BIOLOGY OF HUMAN CONCERNS



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Human Biology

Suzanne Wakim & Mandeep Grewal

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This text was compiled on 05/03/2026

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Licensing

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PREFACE AND ACKNOWLEDGMENTS

DEDICATION

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

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

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

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

VOCABULARY

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

ACKNOWLEDGMENTS

TECHNICAL SUPPORT: LIBRETEXTS LIBRARIES, UC DAVIS

This project could not have been possible without the voluminous support of Dr. Delmar Larsen and Henry Agnew. They helped us overcome many technical difficulties during the creation of this book.

ATTRIBUTIONS AND ACKNOWLEDGEMENTS: CK-12 FOUNDATION AND OPENSTAX

This book is a product of a curation of the OER content from many sources. Butte College Biology Department thanks the following authors:

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- Dr. Katherine Harris
- Jean Brainard
- Jessica Harwood
- Laura Guerin
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- Marcos Gridi-Papp
- Milton Huling Ph.D.
- Niamh Gray-Wilson
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Printed: January 5, 2017

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FINANCIAL SUPPORT: THE ACADEMIC SENATE FOR CALIFORNIA COMMUNITY COLLEGES OPEN EDUCATIONAL RESOURCE INITIATIVE (ASCCC OERI)

- Award number 54 (2019)
- Award number 207 (2020)



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



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



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CHAPTER OVERVIEW

1: THE NATURE AND PROCESS OF SCIENCE

This chapter explains how scientists think and how they "do" science. It describes how scientific theories develop and how scientists investigate questions to advance scientific knowledge. The chapter also explains how science may be misused and how and why human subjects are protected in scientific research.

1.1: Case Study- Why Should You Learn About Science?

1.2: What Is Science?

1.3: The Nature of Science

1.4: Theories in Science

1.5: Scientific Investigations

1.6: Scientific Experiments

1.7: Extrapolations of Scientific Investigations

1.8: Case Study Conclusion- Shot and Chapter Summary

Thumbnail: This image describes the Scientific Method as a cyclic/iterative process of continuous improvement. (Public Domain).

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1.1: CASE STUDY- WHY SHOULD YOU LEARN ABOUT SCIENCE?

CASE STUDY: TO GIVE A SHOT OR NOT

Elena and Daris are expecting their first child. They are excited for the baby to arrive, but they are nervous as well. Will the baby be healthy? Will they be good parents? In addition to these big concerns, it seems like there are a million decisions to be made. Will Elena breastfeed or will they use formula? Will they buy a crib or let the baby sleep in their bed?



Figure **1.1.1**: Pregnant Woman

Elena goes online to try to find some answers. She finds a website from an author who writes books on parenting. On this site, she reads an article that argues that children should not be given many of the standard childhood vaccines, including the measles, mumps, and rubella (MMR) vaccine.

The article claims that the MMR vaccine has been proven to cause autism and gives examples of three children who came down with autism-like symptoms shortly after their first MMR vaccination at one year of age. The author believes that the recent increase in the incidence of children diagnosed with autism spectrum disorders is due to the fact that the number of vaccinations given in childhood has increased.

Elena is concerned. She does not want to create lifelong challenges for their child. Besides, aren't diseases like measles, mumps, and rubella basically eradicated by now? Why should they risk the health of their baby by injecting them with vaccines for diseases that are a thing of the past?

Once baby Juan is born, Elena brings them to the pediatrician's office. Dr. Rodriguez says Juan needs some shots. Elena is reluctant and shares what she has read online. Dr. Rodriguez assures Elena that the study that originally claimed a link between the MMR vaccine and autism has been found to be fraudulent and that vaccines have repeatedly been demonstrated to be safe and effective in peer-reviewed studies.

Although Elena trusts their doctor, she is not fully convinced. What about the increase in the number of children with autism and the cases where symptoms of autism appeared after MMR vaccination? Elena has a tough decision to make, but a better understanding of science can help her. In this chapter, you will learn about what science is (and what it is not), how it works, and how it relates to human health.

CHAPTER OVERVIEW: THE NATURE AND PROCESS OF SCIENCE

In the rest of the chapter, you'll learn much more about science, including how scientists think and how they advance scientific knowledge. Specifically, you'll learn that:

- Science is a distinctive way of gaining knowledge about the natural world that is based on evidence and logic. Scientists assume that nature can be understood with systematic study; that scientific ideas are open to revision, although sound scientific ideas can withstand repeated testing; and that science is limited in the types of questions it can answer.
- A scientific theory is at the pinnacle of explanations in science. A theory is a broad explanation for many phenomena that is widely accepted because it is supported by a great deal of evidence. An example of a theory in human biology is the germ theory of disease. It took more than two centuries of research to provide enough evidence that microorganisms ("germs") cause disease for this explanation to become widely accepted and attain the status of a theory.
- The process of science is epitomized by scientific investigation. This is a procedure for gathering evidence to test a hypothesis. A scientific investigation typically involves steps such as asking a question based on observations and formulating a hypothesis as a testable answer to the question. It also generally involves collecting data as evidence for or against the hypothesis, drawing conclusions, and communicating results. In reality, the process of science is not simple and straightforward. The process actually tends to be nonlinear, iterative, creative, and unpredictable. "Doing" science can be very exciting!
- Scientific experiments are a special type of scientific investigation, in which variables are manipulated by the researcher to test expected outcomes. Experiments are performed under controlled conditions to mitigate the effects of other variables on the outcome variable. Experiments provide the best evidence that one variable causes another variable in scientific research. An example of an experiment in human biology is the astounding public health experiment to test Salk's polio vaccine that was undertaken in 1953. Some 600,000 children received a vaccine injection; another 600,000 received a placebo injection of useless salt water. The vaccine group had a significant drop in polio cases relative to the placebo group, providing support for the hypothesis that the vaccine prevented the disease.
- Many questions in human biology are not amenable to experimental research. Consider the question: "Does smoking cause lung cancer?" It would not be ethical to deliberately experiment with human subjects by exposing them to harmful tobacco smoke in order to see whether they develop lung cancer. For questions like this, observational studies are done to look for correlations between variables. For example, Doll and Hill gathered information on past smoking habits from a large sample

of lung cancer patients and another large sample of controls without lung cancer. Smoking and lung cancer were found to be correlated. Correlation does not imply causation, but it can be a big hint!

- Research involving human subjects presents special challenges to scientists. Until the 1970s, there were few ethical guidelines for researchers to follow when studying human subjects. A shamefully unethical syphilis study called the Tuskegee study changed all that. The Tuskegee study was conducted on African-American men in Alabama from 1932 to 1972. This study was done to see the progression of syphilis. In this study, the control group with the disease was not treated for syphilis. When details of the study were leaked to the media, the public was outraged and the U.S. Congress got involved. In 1974, Congress passed important legislation to protect human subjects in scientific research projects. Chief among the protections was the necessity of informed consent.

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

1. What do you think about the quality of Elena's online source of information about vaccines compared to Dr. Rodriguez's sources?
2. Do you think the arguments presented here that claim that the MMR vaccine causes autism are scientifically valid? Could there be alternative explanations for the observations?
3. Why do you think diseases like measles, polio, and mumps are rare these days, and why are we still vaccinating for these diseases?

ATTRIBUTIONS

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1.2: WHAT IS SCIENCE?

OUCH!

This individual in Figure **1.2.1** is getting a flu vaccine. You probably know that getting a vaccine can hurt, but it's usually worth it. A vaccine contains dead or altered forms of "germs" that normally cause a disease, such as flu or measles. The germs in vaccines have been inactivated or weakened so they can no longer cause illness, but they are still "noticed" by the immune system. They stimulate the immune system to produce chemicals that can kill the actual germs if they enter the body, thus preventing future disease. How was such an ingenious way to prevent disease discovered? The short answer is more than two centuries of science.



Figure **1.2.1**: Getting an annual flu shot

SCIENCE AS PROCESS

You may think of science as a large and detailed body of knowledge, but science is actually more of a process than a set of facts. The real focus of science is the accumulation and revision of scientific knowledge. Science is a special way of gaining knowledge that relies on evidence and logic. Evidence is used to continuously test ideas. Through time, with repeated evidence gathering and testing, scientific knowledge advances.

We've been accumulating knowledge of vaccines for more than two centuries. The discovery of the first vaccine, as well as the process of vaccination, dates back to 1796. An English doctor named **Edward Jenner** observed that people who became infected with cowpox did not get sick from smallpox, a similar but much more virulent disease (Figure **1.2.2**). Jenner decided to transmit cowpox to a young child to see if it would protect them from smallpox. He gave the child cowpox by scratching liquid from cowpox sores into the child's skin. Then, six weeks later, he scratched liquid from smallpox sores into the child's skin. As Jenner predicted, the child did not get sick from smallpox. Jenner had discovered the first vaccine, although additional testing was needed to show that it really was effective.

Almost a century passed before the next vaccine was discovered, a vaccine for cholera in 1879. Around the same time, French chemist Louis Pasteur found convincing evidence that many human diseases are caused by germs. This earned Pasteur the title of "father of germ theory." Since Pasteur's time, vaccines have been discovered for



Figure **1.2.2**: A young child covered with skin lesions from smallpox. Until it was eradicated, this highly contagious infection caused many deaths, and those that survived were often severely scarred for life.

scores of additional diseases caused by "germs," and scientists are currently researching vaccines for many others.

BENEFITS OF SCIENCE

Medical advances such as the discovery of vaccines are one of the most important benefits of science, but science and scientific knowledge are also crucial for most other human endeavors. Science is needed to design safe cars, predict storms, control global warming, develop new technologies of many kinds, help couples have children, and put humans on the moon! Clearly, the diversity of applications of scientific knowledge is vast!

REVIEW

1. Explain why science is more accurately considered a process than a body of knowledge.
2. State three specific examples of human endeavors that are based on scientific knowledge.
3. Jenner used a young boy as a research subject in his smallpox vaccine research. Today, scientists must follow strict guidelines when using human subjects in their research. What unique concerns do you think might arise when human beings are used as research subjects?
4. What gave Jenner the idea to develop a vaccine for smallpox?
5. Why do you think almost a century passed between the development of the first vaccine (for smallpox) and the development of the next vaccine (for cholera)?
6. How does science influence your daily life?

EXPLORE MORE

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1.3: THE NATURE OF SCIENCE

WHY DOES A MOOSE HAVE ANTLERS?

Did you ever wonder why a moose, like the one in Figure **1.3.1**, grows large antlers? The antlers may grow as wide as 1.8 m (6 ft) from tip to tip! The antlers use up a lot of energy to grow and carry around. They can even get caught in brush and trees. In these ways, they would seem to be more of a detriment than a help, so what purpose do the antlers serve? And why do only male moose grow them? If you've ever asked questions such as these about the natural world, then you were thinking like a scientist.



Figure **1.3.1**: Bull moose in Superior National Forest

DEFINING SCIENCE

Science is a distinctive way of gaining knowledge about the natural world that starts with a question and then tries to answer the question with evidence and logic. Science is an exciting exploration of all the whys and hows that any curious person might have about the world. You can be part of that exploration. Besides your curiosity, all you need is a basic understanding of how scientists think and how science is done. In this section, you'll learn how to think like a scientist.

THINKING LIKE A SCIENTIST

Thinking like a scientist rests on certain underlying assumptions. Scientists assume that:

- Nature can be understood through systematic study.
- Scientific ideas are open to revision.
- Sound scientific ideas withstand the test of time.
- Science cannot provide answers to all questions.

NATURE IS UNDERSTANDABLE

Scientists think of nature as a single system controlled by natural laws. By discovering natural laws, scientists strive to increase their understanding of the natural world. Laws of nature are expressed as scientific laws. A **scientific law** is a statement that describes what always happens under certain conditions in nature.

Examples of scientific laws include Mendel's Laws of Inheritance. These laws were discovered by an Austrian Monk, named Gregor Mendel (Figure **1.3.2**), in the mid-1800s. The laws describe how certain traits are inherited from parents by their offspring. Although Mendel discovered his laws of inheritance by experimenting with pea plants, we now know that the laws apply to many other organisms, including human beings. The laws describe how we inherit relatively simple genetic traits, such as blood type, from our parents. For example, if you know the blood types of your parents, you can use Mendel's laws to predict your chances of having a particular blood type.

Barbara McClintock (Figure **1.3.2**) added to our understanding of inheritance in the 1950s by discovering how chromosomes exchange information during meiosis. Meiosis is how organisms produce reproductive cells (such as egg or sperm). McClintock worked with corn and, using the color traits in the kernels demonstrated how crossing-over is used to exchange information between chromosomes. An understanding of how crossing-over works is essential to our understanding of inheritance because it explains why using Mendelian rules of inheritance does not always produce the correct ratios.





