poles, decondense, and are surrounded by new nuclear envelopes

temperature

a measure of molecular motion

template strand

the strand of DNA that specifies the complementary mRNA molecule

temporal lobe

the part of the cerebral cortex that processes auditory input; parts of the temporal lobe are involved in speech, memory, and emotion processing

testes

a pair of male reproductive organs

testosterone

a reproductive hormone in men that assists in sperm production and promoting secondary sexual characteristics

tetrad

two duplicated homologous chromosomes (four chromatids) bound together by chiasmata during prophase I

thalamus

the brain area that relays sensory information to the cortex

thalassemia

inherited blood disorder in which maturation of RBCs does not proceed normally, leading to abnormal formation of hemoglobin and the destruction of RBCs

thermodynamics

the science of the relationships between heat, energy, and work

thick filament

a group of myosin molecules

thin filament

two polymers of actin wound together along with tropomyosin and troponin

thoracic wall compliance

ability of the thoracic wall to stretch while under pressure

thoroughfare channel

continuation of the metarteriole that enables blood to bypass a capillary bed and flow directly into a venule, creating a vascular shunt

threshold of excitation

level of depolarization needed for an action potential to fire

threshold of excitation

the level of depolarization needed for an action potential to fire

thymus

the gland located behind the sternum that produces thymosin hormones that contribute to the development of the immune system

thyroid cartilage

largest piece of cartilage that makes up the larynx and consists of two lamina

thyroid gland

an endocrine gland located in the neck that produces thyroid hormones thyroxine and triiodothyronine

tidal volume (TV)

amount of air that normally enters the lungs during quiet breathing

tight junction

a firm seal between two adjacent animal cells created by protein adherence

tissue

a group of similar cells carrying out the same function

tissue

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

tonic activity

in a neuron, slight continuous activity while at rest

tonicity

the amount of solute in a solution.

total dead space

sum of the anatomical dead space and alveolar dead space

total lung capacity (TLC)

total amount of air that can be held in the lungs; sum of TV, ERV, IRV, and RV

total pressure

sum of all the partial pressures of a gaseous mixture

trabeculae

(singular = trabecula) spikes or sections of the lattice-like matrix in spongy bone

trabeculae carneae

ridges of muscle covered by endocardium located in the ventricles

trachea

tube composed of cartilaginous rings and supporting tissue that connects the lung bronchi and the larynx; provides a route for air to enter and exit the lung

trachealis muscle

smooth muscle located in the fibroelastic membrane of the trachea

trans-fat

a form of unsaturated fat with the hydrogen atoms neighboring the double bond across from each other rather than on the same side of the double bond

transcription bubble

the region of locally unwound DNA that allows for transcription of mRNA

transferrin

plasma protein that binds reversibly to iron and distributes it throughout the body

transport maximum

maximum amount of solute that can be transported out of the renal tubules during reabsorption

transpulmonary pressure

pressure difference between the intrapleural and intra-alveolar pressures

tricuspid valve

term used most often in clinical settings for the right atrioventricular valve

triglyceride

a fat molecule; consists of three fatty acids linked to a glycerol molecule

tRNA

transfer RNA; an RNA molecule that contains a specific three-nucleotide anticodon sequence to pair with the mRNA codon and also binds to a specific amino acid

tropomyosin

acts to block myosin binding sites on actin molecules, preventing cross-bridge formation and preventing contraction until a muscle receives a neuron signal

troponin

binds to tropomyosin and helps to position it on the actin molecule, and also binds calcium ions

true vocal cord

one of the pair of folded, white membranes that have a free inner edge that oscillates as air passes through to produce sound

tubular reabsorption

reclamation of water and solutes that got filtered out in the glomerulus

tubular secretion

process of secretion of wastes that do not get reabsorbed

tunica externa

(also, tunica adventitia) outermost layer or tunic of a vessel (except capillaries)

tunica intima

(also, tunica interna) innermost lining or tunic of a vessel

tunica media

middle layer or tunic of a vessel (except capillaries)

tympanum

(also, tympanic membrane or ear drum) thin diaphragm between the outer and middle ears

type I alveolar cell

squamous epithelial cells that are the major cell type in the alveolar wall; highly permeable to gases

type II alveolar cell

cuboidal epithelial cells that are the minor cell type in the alveolar wall; secrete pulmonary surfactant