Figure **1.3.2**: Science is an ongoing process of gaining knowledge. Gregor Mendel discovered laws of inheritance in the mid-1800s. Barbara McClintock refined these laws in the 1950s. Many other scientists have also contributed to our understanding of inheritance.

SCIENTIFIC IDEAS ARE OPEN TO CHANGE

Science is more of a process than a set body of knowledge. Scientists are always testing and revising their ideas, and as new observations are made, existing ideas may be challenged. Ideas may be replaced with new ideas that better fit the facts, but more often

existing ideas are simply revised. For example, when scientists discovered how genes control genetic traits, they didn't throw out Mendel's laws of inheritance. The new discoveries helped to explain why Mendel's laws applied to certain traits but not others. They showed that Mendel's laws are part of a bigger picture. Through many new discoveries over time, scientists gradually build an increasingly accurate and detailed understanding of the natural world.

Occasionally, scientific ideas change radically. Radical changes in scientific ideas were given the name **paradigm shifts** by the philosopher Thomas Kuhn in 1962. Kuhn agreed that scientific knowledge typically accumulates gradually, as new details are added to established theories. However, Kuhn also argued that from time to time, a scientific revolution occurs in which current theories are abandoned and completely new ideas take their place.

Although there is debate among scientists as to what constitutes a paradigm shift, the theory of evolution is widely accepted as a good example in biology. In fact, some scientists argue that it is the only example of a paradigm shift in biology. Prior to Charles Darwin's publication of his theory of evolution in the 1860s, most scientists believed that God had created living species and that the species on Earth had not changed since they were created. Drawing on a great deal of evidence and logical arguments, Darwin demonstrated that species could change and that new species could arise from pre-existing ones. This was such a radical change in scientific thinking that Darwin was reluctant to publish his ideas for fear of a backlash from other scientists and the public. Indeed, Darwin was at first ridiculed for his evolutionary theory, but in time, it was widely accepted and became a cornerstone of all life sciences.

SCIENTIFIC KNOWLEDGE MAY BE LONG LASTING

Many scientific ideas have withstood the test of time. For example, about 200 years ago, the scientist John Dalton proposed atomic theory — the theory that all matter is made of tiny particles called atoms. This theory is still valid today. During the two centuries since the theory was first proposed, a great deal more has been learned about atoms and the even smaller particles of which they are composed. Nonetheless, the idea that all matter consists of atoms remains valid. There are many other examples of basic scientific ideas that have been tested repeatedly and found to be sound. You will learn about many of them as you study human biology.

NOT ALL QUESTIONS CAN BE ANSWERED BY SCIENCE

Science rests on evidence and logic, and evidence comes from observations. Therefore, science deals only with things that can be observed. An **observation** is anything that is detected through human senses or with instruments and measuring devices that extend human senses. Things that cannot be observed or measured by current means — such as supernatural beings or events — are outside the bounds of science. Consider these two questions about life on Earth:

- Did life on Earth evolve over time?
- Was life on Earth created by a supernatural deity?

The first question can be answered by science on the basis of scientific evidence such as fossils and logical arguments. The second question could be a matter of belief but no evidence can be gathered to support or refute it. Therefore, it is outside the realm of science.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Scientific research is often reported in the popular media. In fact, that's how most people learn about new scientific findings. Informing the public about scientific research is a valuable media service, but the types of scientific investigations that are reported may lead to a distorted public perception of what science is and how reliable its results are. Why? There are actually two types of science, often referred to as consensus science and frontier science. The latter type of science is the type that usually makes the news, but the media generally do not distinguish between the two types. Therefore, many people may infer that what they read about frontier science is typical of all science.

- **Consensus science** refers to scientific ideas that have been researched for a long period of time and for which a great deal of evidence has accumulated. This type of research generally fits well within current scientific paradigms. A good example of consensus science is global climate change. Data showing the impact of increasing levels of atmospheric carbon dioxide, due to human activities, on global warming have been accumulating for many decades. Today, virtually all climate scientists agree that global warming is occurring and that human actions are largely responsible for it. However, the few scientists — and many politicians — who do not agree with the consensus view receive greater media attention because the consensus view is "old" news. The findings have been coming in for years, and new research in the area keeps finding similar results.
- **Frontier science,** in contrast, refers to scientific ideas that are relatively new and have not yet been supported by years of scientific evidence. Frontier research takes place at the frontiers of knowledge in a particular field. A good example of frontier science is research into the presumed link between cholesterol in the diet and cholesterol in the blood. The consensus view for many years was that a diet high in cholesterol increases blood levels of cholesterol, which may lead, in turn, to cardiovascular disease. Recent research challenging this accepted view found that genes play a more significant role than diet in blood levels of cholesterol and risk of cardiovascular disease.

The media tend to focus on frontier science because it seems controversial and may lead to major new scientific breakthroughs. With more research, ideas in frontier science may be supported by more evidence, gain wider acceptance, and become consensus science. In some cases, frontier science that

is at odds with a current paradigm may even lead to a paradigm shift. However, the opposite may happen instead. Additional research may undermine the initial findings of frontier research so that the new and exciting ideas are rejected. Unfortunately, when frontier science is later shown to be mistaken, people may infer that all science, including consensus science, is unreliable.

REVIEW

1. Define science.
2. What is the general goal of science?
3. Identify four basic assumptions that scientists make when they study the natural world.
4. Explain why science cannot provide answers to all questions.
5. Do observations in science have to be made by the naked eye? Can you think of a way in which scientists might be able to make observations about something they cannot directly see?
6. If something cannot be observed, can it be tested scientifically?
7. What do you think would be more susceptible to being disproved — conclusions drawn from frontier science or consensus science? Explain your reasoning.
8. Scientific knowledge builds upon itself. Give an example of a scientific idea from the reading where the initial idea became extended as science advanced.
9. What is a dramatic change in scientific understanding is called?
10. Discuss this statement: “Scientific ideas are always changing, so they can't be trusted.” Do you think this is true?
11. True or False: Science is a process.
12. True or False: A scientific law describes what happens most of the time under certain conditions.
13. What is one piece of evidence that life on Earth evolved over time?
14. Why do you think that as technology advances, scientific knowledge expands?

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1.4: THEORIES IN SCIENCE

OH VAPOR SO FOUL!

An individual in this sketch is holding his nose to avoid breathing in the miasma. Miasma refers to a toxic vapor that people believed for centuries was a cause of many diseases, including cholera and plague. The idea that miasma causes diseases was first proposed in the second century B.C.E. by a prominent Greek physician named Galen. They believed that miasma, which is identifiable by its foul smell, emanates from rotting organic matter and sickens people who live close enough to inhale it. Miasma was the predominant explanation for disease transmission from the time of Galen until the germ theory of disease became widely accepted in the late 1800s.



Figure **1.4.1**: A man holding his nose to avoid breathing in a miasma

WHAT IS A SCIENTIFIC THEORY?

Germ theory, which is described in detail below, is one of several scientific theories you will read about in human biology. A **scientific theory** is a broad explanation of events that is widely accepted by the scientific community. To become a theory, an explanation must be strongly supported by a great deal of evidence.

People commonly use the word *theory* to describe a guess or hunch about how or why something happens. For example, you might say, "I think a woodchuck dug this hole in the ground, but it's just a theory." Using the word *theory* in this way is different from the way it is used in science. A scientific theory is not just a guess or hunch that may or may not be true. In science, a theory is an explanation that has a high likelihood of being correct because it is so well supported by evidence.

GERM THEORY: A HUMAN BIOLOGY EXAMPLE

The **germ theory of disease** states that contagious diseases are caused by "germs," or microorganisms, which are organisms that are too small to be seen without magnification. Microorganisms that cause disease are called **pathogens**. Human pathogens include bacteria and viruses, among other microscopic entities. When pathogens invade humans or other living hosts, they grow, reproduce, and make their hosts sick. Diseases caused by germs are contagious because the microorganisms that cause them can spread from person to person.

FIRST STATEMENT OF GERM THEORY

Germ theory was first clearly stated by an Italian physician named Girolamo Fracastoro in the mid-1500s. Fracastoro proposed that contagious diseases are caused by transferable "seed-like entities," which we now call germs. According to Fracastoro, germs spread through populations, making many people sick, through direct or indirect contact between individuals.

Fracastoro's idea, though essentially correct, was disregarded by other physicians. Instead, Galen's idea of miasma remained the accepted explanation for the spread of disease for another 300 years. However, evidence for Fracastoro's idea accumulated during that time. Some of the earliest evidence was provided by the Dutch lens and microscope maker Anton van Leeuwenhoek, who discovered microorganisms. By the 1670s, van Leeuwenhoek had directly observed many different types of microorganisms, including bacteria.

EVIDENCE FROM PUERPERAL FEVER

One of the first physicians to demonstrate that a microorganism is the cause of a specific human disease was the Hungarian obstetrician Ignaz Semmelweis in the 1840s. The disease was puerperal fever, an often-fatal infection of the female reproductive organs. Puerperal fever is also called childbed fever because it usually affects women who have just given birth.

Semmelweis observed that deaths from puerperal fever occurred much more often when women had been attended by doctors at his hospital than by midwives at home. Semmelweis also noticed that doctors often came directly from autopsies to the beds of women about to give birth. From his observations, Semmelweis inferred that puerperal fever was a contagious disease caused by some type of matter carried to pregnant patients on the hands of doctors from autopsied bodies. As a consequence, Semmelweis urged doctors and medical students at his hospital to wash their hands with chlorinated lime water before examining pregnant women. After this change, the hospital's death rate for women who had just given birth fell from 18 to 2 percent, which was a 90 percent reduction. Some of Semmelweis' findings are presented in Figure **1.4.3**.

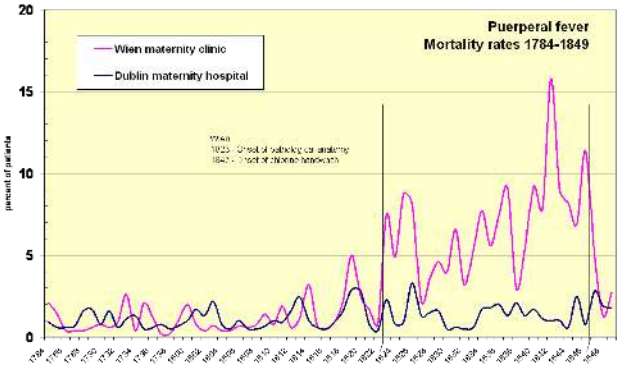


Figure **1.4.2**: This graph compares mortality rates from 1784-1849 in two maternity clinics (Wien and Dublin). Rates increased in the Wien clinic when they started studying pathological anatomy in 1823. The rates decreased sharply in 1847 when they started using chlorine handwashing. The Dublin clinic, which did not study pathological anatomy, shows a low rate of infection throughout the timeframe.

Semmelweis published his results, but they were derided by the medical profession. The idea that doctors themselves were the carriers of a fatal disease was taken as a personal affront by his fellow physicians. One of Semmelweis' peers protested indignantly that doctors are gentlemen and that gentlemen's hands are always clean. As a result of attitudes such as this, Semmelweis became the target of a vicious smear campaign. Eventually, Semmelweis had a mental breakdown and was committed to a mental hospital, where he died.

DISCOVERING MICROBES

Throughout the later 1800s, more formal investigations were conducted on the relationship between germs and disease. Some of the most important was undertaken by Louis Pasteur (pictured in his lab in Figure **1.4.4**). Pasteur was a French chemist who did careful experiments to show that fermentation, food spoilage, and certain diseases are caused by microorganisms.

He discovered the cause of puerperal fever in 1879 and determined it was an infection caused by the bacterium *Streptococcus pyogenes* (Figure **1.4.5**). Although Pasteur was not the first person to propose germ theory, his investigations clearly supported it. He also became a strong proponent of the theory and managed to convince most of the scientific community of its validity.

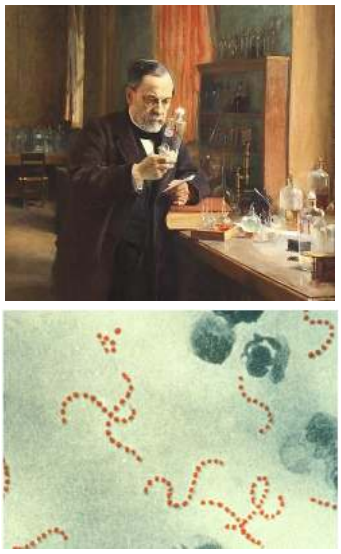


Figure **1.4.3**: Louis Pasteur (left) discovered that the bacterium *Streptococcus pyogenes* (right) causes puerperal fever.

EMERGING DISEASES

Scientific theories are not static and neither is the world around us. While we have been studying disease for hundreds of years, there is always more to learn. One reason for this is that organisms (such as those that cause disease) are always changing. This evolution of organisms leads to new diseases such as the COVID-19 pandemic. This resulted from a novel coronavirus (SARS-CoV-2) which is a descendent of coronaviruses that did not infect humans. Scientists are continually developing new strategies for learning about and curing emerging diseases.



Figure **1.4.4**: Pennsylvania Commonwealth microbiologist Kerry Pollard performs a manual extraction of the coronavirus inside the extraction lab at the Pennsylvania Department of Health Bureau of Laboratories on Friday, March 6, 2020.

REVIEW

1. Define scientific theory.
2. Contrast how the word theory is used in science and in everyday language.
3. What is the germ theory of disease? How did it develop?
4. Explain why Pasteur, rather than Fracastoro or Semmelweis, is called the father of germ theory.
5. Galen and Fracastoro may have come up with different explanations for how a disease is spread, but what observations do you think they made that were similar?

6. Use the explanation of Semmelweis' research and the graph in Figure **1.4.2** to answer the following questions.
    A. What was Semmelweis' observation that led him to undertake this study? What question was he trying to answer?
    B. What was the hypothesis (i.e. proposed answer for a scientific question) that Semmelweis was testing?
    C. Why did Semmelweis track death rates from puerperal fever at Dublin Maternity Hospital where autopsies were not performed?
    D. What were the two pieces of evidence shown in the graph that supported Semmelweis' hypothesis?
    E. Why do you think it was important that Semmelweis compared Dublin Maternity Hospital and Wien Maternity Clinic over the same years?
7. What is the difference between a microorganism and a pathogen?
8. Explain why the development of the microscope lent support to the germ theory of disease.
9. Does the observation of microorganisms alone conclusively prove that germ theory is correct? Why or why not?
10. Who do you think was using more scientific reasoning - Semmelweis or the physicians that derided his results? Explain your answer.

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1.5: SCIENTIFIC INVESTIGATIONS

WHAT TURNED THE WATER ORANGE?

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



Figure **1.5.1**:Rio Tinto river

"DOING" SCIENCE

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

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

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

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

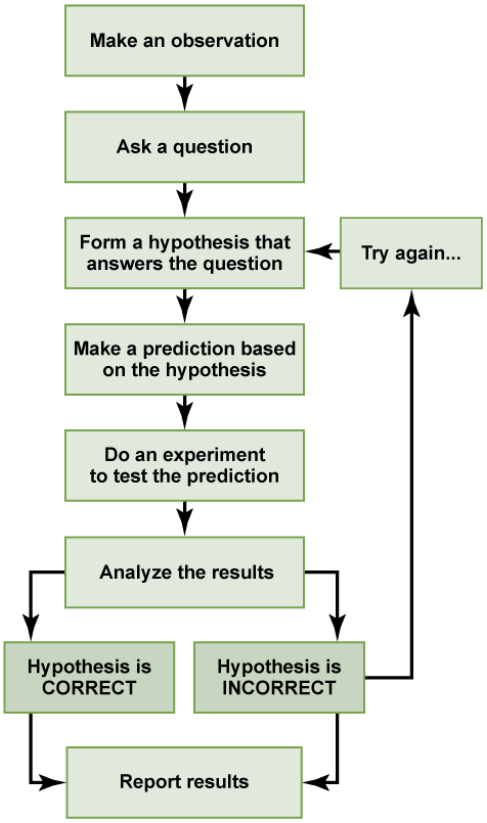


Figure **1.5.2**: The Scientific Method: The scientific method is a process for gathering data and processing information. It provides well-defined steps to standardize how scientific knowledge is gathered through a logical, rational problem-solving method. This diagram shows the steps of the scientific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

MAKING OBSERVATIONS

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

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

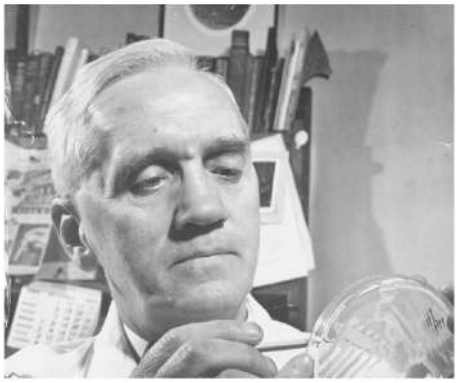


Figure **1.5.3**: Alexander Fleming experimenting with penicillin and bacteria in his lab in the 1940s.

ASKING QUESTIONS

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

HYPOTHESIS FORMATION

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

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

HYPOTHESIS TESTING

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

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

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

TESTING FLEMING'S HYPOTHESIS

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

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

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

ANALYZING AND INTERPRETING DATA

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

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

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

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

DRAWING CONCLUSIONS

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

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

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

CORRELATION-CAUSATION FALLACY

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

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

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

COMMUNICATING RESULTS

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

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

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

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

REVIEW

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

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1.6: SCIENTIFIC EXPERIMENTS

SEEING SPOTS

The spots on this child's tongue are an early sign of vitamin C deficiency, which is also called scurvy. This disorder, which may be fatal, is uncommon today because foods high in vitamin C are readily available. They include tomatoes, peppers, and citrus fruits such as oranges, lemons, and limes. However, scurvy was a well-known problem on navy ships in the 1700s. It was said that scurvy caused more deaths in the British fleet than French and Spanish arms. At that time, the cause of scurvy was unknown and vitamins had not yet been discovered. Anecdotal evidence suggested that eating citrus fruits might cure scurvy. However, no one knew for certain until 1747, when a Scottish naval physician named John Lind did an experiment to test the idea. Lind's experiment was one of the first clinical experiments in the history of medicine.



Figure **1.6.1**: Scorbutic tongue

WHAT IS AN EXPERIMENT?

An **experiment** is a special type of scientific investigation that is performed under controlled conditions. Like all investigations, an experiment generates evidence to test a hypothesis. But unlike some other types of investigations, an experiment involves manipulating some factors in a system in order to see how it affects the outcome. Ideally, experiments also involve controlling as many other factors as possible in order to isolate the cause of the experimental results.

An experiment generally tests how one particular variable is affected by some other specific variable. The affected variable is called the **dependent variable** or outcome variable. The variable that affects the dependent variable is called the **independent variable.** It is also called the manipulated variable because this is the variable that is manipulated by the researcher. Any other variables (**control variable**) that might also affect the dependent variable are held constant, so the effects of the independent variable alone are measured.

LIND'S SCURVY EXPERIMENT

Lind began his scurvy experiment onboard a British ship after it had been at sea for two months and sailors had started showing signs of scurvy. He chose a group of 12 sailors with scurvy and divided the group into 6 pairs. All 12 sailors received the same diet, but each pair also received a different daily supplement to the diet (Table **1.6.1**).

Table **1.6.1**: Lind's Scurvy Experiment

Pair of Subjects	Daily Supplement to the Diet Received by this Pair
1	1 quart of cider
2	5 drops of sulfuric acid
3	6 spoons of vinegar
4	1 cup of seawater
5	2 oranges and 1 lemon
6	spicy paste and a drink of barley water

Lind's experiment ended after just five days when the fresh citrus fruits ran out for pair 5. However, the two sailors in this pair had already fully recovered or greatly improved. The sailors in pair 1 (receiving the quart of cider) also showed some improvement, but sailors in the other pairs showed none.

Can you identify the independent and dependent variables in Lind's experiment? The independent variable is the daily supplement received by the pairs. The dependent variable is the improvement/no improvement in scurvy symptoms. Lind's results supported the citrus fruit cure for scurvy, and it was soon adopted by the British navy with good results. However, the fact that scurvy is caused by a vitamin C deficiency was not discovered until almost 200 years later.

SAMPLING

Lind's scurvy experiment included just 12 subjects. This is a very small sample by modern scientific standards. The **sample** in an experiment or other investigation consists of the individuals or events that are actually studied. It rarely includes the entire population because doing so would likely be impractical or even impossible.

There are two types of errors that may occur by studying a sample instead of the entire population: chance error and bias.

- A chance error occurs if the sample is too small. The smaller the sample is, the greater the chance that it does not fairly represent the whole population. Chance error is mitigated by using a larger sample.
- Bias occurs if the sample is not selected randomly with respect to a variable in the study. This problem is mitigated by taking care to choose a randomized sample.

A reliable experiment must be designed to minimize both of these potential sources of error. You can see how the sources of error were addressed in another landmark experiment: Jonas Salk's famous 1953 trial of his newly developed polio vaccine. Salk's massive experiment has been called the "greatest public health experiment in history."

SALK'S POLIO VACCINE EXPERIMENT

Imagine a nationwide epidemic of a contagious flu-like illness that attacks mainly children and often causes paralysis. That's exactly what happened in the U.S. during the first half of the 20th century. Starting in the early 1900s, there were repeated cycles of polio epidemics, and each seemed to be stronger than the one before. Many children ended up on life support in so-called "iron lungs" (see photo below) because their breathing muscles were paralyzed by the disease.



Figure **1.6.2**: This photo shows the iron lung ward in a California hospital in 1953, the same year that Salk undertook his nationwide vaccine experiment.

Polio is caused by a virus, and there is still no cure for this potentially devastating illness. Fortunately, it can now be prevented with vaccines. The first polio vaccine was discovered by Jonas Salk in 1952. After testing the vaccine on himself and his family members to assess its safety, Salk undertook a nationwide experiment to test the effectiveness of the vaccine using more than a million schoolchildren as subjects. It's hard to imagine a nationwide trial of an experimental vaccine using children as "guinea pigs." It would never happen today. However, in 1953, polio struck such fear in the hearts of parents that they accepted Salk's word that the vaccine was safe and gladly permitted their children to participate in the study.

Salk's experiment was very well designed. First, it included two very large, random samples of children — 600,000 in the treatment group, called the **experimental group**, and 600,000 in the untreated group, called the **control group**. Using very large and randomized samples reduced the potential for chance error and bias in the experiment. Children in the experimental group were injected with the experimental polio vaccine. Children in the control group were injected with a harmless saline (saltwater) solution. The saline injection was a placebo. A **placebo** is a "fake" treatment that actually has no effect on health. It is included in trials of vaccines and other medical treatments, so subjects will not know in which group (control or experimental) they have been placed. The use of a placebo helps researchers control for the **placebo effect**. This is a psychologically-based reaction to a treatment that occurs just because the subject is treated, even if the treatment has no real effect.

Experiments in which a placebo is used are generally **blind experiments** because the subjects are "blind" to their experimental group. This helps prevent bias in the experiment. Often, even the researchers do not know which subjects are in each group. This type of experiment is called a **double-blind experiment** because both subjects and researchers are "blind" to which subjects are in each group. Salk's vaccine trial was a double-blind experiment, and double-blind experiments are now considered the gold standard of clinical trials of vaccines, therapeutic drugs, and other medical treatments.

Salk's polio vaccine proved to be highly successful. Analysis of data from his study revealed that the vaccine was 80 to 90 percent effective in preventing polio. Almost overnight, Salk was hailed as a national hero. He appeared on the cover of *Time* magazine and was invited to the White House. Within a few years, millions of children had received the polio vaccine. By 1961, the incidence of polio in the U.S. had been reduced by 96 percent.

LIMITS ON EXPERIMENTATION

Well-done experiments are generally the most rigorous and reliable scientific investigations. However, their hallmark feature of manipulating variables to test outcomes is not possible, practical, or ethical in all investigations. As a result, many ideas cannot be tested through experimentation. For example, experiments cannot be used to test ideas about what our ancestors ate millions of years ago or how long-term cigarette smoking contributes to lung cancer. In the case of our ancestors, it is impossible to study them directly. Researchers must rely instead on indirect evidence, such as detailed observations of their fossilized teeth. In the case of smoking, it is unethical to expose human subjects to harmful cigarette smoke. Instead, researchers may use large observational studies of people who are already smokers, with nonsmokers as controls, to look for correlations between smoking habits and lung cancer.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Lind undertook his experiment to test the effects of citrus fruits on scurvy at a time when seamen were dying by the thousands from this nutritional disease as he explored the world. Today's explorers are astronauts in space, and their nutrition is also crucial to the success of their missions. However, maintaining good nutrition in astronauts in space can be challenging. One problem is that astronauts tend to eat less while in space. Not only are they very busy on their missions, but they may also get tired of the space food rations. The environment of space is another problem. Factors such as microgravity and higher radiation exposure can have major effects on human health and require nutritional adjustments to help counteract them. A novel way of studying astronaut nutrition and health is provided by identical twin astronauts Scott and Mark Kelly (Figure **1.6.3**).



Figure **1.6.3**: Homozygote twin astronauts Mark and Scott Kelly at the Johnson Space Center.