U

ultrasound

sound frequencies above the human detectable ceiling of approximately 20,000 Hz

umami

one of the five basic tastes, which is described as "savory" and which may be largely the taste of L-glutamate

universal donor

individual with type O^- blood

universal recipient

individual with type AB^+ blood

unsaturated fatty acid

a long-chain hydrocarbon that has one or more than one double bonds in the hydrocarbon chain

up-regulation

an increase in the number of hormone receptors in response to increased hormone levels

ureter

the urine-bearing tubes coming out of the kidney

ureter

urine-bearing tube coming out of the kidney; carries urine to the bladder

urethra

the tube that conducts urine from the urinary bladder to the external environment

urinary bladder

structure that the ureters empty the urine into; stores urine

urinary bladder

the structure that the ureters empty the urine into

urine

filtrate produced by kidneys that gets excreted out of the body

uterus

a female reproductive structure in which an embryo develops

V

vacuole

a membrane-bound sac, somewhat larger than a vesicle, that functions in cellular storage and transport

vagina

a muscular tube for the passage of menstrual flow, copulation, and birth of offspring

valve

in the cardiovascular system, a specialized structure located within the heart or vessels that ensures one-way flow of blood

van der Waals interaction

a weak attraction or interaction between molecules caused by slightly positively charged or slightly negatively charged atoms

variable

a part of an experiment that can vary or change

vasa recta

peritubular network that surrounds the loop of Henle of the juxtamedullary nephrons

vasa vasorum

small blood vessels located within the walls or tunics of larger vessels that supply nourishment to and remove wastes from the cells of the vessels

vascular shunt

continuation of the metarteriole and thoroughfare channel that allows blood to bypass the capillary beds to flow directly from the arterial to the venous circulation

vasoconstriction

constriction of the smooth muscle of a blood vessel, resulting in a decreased vascular diameter

vasodilation

relaxation of the smooth muscle in the wall of a blood vessel, resulting in an increased vascular diameter

vasodilator

compound that increases the diameter of blood vessels

vasomotion

irregular, pulsating flow of blood through capillaries and related structures

vasopressin

another name for anti-diuretic hormone

vein
blood vessel that conducts blood toward the heart

venous reserve
volume of blood contained within systemic veins in the integument, bone marrow, and liver that can be returned to the heart for circulation, if needed

ventilation
movement of air into and out of the lungs; consists of inspiration and expiration

ventral respiratory group (VRG)
region of the medulla oblongata that stimulates the contraction of the accessory muscles involved in respiration to induce forced inspiration and expiration

ventricle
one of the primary pumping chambers of the heart located in the lower portion of the heart; the left ventricle is the major pumping chamber on the lower left side of the heart that ejects blood into the systemic circuit via the aorta and receives blood from the left atrium; the right ventricle is the major pumping chamber on the lower right side of the heart that ejects blood into the pulmonary circuit via the pulmonary trunk and receives blood from the right atrium

ventricular ejection phase
second phase of ventricular systole during which blood is pumped from the ventricle

venule
small vessel leading from the capillaries to veins

vesicle
a 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

vestibular fold
part of the folded region of the glottis composed of mucous membrane; supports the epiglottis during swallowing

vision
sense of sight

vital capacity (VC)
sum of TV, ERV, and IRV, which is all the volumes that participate in gas exchange

vitamin
an organic substance necessary in small amounts to sustain life

W

white blood cell
a nucleated cell found in the blood that is a part of the immune system; also called leukocytes

white blood cells (WBCs)
(also, leukocytes) one of the formed elements of blood that provides defense against disease agents and foreign materials

Y

yellow marrow
connective tissue in the interior cavity of a bone where fat is stored

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Keywords are listed by the section with that keyword (page numbers are in parentheses). Keywords do not necessarily appear in the text of the page. They are merely associated with that section. *Ex.* apples, § 1.1 (1) **Terms** are referenced by the page they appear on. *Ex.* apples, 1

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Human Biology
This is a text book for a one-quarter/semester non-majors human biology course that combines materials from three OpenStax books: Biology, Concepts of Biology, and Anatomy and Physiology.

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