The Kellys are the first identical twin astronauts, but twin studies are nothing new. Scientists have used identical (homozygotic) twins as research subjects for many decades. Identical twins have the same genes, so any differences between them generally can be attributed to environmental influences rather than genetic causes. Mark Kelly spent almost a full year on the International Space Station (ISS) between 2015 and 2016, while his twin, Scott Kelly, stayed on the ground, serving as a control in the experiment. You may have noticed a lot of media coverage of Mark Kelly's return to Earth in March 2016 because his continuous sojourn in space was the longest of any American astronaut at that time. NASA is learning a great deal about the effects of long-term space travel on the human body by measuring and comparing nutritional indicators and other health data in the twins.

REVIEW

1. How do experiments differ from other types of scientific investigations?
2. Identify the independent and dependent variables in Salk's nationwide polio vaccine trial.
3. Compare and contrast chance error and bias in sampling. How can each type of error be minimized?
4. What is the placebo effect? Explain how Salk's experimental design controlled for it.
5. *Fill in the blanks.* The _____ variable is manipulated to see the effects on the _____ variable.
6. *True or False.* In studies of identical twins, the independent variable is their genetics.
7. *True or False.* Experiments cannot be done on humans.
8. *True or False.* Larger sample sizes are generally better than smaller ones in scientific experiments.
9. Answer the following questions about Lind's scurvy experiment.
    A. Why do you think it was important that the sailors' diets were all kept the same, other than the daily supplement?
    B. Can you think of some factors other than diet that could have potentially been different between the sailors that might have affected the outcome of the experiment?
    C. Why do you think the sailors who drank cider had some improvement in their scurvy symptoms?
10. Explain why double-blind experiments are considered to be more rigorous than regular blind experiments.
11. Why are studies using identical twins so useful?
12. Do you think it is necessary to include a placebo (such as an injection with saline in a drug testing experiment) in experiments that use animals? Why or why not?

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1.7: EXTRAPOLATIONS OF SCIENTIFIC INVESTIGATIONS

UP IN SMOKE

You've probably seen this warning label dozens of times. It's been required on cigarette packs in the U.S. since 1965, one year after the U.S. Surgeon General first issued a report linking cigarette smoking with diseases such as lung cancer. The report was based on thousands of research articles, including important research results published by British scientists Richard Doll and Austin Bradford Hill. Starting in 1950, Doll and Hill conducted large-scale, long-term observational studies on smoking and lung cancer and demonstrated a strong correlation between the two.



Figure **1.7.1**: Surgeon General's warning on a box of cigarettes: Smoking causes lung cancer, heart disease, emphysema and may complicate pregnancy.

OBSERVATIONAL STUDIES

Many questions in human biology are investigated with observational as opposed to experimental studies. An **observational study** measures characteristics in a sample but does not attempt to manipulate variables of interest. A simple example of an observational study is a political poll. A sample of adults might be asked how old they are and which of two candidates they favor. The study provides a snapshot in time of potential voters' opinions and how they differ by age of the respondent. Whether the results of the study apply to the population as a whole depends mainly on how large and random the sample is.

How is an observational study different from an experiment — the gold standard of scientific research studies? The main difference is how subjects are treated. In an observational study, no attempt is made to influence the subjects in any way. In an experiment, in contrast, the researcher applies a treatment to a group of subjects and attempts to isolate the effects of the treatment on an outcome variable by comparing the experimental group with a control group. For example, in 1954, Jonas Salk did an experimental trial of his newly discovered polio vaccine by giving it to a very large sample of children. Children in an equally large control group were given a harmless injection of a saline solution but no vaccine. Salk then compared the two groups of children and determined that the vaccine was 80 to 90 percent effective in preventing polio.

TYPES OF OBSERVATIONAL STUDIES

There are three different types of observational studies: cross-sectional, case-control, and cohort studies. All three types have pros and cons.

CROSS-SECTIONAL STUDIES

A **cross-sectional study** is a type of observational study that collects data from a sample of subjects just once at a certain point in time. The political poll described above is a simple example of a cross-sectional study. A possible link between smoking and lung cancer was also first suggested by cross-sectional studies. Researchers found a higher rate of lung cancer in people who smoked than in those who did not smoke at the time of the study. In other words, the two variables seemed to be associated.

Cross-sectional studies are relatively cheap and easy to do, but their results are weak, so they are rarely used alone. More often, a researcher uses a cross-sectional study to find variables that may be linked and then does a case-control or cohort study to further investigate a possible relationship between the two variables.

CASE-CONTROL STUDIES

A **case-control study** is a type of observational study that compares a group of subjects having a trait of interest (cases) with a group of similar subjects not having the trait (controls). This type of study is retrospective. Subjects are asked to report their behaviors in the past in an attempt to find correlations between specific past behaviors and current status. The retrospective nature of case-control studies is their main weakness. Subjects' responses may be inaccurate because they forget or are dishonest about past habits.

A classic example of a case-control study is the early research on smoking and lung cancer carried out by Doll and Hill (Figure **1.7.2**). In 1950, the two scientists interviewed 700 lung cancer patients (cases) and 700 people without lung cancer (controls). They gathered information on past smoking habits and other characteristics of people in the two groups. When they compared the two groups, they found a strong association between past smoking behavior and current lung cancer status.



Figure **1.7.2**: Austin Bradford Hill was named a British knight for his important research in public health, including his work with Richard Doll establishing a link between tobacco smoking and lung cancer.

COHORT STUDIES

A **cohort study** is an observational study in which a group of similar subjects (the cohort) is selected at the start of the study and then followed over time. This type of study is prospective. The researchers collect data on the cohort periodically for months or

even years into the future. Because the researchers collect the information directly, the data are likely to be more accurate than the self-reported recall data in case-control studies. Prospective data also allow researchers to establish the sequence of progression of disease states or other conditions of interest. On the other hand, cohort studies are the most costly and difficult observational studies to undertake.

One of the largest-ever cohort studies was undertaken by Doll and Hill in 1951. It was based on their earlier case-control study and further investigated the link between smoking and lung cancer. The cohort that began the study included almost 50,000 British male physicians, and they were followed by the researchers over the next 50 years. Initial findings of the study were first reported in 1954, and then updated results were reported periodically after that. The last report was published in 2004, and it reflected on the previous 50 years of research findings. This study provided even stronger evidence for the correlation between smoking and lung cancer.

Numerous other research studies, including experimental studies, have shown conclusively that smoking causes lung cancer, among many other health problems. Figure **1.7.3** shows some of the ill effects that have since been demonstrated to be caused by smoking.

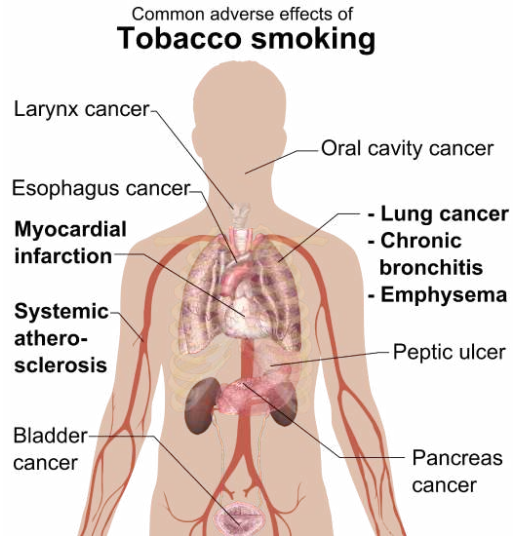


Figure **1.7.3**: Lung cancer is just one of many adverse effects on the human body that research studies have shown to be caused by smoking. The more common adverse effects are in bold and include myocardial infarction, system atherosclerosis, lung cancer, chronic bronchitis, and emphysema. Other effects include larynx cancer, esophagus cancer, bladder cancer, oral cavity cancer, peptic ulcer, and pancreas cancer.

CORRELATION VS. CAUSATION IN OBSERVATIONAL STUDIES

Observational studies can generally establish correlation but not necessarily causation. **Correlation** is an association between two variables in which a change in one variable is associated with a change in the other variable. Correlation may be strong or weak. It can also be positive or negative.

- If two variables are shown to have a positive correlation, both variables change in the same direction. For example, an observational study might find that more smoking is correlated with a higher risk of lung cancer. In other words, as smoking goes up, so does lung cancer.
- If two variables are shown to have a negative correlation, they change in opposite directions. For example, an observational study might find that people who exercise more are less likely to develop lung cancer. In other words, as exercise increases, lung cancer decreases.

One of the main differences between observational studies and experiments is the issue of correlation vs. causation. Because observational studies do not control all variables, any correlations they show between variables cannot be interpreted as one variable causes another. In experiments, in contrast, all possible variables are controlled, making it safer to conclude that changes in one variable cause changes in another. Unfortunately, when observational studies are reported in the news media, this distinction is not often made. Instead, a variable that is correlated with another in an observational study may be reported incorrectly as causing changes in the other variable.

In observational studies, it is always possible that some other variable affects both of the variables of interest and explains the correlation. An example of the confusion of correlation and causation in observational studies is the case of the health effects of coffee. Many early observational studies of coffee consumption and health found a positive correlation between drinking coffee and health problems such as heart disease and cancer. Does this mean that drinking coffee causes these health problems? Not necessarily, although news media have reported this conclusion. Looking more deeply into the issue reveals that coffee drinking is also associated with a less health-conscious lifestyle. People who drink coffee tend to practice other behaviors that may negatively impact their health, such as smoking cigarettes or drinking alcohol. Larger observational studies in which such lifestyle differences were taken into account have found no correlation between coffee consumption and health problems. In fact, they have found that moderate coffee consumption may actually have some health benefits.

RATIONALE FOR OBSERVATIONAL STUDIES

If observational studies cannot establish causation, why are they done? Why aren't all research questions investigated experimentally? There are several important reasons to do observational studies:

- An observational study may be the only type of study that is feasible for certain research questions because experiments are impossible, impractical, or unethical to undertake. For example, it would be unethical to do an experiment on smoking and health in which subjects in the smoking sample are deliberately exposed to tobacco smoke and then observed to see if they develop lung cancer.
- An observational study is generally cheaper and easier to conduct than an experimental study.
- An observational study usually can study more subjects and obtain a larger set of data than an experimental study.

MODELS

Another way to gain scientific knowledge without experimentation is with modeling. A **model** is a representation of part of the real world. Did you ever build a model car or airplane? Scientific models are something like that. They represent the real world but are simpler. This is one reason that models are especially useful for investigating complex systems. By studying a much simpler model, it is easier to learn how the real system works.

As a hypothesis, a model must be evaluated. It is assessed by criteria such as how well it represents the real world, what limitations it has, and how useful it is. The usefulness of a model depends on how well its predictions match observations of the real world. Keep in mind that even when a model's predictions match real-world observations, it doesn't prove that the model is correct or that it is the only model that works.

MODELING BIOLOGICAL SYSTEMS

Many phenomena in biology occur as part of a complex system, whether the system is a cell, a human organ such as the brain, or an entire ecosystem. Models of biological systems can range from simple two-dimensional diagrams to complex computer simulations. Figure **1.7.3** depicts a model of nicotine's effect on cells in the nervous system.

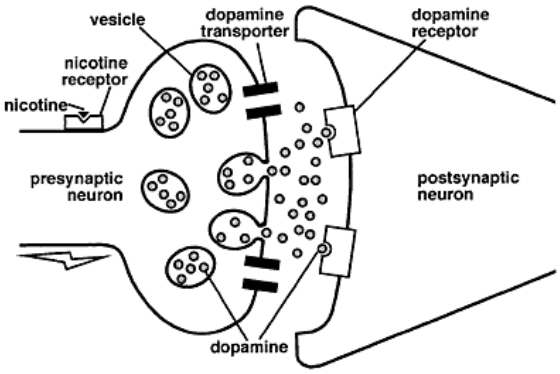


Figure **1.7.4**: Nicotine binds to specific receptors on the presynaptic neuron. When nicotine binds to receptors at the cell body, it excites the neuron so that it fires more action potentials (electrical signals, represented by the jagged shape in the lower left of the figure) that move toward the synapse, causing more dopamine release (not shown in the figure). When nicotine binds to nicotine receptors at the nerve terminal, the amount of dopamine released in response to an action potential is increased.

MODEL ORGANISMS

Using other organisms as models of the human body is another way models are used in human biology research. A **model organism** is a nonhuman species that is extensively studied to understand particular biological phenomena. The expectation is that discoveries made in the model organism will provide insights into the workings of the human organism. In researching human diseases, for example, model organisms allow for a better understanding of the disease process without the added risk of harming actual human beings. The model species chosen should react to the disease or its treatment in a way that resembles human physiology. Although biological activity in a model organism does not ensure the same effect in humans, many drugs, treatments, and cures for human diseases are developed in part with the guidance of model organisms.

Model organisms that have been used in human biology research range from bacteria such as *E. coli* to nonhuman primates such as chimpanzees. The mouse *Mus musculus*, pictured below, is a commonly used model organism in human medical research. For example, it has been widely used to study diet-induced obesity and related health problems. In fact, the mouse model of diet-induced obesity has become one of the most important tools for understanding the interplay of high-fat Western diets and the development of obesity.



Figure **1.7.5**: The mouse *Mus musculus* is commonly used as a model organism in human biology research.

FEATURE: RELIABLE SOURCES

You may get most of your news from the Internet. You probably also research personal questions and term paper topics online. Unlike the information in newspapers and most television news broadcasts, information on the Internet is not regulated for quality or accuracy. Almost anybody can publish almost anything they wish on the web. The responsibility is on the user to evaluate Internet resources. How do you know if the resources you find online are reliable? The questions below will help you assess their reliability.

1. How did you find the web page? If you just "googled" a topic or question, the search results may or may not be reliable. More likely to be trustworthy are web pages recommended by a faculty member, cited in an academic source, or linked with a reputable website.
2. What is the website's domain? If its URL includes .edu, it is affiliated with a college or university. If it includes .gov, it is affiliated with the federal government, and if it includes .org it is affiliated with a nonprofit organization. Such websites are generally more trustworthy sources of information than .com websites, which are commercial or business websites.
3. Who is the author of the web page? Is the author affiliated with a recognized organization or institution? Are the author's credentials listed, and are they relevant to the information on the page? Is current contact information for the author provided?
4. Is the information trustworthy? Are sources cited for facts and figures? Is a bibliography provided? Does there seem to be a particular bias or point of view presented, or does the

information seem fair and balanced? Does the page contain advertising that might impact the content of information that is included?
5. Is the information current? When was the page created and last updated? Are the links on the page current and functional?

Put this advice into practice. Go online and find several web pages that provide information on the topic of smoking and lung cancer. Which websites do you think provide the most reliable information? Why?

REVIEW

1. Explain why observational studies cannot establish causation. Describe an example to illustrate your explanation.
2. Compare and contrast the three types of observational studies described above.
3. Identify three possible reasons for doing an observational study.
4. Why are models commonly used in human biology research?
5. *Multiple answers*: What kind of a study involves the recall of variables that occurred in the past? What kind involves the observation of variables from the beginning?
   A. positive correlation; negative correlation
   B. negative correlation; positive correlation
   C. retrospective; prospective
   D. prospective; retrospective
6. *True or False*. A positive correlation means there are health benefits to the variable under investigation.
7. *True or False*. A cohort is a group of subjects of different ages, weights, genders, and health statuses.
8. A study is done to investigate whether soda consumption influences the development of diabetes. The subjects are individuals recently diagnosed with diabetes compared to controls who do not have diabetes. All of the respondents are asked how many times a week they drank soda over the last two years. Answer the following questions about this scientific investigation.
   A. What type of observational study is this?
   B. The subjects with diabetes are "matched" to the controls, meaning that the researchers tried to minimize the effect of other variables outside of the variable of interest (i.e. soda consumption). What do you think some of those other variables could be?
   C. Do you think the data about soda consumption will be accurate? Why or why not?
   D. How could you change the study to get more accurate data on whether there is a relationship between soda consumption and diabetes? Explain why your new study would be more accurate.
9. Do you think that computer simulation models of biological systems can be accurate without observations or experiments on actual living organisms or tissues?
10. Explain why both observational and experimental investigations are useful in science.

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1.8: CASE STUDY CONCLUSION- SHOT AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: TO GIVE A SHOT OR NOT

New mother Elena left her pediatrician's office still unsure whether to vaccinate baby Juan. Dr. Rodriguez gave Elena a list of reputable sources where she could look up information about the safety of vaccines herself, such as the Centers for Disease Control and Prevention (CDC). Elena reads that the consensus within the scientific community is that there is no link between vaccines and autism. She finds a long list of studies published in peer-reviewed scientific journals that disprove any link. Additionally, some of the studies are "meta-analyses" that analyzed the findings from many individual studies. Elena is reassured by the fact that many different researchers, using a large number of subjects in numerous well-controlled and well-reviewed studies, all came to the same conclusion.



Figure **1.8.1**: Infant on parent's lap

Elena also went back to the author's website that originally scared her about the safety of vaccines. She found that the author was not a medical doctor or scientific researcher, but rather was a self-proclaimed "child wellness expert." Also, the doctor sold books and advertising on their site, some of which were related to claims of vaccine injury. Elena realized that the doctor was both an unqualified and potentially biased source of information.

Also, Elena realized that some of the doctor's arguments were based on correlations between autism and vaccines, but, as the saying goes, "correlation does not imply causation." For instance, the recent rise in autism rates may have occurred during the same time period as an increase in the number of vaccines given in childhood, but Elena could think of many other environmental and social factors that have also changed during this time period. There are just too many variables to come to the conclusion that vaccines, or anything else, are the cause of the rise in autism rates based on that type of argument alone. Also, Elena learned that the age of onset of autism symptoms happens to typically be around the time that the MMR vaccine is first given, so the apparent association in the timing may just be a coincidence.

Public health, sanitation, and the use of antibiotics and vaccines have lessened the impact of infectious disease on human populations. Through vaccination programs, better nutrition, and vector control (carriers of disease), international agencies have significantly reduced the global infectious disease burden. Reported cases of measles in the United States dropped from around 700,000 a year in the 1950s to practically zero by the late 1990s and declared eradicated by the year 2000 (Figure **1.8.2**). Globally, measles fell 60 percent from an estimated 873,000 deaths in 1999 to 164,000 in 2008. This advance is attributed entirely to a comprehensive vaccination program.

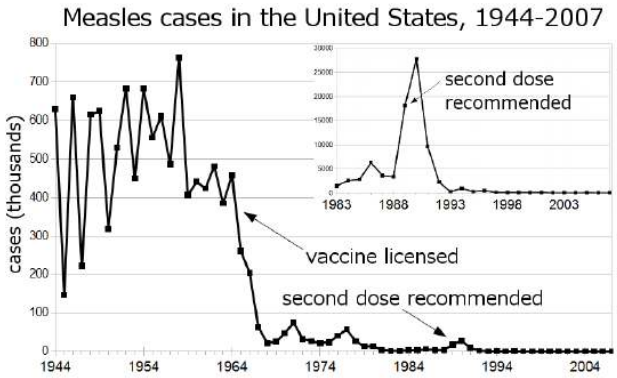


Figure **1.8.2**: Measles cases reported in the United States, 1944-2007. From 1944 to 1963 measles cases fluctuated between 100 - 800 cases per thousand individuals. The measles vaccine was licensed in 1963 and the number of cases plummeted to less than 100 per thousand individuals. A second dose was recommended in 1988 an causes the total number of cases to fall to nearly zero.

However, Elena came across news about a measles outbreak that originated in California in 2014, 2015, and the latest outbreak of 2019 (Figure **1.8.3**). Measles wasn't just a disease of the past as she had thought! She learned that measles and whooping cough, which had previously been rare thanks to widespread vaccinations, are now on the rise, and that people choosing not to vaccinate their children seems to be one of the contributing factors. Elena realized that it is important to vaccinate their baby against these diseases, not only to protect the baby from their potentially deadly effects but to also protect others in the population.

In her reading, Elena learns that scientists do not yet know the causes of autism, but she feels reassured by the abundance of data that disproves any link with vaccines. She thinks that the potential benefit of protecting their baby's health against deadly diseases outweighs any unsubstantiated claims about vaccines. She will be making an appointment to get baby Juan their shots soon.

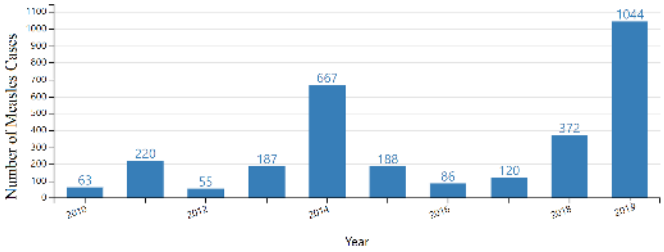


Figure **1.8.3**: Measles cases reported in the US as of June 2019 - 1044 cases of measles were reported in the states of Arizona, California, Colorado, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, Missouri, New Mexico, Nevada, New Hampshire, New Jersey, New York, Oklahoma, Oregon, Pennsylvania, Texas, Tennessee, Virginia, and Washington. This is much higher than any year in the past decade where the number of cases flucuated from 55 to 667.

CHAPTER SUMMARY

- Science is a distinctive way of gaining knowledge about the natural world that is based on the use of evidence to logically test ideas. As such, science is more of a process than a body of knowledge.
- A scientific theory, such as the germ theory of disease, is the highest level of explanation in science. A theory is a broad explanation for many phenomena that is widely accepted because it is supported by a great deal of evidence.
- The scientific investigation is the cornerstone of science as a process. An investigation is a procedure for gathering evidence to test a hypothesis.
- A scientific experiment is a type of scientific investigation in which the researcher manipulates variables under controlled conditions to test expected outcomes. Experiments are the gold standard for scientific investigations and can establish causation between variables.
- Nonexperimental scientific investigations such as observational studies and modeling may be undertaken when experiments are impractical, unethical, or impossible. Observational studies generally can establish correlation but not causation between variables.

CHAPTER SUMMARY REVIEW

1. Which of the following is the best example of “doing science?”
   A. memorizing the processes of the water cycle
   B. learning how to identify trees from their leaves
   C. learning the names of all the bones in the human body
   D. making observations of wildlife while hiking in the woods
2. A scientist develops a new idea based on their observations of nature. What should they do next?
   A. think of a way to test the idea
   B. claim that they have discovered a new theory
   C. reject any evidence that conflicts with the idea
   D. look only for evidence that supports the idea
3. Which of the following is defined as a possible answer to a scientific question?
   A. an observation
   B. data
   C. a hypothesis
   D. statistics
4. Do scientists usually come up with a hypothesis in the absence of any observations? Explain your answer.
5. Why does a good hypothesis have to be falsifiable?
6. Name one scientific law.
7. Name one scientific theory.
8. Give an example of a scientific idea that was later discredited.
9. Would the idea that the Earth revolves around the Sun be considered consensus science or frontier science?
10. *True or False.* A scientific investigation always follows the same sequence of steps in a linear fashion.
11. *True or False.* Data that does not support a hypothesis is not useful.
12. *True or False.* Experimentation is the only valid type of scientific investigation.
13. *True or False.* Correlation does not imply causation.
14. Explain why science is considered an iterative process.
15. A statistical measurement called a P-value is often used in science to determine whether or not a difference between two groups is actually significant or simply due to chance. A P-value of 0.03 means that there is a 3% chance that the difference is due to chance alone. Do you think a P-value of 0.03 would indicate that the difference is likely to be significant? Why or why not?
16. a. Why is it important that scientists communicate their findings to others? How do they usually do this?
17. What is a “control group” in science?
18. In a scientific experiment, why is it important to only change one variable at a time?
19. Which is the *dependent variable* – the variable that is manipulated or the variable that is being affected by the change?
20. Which is most likely to show or disprove causation between two variables?
    A. a controlled experiment
    B. an observational study
    C. the development of a hypothesis
    D. an observation
21. You see an ad for a “miracle supplement” called NQP3 that claims the supplement will reduce belly fat. They say it works by reducing the hormone cortisol and by providing your body with missing unspecified “nutrients”, but they do not cite any peer-reviewed clinical studies. They show photographs of three people who appear slimmer after taking the product. A board-certified plastic surgeon endorses the product on television. Answer the following questions about this product.
    A. Do you think that because a doctor endorsed the product, it really works? Explain your answer.
    B. Do you think the photographs are good evidence that the product works? Why or why not?

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CHAPTER OVERVIEW

2: CHEMISTRY OF LIFE

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

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

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

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2.1: CASE STUDY- CHEMISTRY AND YOUR LIFE

CASE STUDY: DIET DILEMMA

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



Figure **2.1.1**: Diabetes Detritus

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

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

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

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

CHAPTER OVERVIEW: CHEMISTRY OF LIFE

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

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

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

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

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2.2: ELEMENTS AND COMPOUNDS

WHAT ARE YOU MADE OF?

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



Figure **2.2.1**: Diversity and Unity

ELEMENTS AND ATOMS

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

PERIODIC TABLE OF THE ELEMENTS

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

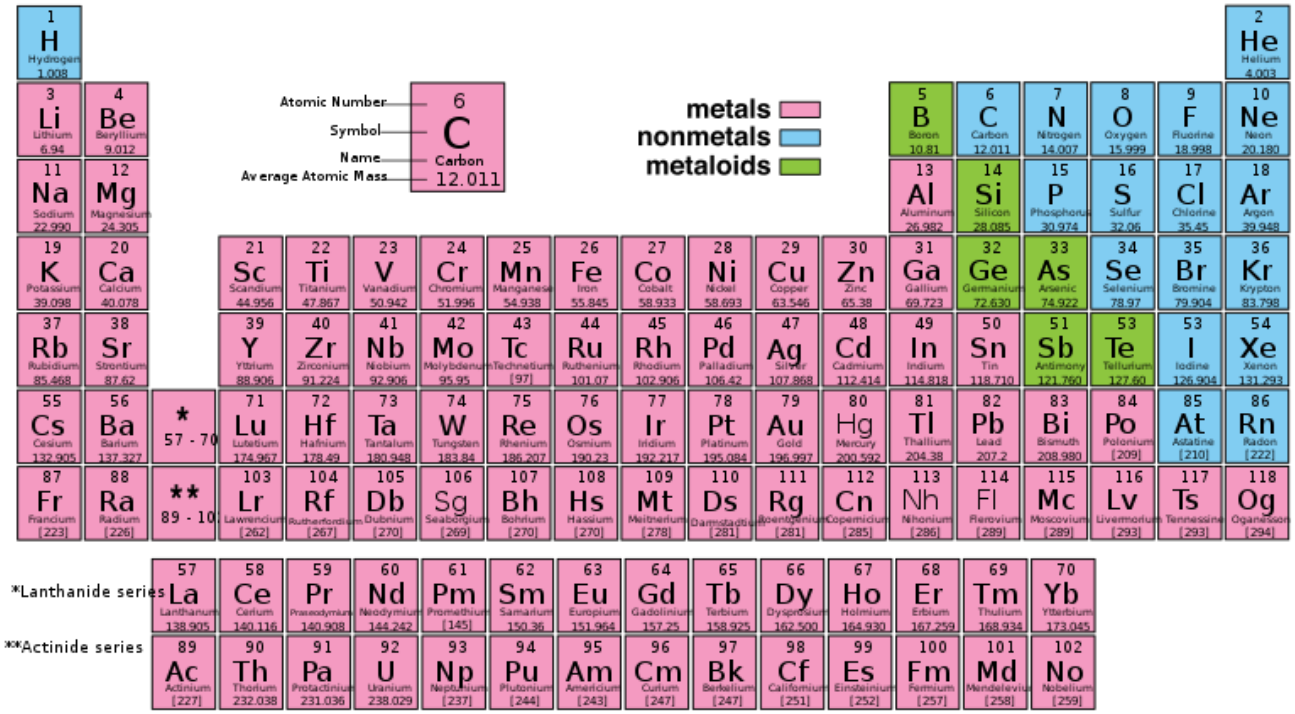


Figure **2.2.3**: Periodic Table of the Elements. The periodic table of the elements arranges elements in groups based on their properties. You may prefer to use an interactive periodic table or an accessible periodic table.

STRUCTURE OF AN ATOM

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

Table **2.2.1**: Subatomic Particles

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

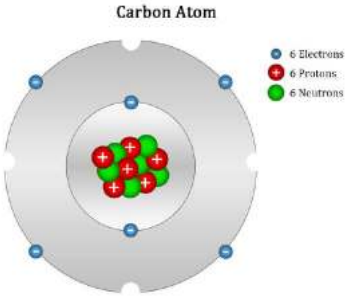


Figure **2.2.2**: A model of a Carbon atom. Carbon has 6 protons and 6 neutrons (found in the nucleus). The image also shows the 6 electrons outside of the nucleus in 2 separate orbitals.

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

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

COMPOUNDS AND MOLECULES

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

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

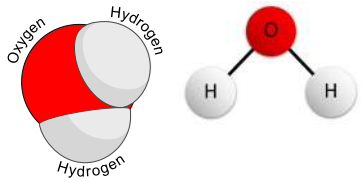


Figure **2.2.4**: Water Molecule. A water molecule always has this composition, one atom of oxygen, and two atoms of hydrogen.

REVIEW

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

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2.3: CHEMICAL BONDING

CHEMICAL BONDING

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



Figure **2.3.1**: Mother and daughter

WHY BONDS FORM

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

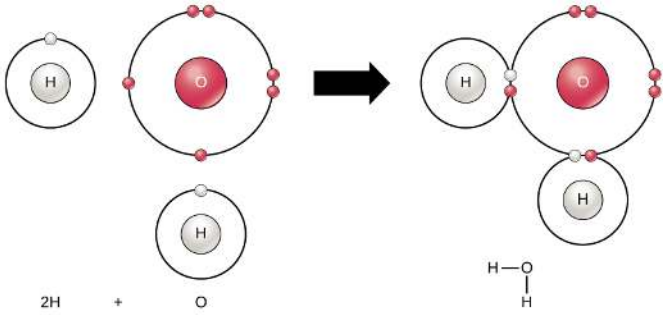


Figure **2.3.2**: Bonds between hydrogen and oxygen atoms in a water molecule. Electrons are drawn as spheres on the circle indicating an electron orbit. The nucleus is shown as the big sphere in the center of the atom.

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

TYPES OF CHEMICAL BONDS

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

NON-POLAR COVALENT BONDS

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

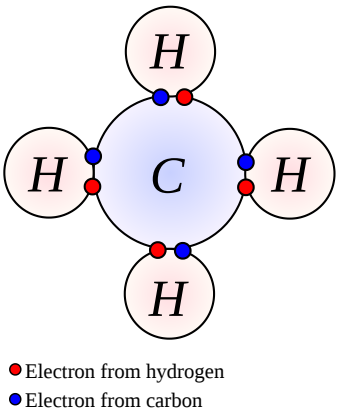


Figure **2.3.3**: Methane is formed when four hydrogens and one carbon covalently bond.

POLAR COVALENT BONDS AND HYDROGEN BONDS

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

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

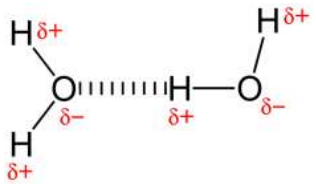


Figure **2.3.4**: A hydrogen bond in water occurs between the hydrogen atom of one water molecule and the lone pair of electrons on an oxygen atom of a neighboring water molecule

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

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

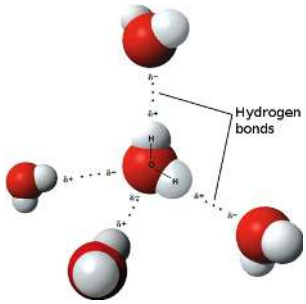


Figure **2.3.5**: Multiple hydrogen bonds occur simultaneously in water because of its bent shape and the presence of two hydrogen atoms per molecule.

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

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

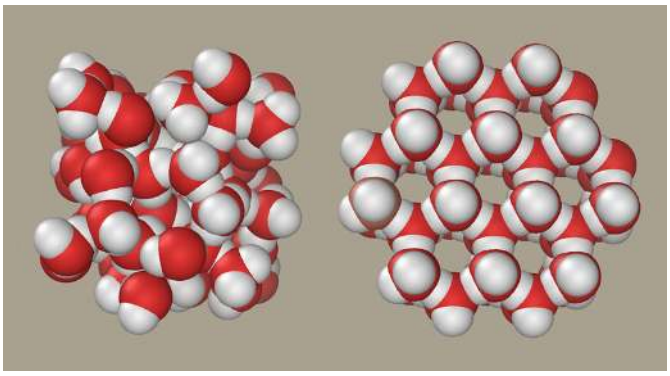


Figure **2.3.6**: When water freezes to ice, the hydrogen bonding network becomes more stable. Each oxygen atom has an approximately tetrahedral geometry – two covalent bonds and two hydrogen bonds.

IONIC BONDS

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

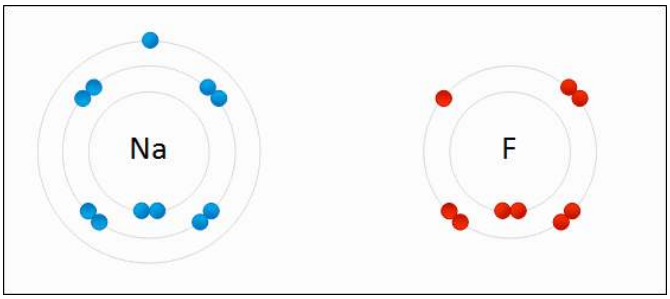


Figure **2.3.7**: Sodium (left) and fluorine (right) form an ionic compound called Sodium fluoride. The animation shows sodium (Na) losing an electron. This electron is taken by fluorine (F). This makes Na positively charged and F negatively charged. These ions are then attracted to each other.

REVIEW

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

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2.4: BIOCHEMICAL COMPOUNDS

CARBS GALORE

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



Figure **2.4.1**: Grain product food

CHEMICAL COMPOUNDS IN LIVING THINGS

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

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

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



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

CLASSES OF BIOCHEMICAL COMPOUNDS

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

CARBOHYDRATES

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

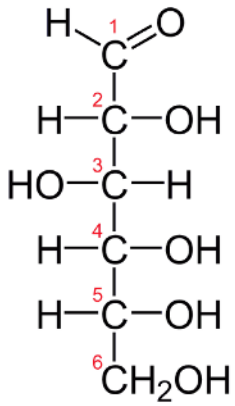


Figure **2.4.3**: Model of a monosaccharide (glucose) molecule. Glucose has 6 carbons forming a backbone. Each carbon has a total of 4 bonds. Each bond connects carbon to a carbon, hydrogen, or oxygen atom.

LIPIDS

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

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

PROTEINS

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

NUCLEIC ACIDS

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

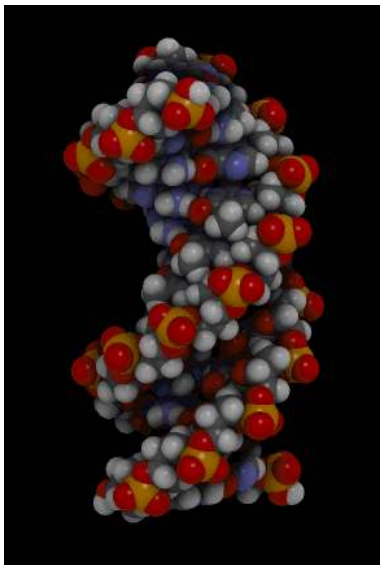


Figure **2.4.4**: This rotating DNA model shows the complexity of this two-stranded nucleic acid. There are many different atoms making the double helix structure.

REVIEW

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

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2.5: CARBOHYDRATES

THE CELLULOSE OF OUR LIVES

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



Figure 2.5.1: Body paint and jeans

WHAT ARE CARBOHYDRATES?

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

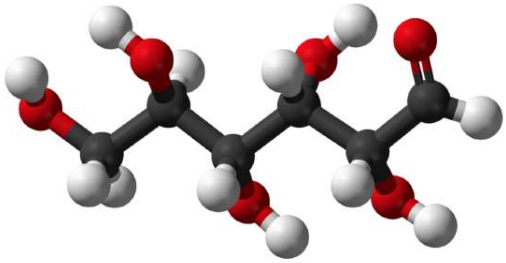


Figure 2.5.2: The six black balls in this model of the monosaccharide glucose represent carbon atoms. These six carbons make up the backbone in the center of glucose. The red balls are oxygen, and the white ones are hydrogen.

SUGARS

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

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

COMPLEX CARBOHYDRATES

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

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

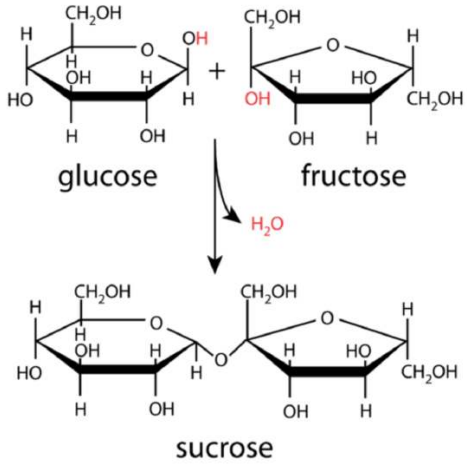


Figure 2.5.3: Glucose and fructose combine to produce the disaccharide sucrose in a condensation reaction. The diagram shows how water is produced when the reaction occurs. This is because the oxygen in glucose binds to the carbon in fructose. That removes an oxygen and two hydrogens from the new molecule.

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

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

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



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

STARCH

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

GLYCOGEN

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

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

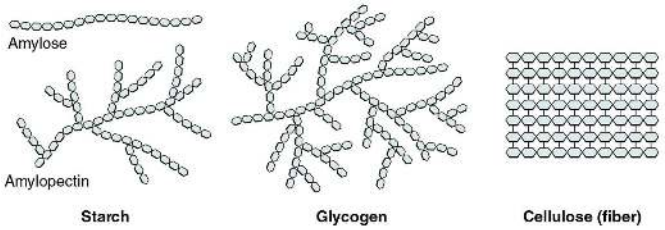


Figure **2.5.5**: Starch, Glycogen, and Cellulose have different arrangements of monosaccharides.

CELLULOSE

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

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

CHITIN

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

FEATURE: MY HUMAN BIOLOGY



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

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

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

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

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

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

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

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

SUMMARY

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

REVIEW

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

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

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2.6: LIPIDS

YUM!

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



Figure **2.6.1**: Philly Cheesesteak Sandwich

LIPIDS AND FATTY ACIDS

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

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

SATURATED FATTY ACIDS

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

UNSATURATED FATTY ACIDS

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

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

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

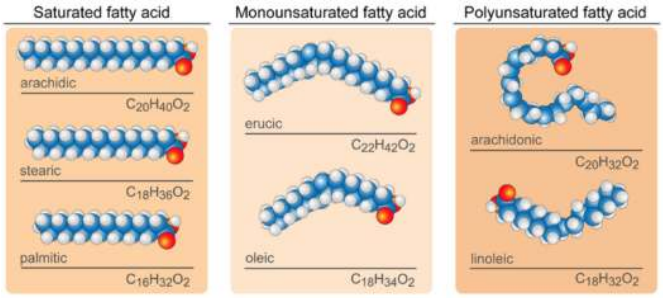


Figure **2.6.2**: Fatty Acids models. The blue balls, white balls, and red balls represent carbon, hydrogen, and oxygen, respectively. Saturated fatty acids, such as arachidic, stearic and palmitic, have straight chains. Unsaturated fatty acids have bent chains. Monounsaturated fatty acids, such as erucic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

TYPES OF LIPIDS

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

TRIGLYCERIDES

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

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

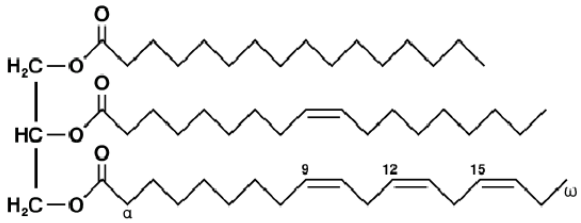


Figure **2.6.3**: Triglyceride Molecule. The left part of this triglyceride molecule represents glycerol. Each of the three long chains on the right represents a different fatty acid. From top to bottom, the fatty acids are palmitic acid, oleic acid, and alpha-linolenic acid. These fatty acids are shown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

PHOSPHOLIPIDS

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

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

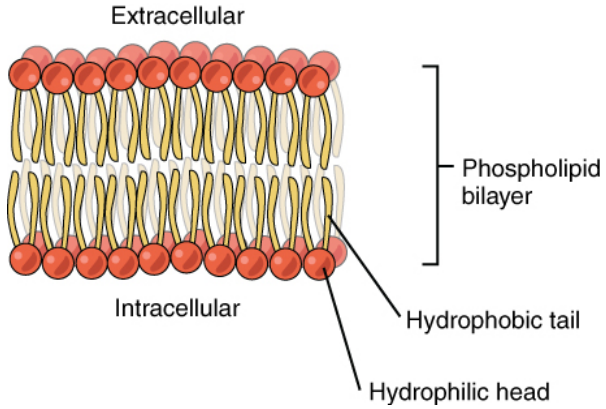


Figure **2.6.4**: The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads contact the fluid inside and outside of the cell.

STEROIDS

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

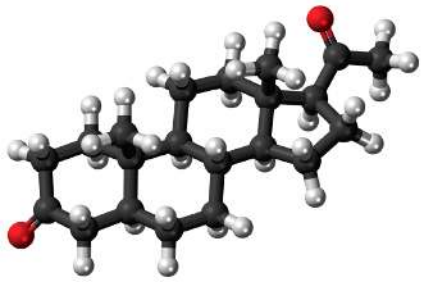


Figure **2.6.5**: Each steroid molecule consists of a four-ring core of 17 carbon atoms (black balls in the model). The red balls are representing oxygen and the white balls are representing hydrogen in the model. The components of the molecule may vary and determine the steroid's function.

FEATURE: MY HUMAN BODY

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

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

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

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

REVIEW

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

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2.7: PROTEINS

PROTEIN SHAKE

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



Figure 2.7.1: Protein shake

WHAT ARE PROTEINS?

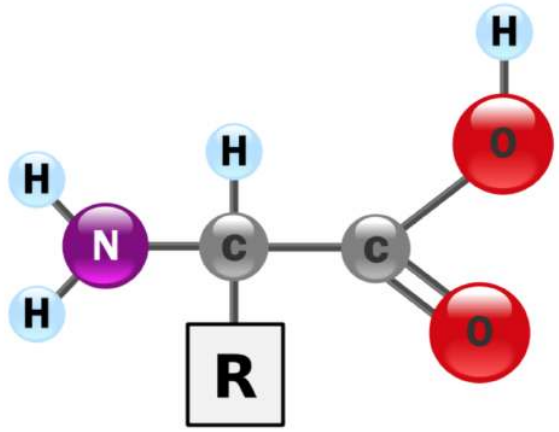


Figure 2.7.2: General Structure of Amino Acids. This model shows the general structure of all amino acids. Only the side chain, R, varies from one amino acid to another. For example, in the amino acid glycine, the side chain is simply hydrogen (H). In glutamic acid, in contrast, the side chain is CH_2CH_2COOH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

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

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

PROTEIN STRUCTURE

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

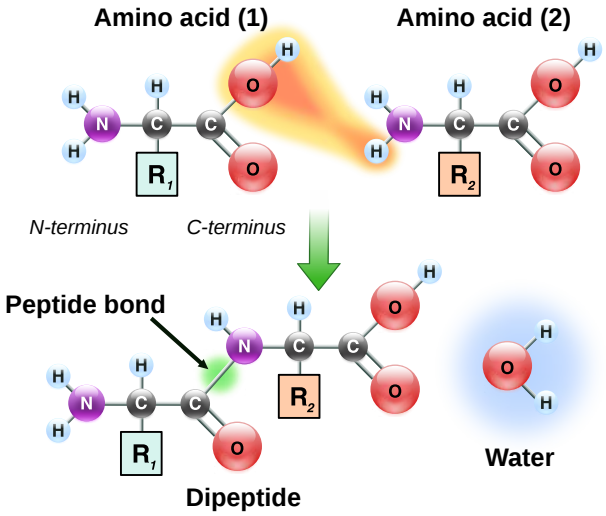


Figure 2.7.3: Amino acids join together to form a molecule called a dipeptide. The C–N bond is called a peptide bond. The order of amino acids is by convention shown with the free amino group on the left and the free carboxyl group on the right.

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

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

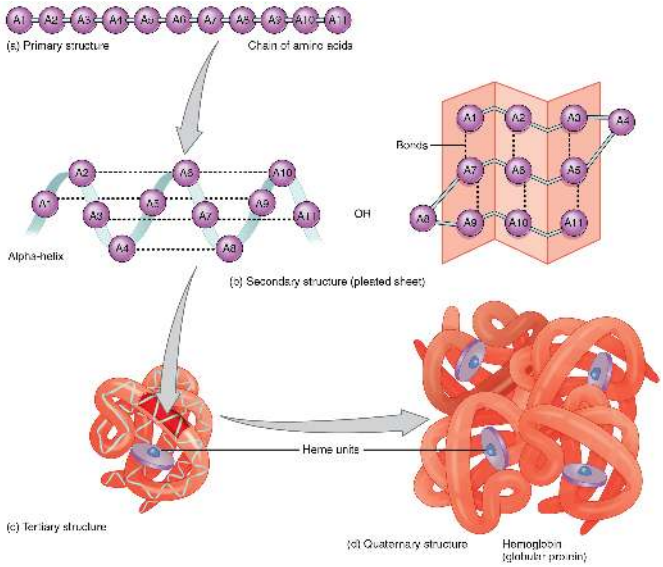


Figure **2.7.4**: The levels of structure of a protein called hemoglobin.

FUNCTIONS OF PROTEINS

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

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

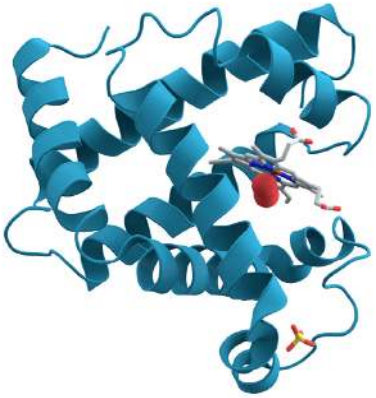


Figure **2.7.5**: Myoglobin is a protein found in the muscle tissues of most mammals. It binds with oxygen to supply the cells with this element. The modle shows the 3D structure of the protein.

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

PROTEIN CONSUMPTION, DIGESTION, AND SYNTHESIS

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

REVIEW

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

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

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2.8: NUCLEIC ACIDS

WHO'S WHO?

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



Figure **2.8.1**: Twins

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

STRUCTURE OF NUCLEIC ACIDS

Each nucleotide consists of three smaller molecules:

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

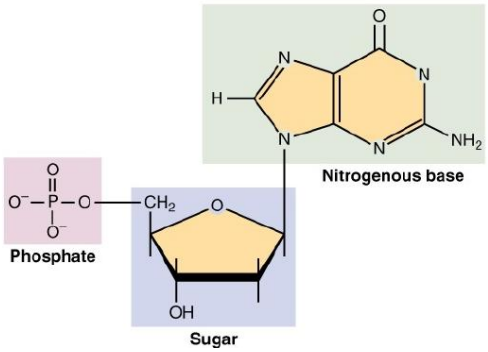


Figure **2.8.2**: Nucleotides consist of a sugar, a nitrogenous base, and a phosphate group

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

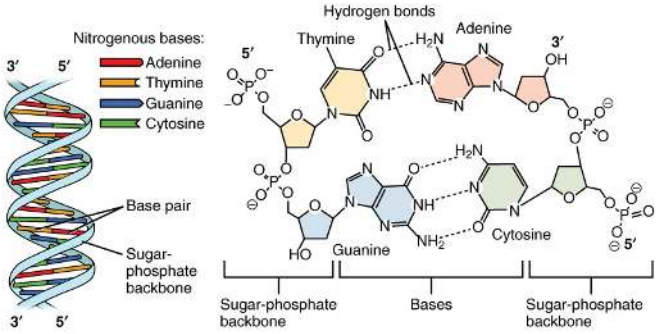


Figure **2.8.3**: Nucleic Acid

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

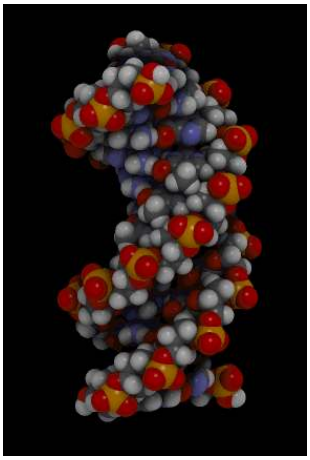


Figure **2.8.4**: DNA molecule

ROLES OF NUCLEIC ACIDS

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

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

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

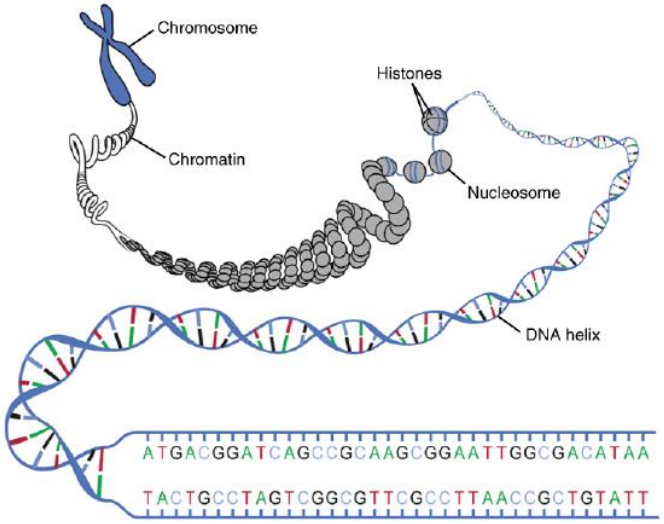


Figure **2.8.5**: The organization of a chromosome

FEATURE: HUMAN BIOLOGY IN THE NEWS

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



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

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



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

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

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

REVIEW

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

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

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2.9: ENERGY IN CHEMICAL REACTIONS

SLOW BURN

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



Figure **2.9.1**: Rusty chain

WHAT IS A CHEMICAL REACTION?

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

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



Figure **2.9.2**: Flames from methane burning

CHEMICAL EQUATIONS

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

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

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

ROLE OF ENERGY IN CHEMICAL REACTIONS

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

EXERGONIC REACTIONS

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

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

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



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

ENDERGONIC REACTIONS

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

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

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



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

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

ACTIVATION ENERGY

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

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

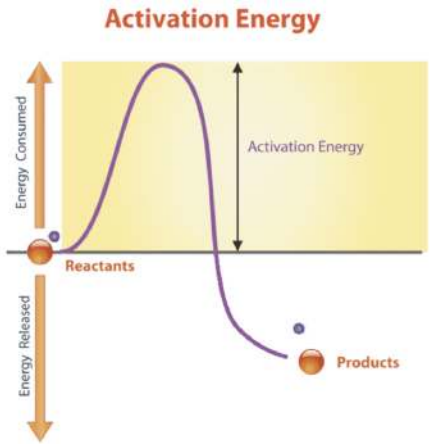


Figure **2.9.5**: This diagram of activation energy shows the reactants on the far left and the products on the right. Notice that the reactants are at a higher energy level than the products, so this reaction releases energy overall. But the reaction consumes energy to get started - this is the activation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

REVIEW

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

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

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

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2.10: CHEMICAL REACTIONS IN LIVING THINGS

ASSEMBLY LINE

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



Figure **2.10.1**: Assembly line

WHAT ARE BIOCHEMICAL REACTIONS?

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

CATABOLIC REACTIONS

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

ANABOLIC REACTIONS

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

ENZYMES

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

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

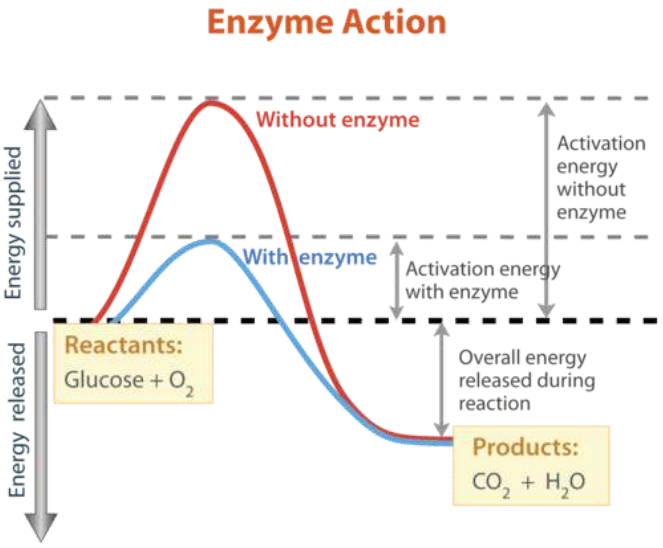


Figure **2.10.2**: Enzyme Action. This graph shows what happens when glucose combines with oxygen. An enzyme speeds up the reaction by lowering the activation energy. Compare the activation energy needed with and without the enzyme.

HOW WELL ENZYMES WORK

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

ENZYME-DEFICIENCY DISORDERS

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

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

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

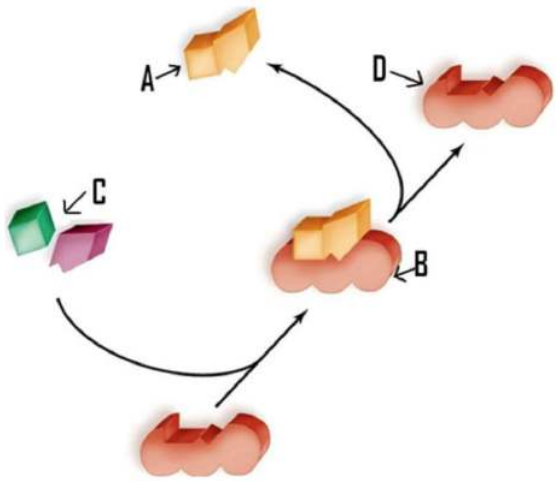


Figure **2.10.3**: The figure shows how enzymes convert substrates into products. the substrate (A) binds at the activation site of the enzyme(D) and makes a substrate-enzyme complex (B). Then, the enzyme converts the substrate into the product (C) by breaking or making bonds between the atoms of the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

FEATURE: RELIABLE SOURCES

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

Choose one of the following topics about G6PD deficiency:

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

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

REVIEW

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

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2.11: BIOCHEMICAL PROPERTIES OF WATER

THE BLUE MARBLE

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



Figure **2.11.1**: Planet Earth

CHEMICAL STRUCTURE AND PROPERTIES OF WATER

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

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

CHEMICAL STRUCTURE OF WATER

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

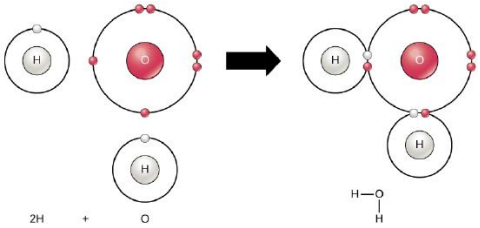


Figure **2.11.2**: This model is an atomic diagram of water, showing the two hydrogen atoms and an oxygen atom in the center.

WATER IS A GOOD SOLVENT

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

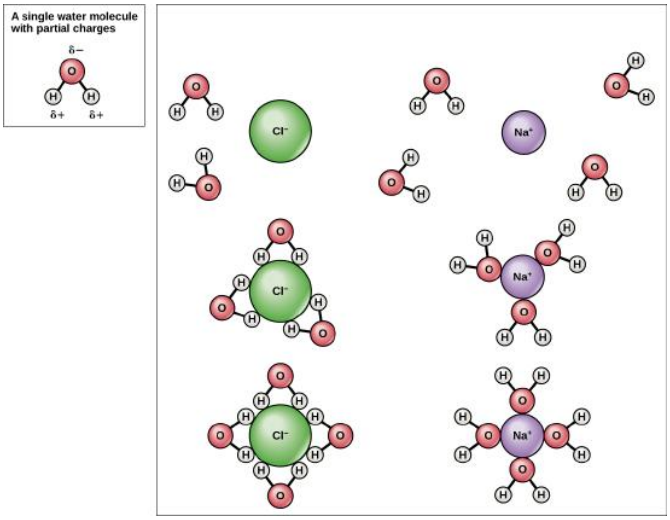


Figure **2.11.3**: This diagram shows the positive and negative parts of a water molecule. It also depicts how a charge, such as on an ion (Na or Cl, for example) can interact with a water molecule.

HYDROGEN BONDING

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

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

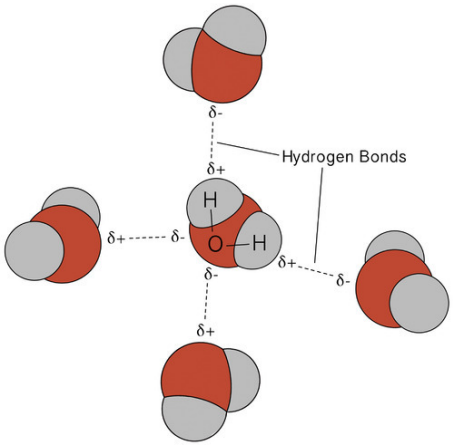


Figure **2.11.4**: Hydrogen bonds form between positively and negatively charged parts of water molecules. The bonds hold the water molecules together. How do you think this might affect water's properties?

STICKY, WET WATER

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



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

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

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

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

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

THE DENSITY OF ICE AND WATER

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

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

REVIEW

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

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2.12: ACIDS AND BASES

DANGER! BATTERY ACID!

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



Figure **2.12.1**: Car battery

WATER AND SOLUTIONS

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

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

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

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

ACIDITY AND PH

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

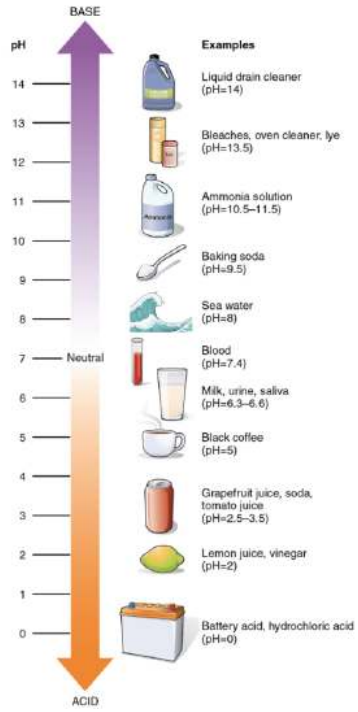


Figure **2.12.2**: This pH scale shows the acidity of many common substances. The lower the pH value, the more acidic a substance is.

Examples of pH

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

ACIDS

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

BASES

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

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

ACIDS, BASES, AND ENZYMES

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

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

FEATURE: MY HUMAN BODY

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

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

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

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

REVIEW

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

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

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

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2.13: NUTRIENTS

FIGHTING PHYTOCHEMICALS

Many wars have been fought to acquire these spices from India. Chemicals and oils in the spices infuse specific smells and tastes in Indian cuisine. Food and culture are intertwined, and people bring their culture with them when they settle in a foreign country. Sometimes their culture is accepted, and sometimes it becomes a cause of discrimination that people have to face for embracing their culture.

This colorful display of Indian spices is not just pretty to look at, the items pictured are also rich in phytochemicals. **Phytochemicals** are a large group of recently discovered chemicals, such as oils and colors, that occur naturally in plants. Many of them are known to protect plants by fighting off insect attacks and infectious diseases. Phytochemicals in the food we eat may also be needed to help keep us healthy. If so, some nutritionists think they should be classified as nutrients.



Figure **2.13.1**: Indian Spices

WHAT ARE NUTRIENTS?

Nutrients are substances the body needs for energy, building materials, and control of body processes. There are six major classes of nutrients based on biochemical properties: carbohydrates, proteins, lipids, water, vitamins, and minerals. Fiber, which consists largely of nondigestible carbohydrates, is sometimes added as the seventh class of nutrients.

Besides the biochemical classification of nutrients, nutrients are also categorized as either essential or nonessential nutrients. **Essential nutrients** cannot be synthesized by the human body, at least not in sufficient amounts for normal functioning, so these nutrients must be obtained from food. **Nonessential nutrients,** in contrast, can be synthesized in the body in sufficient quantities for normal functioning, although they are generally obtained from food as well. Except for dietary fiber, all dietary carbohydrates are considered nonessential. Every other major class of nutrients contains multiple essential compounds. For example, there are nine essential amino acids, at least two essential fatty acids, and many essential vitamins and minerals. Water and fiber are also essential nutrients.

The major classes of nutrients are also categorized as macronutrients or micronutrients depending on how much of them the body needs.

MACRONUTRIENTS

Macronutrients are nutrients that the body needs in relatively large amounts. They include carbohydrates, proteins, lipids, and water. All macronutrients except water are used by the body for energy, although this is not their sole physiological function. The energy provided by macronutrients in food is measured in kilocalories, commonly called **Calories,** where 1 Calorie is the amount of energy needed to raise 1 kilogram of water by 1 degree Celsius.

CARBOHYDRATES

Carbohydrates are organic compounds made up of simple sugars (as in the cotton candy pictured in Figure **2.13.2**). Carbohydrates are classified by the number of sugars they contain as monosaccharides (one sugar), such as glucose and fructose; disaccharides (two sugars), such as sucrose and lactose; and polysaccharides (three or more sugars), including starch, glycogen, and cellulose (the main component of dietary fiber). Dietary carbohydrates come mainly from grains, fruits, and vegetables. All digestible carbohydrates in the diet are used by the body for energy. One gram of dietary carbohydrates provides 4 Calories of energy. **Fiber,** such as the cellulose in plant foods, cannot be digested by the human digestive system, so most of it just passes through the digestive tract. Although it does not provide energy as other carbohydrates do, it is nonetheless considered an essential nutrient for its physiological roles. There are two types of fiber in many plant foods: soluble fiber and insoluble fiber.



Figure **2.13.2**: This cotton candy may look like a big cotton ball made of real cotton, which consists mostly of cellulose, but it actually consists almost entirely of simple sugars.

Soluble fiber consists of nondigestible complex plant carbohydrates that dissolve in water, forming a gel. This type of dietary fiber thickens and slows the movement of chyme through the small intestine and thereby slows the absorption of glucose into the blood. The consistency of food after it has been mechanically digested in the stomach is referred to as chyme. This may lessen insulin spikes

and the risk of type 2 diabetes. Soluble fiber can also help lower blood cholesterol. Good dietary sources of soluble fiber include oats, apples, and beans.

Insoluble fiber consists mainly of cellulose and does not dissolve in water. As insoluble fiber moves through the large intestine, it stimulates peristalsis. Peristalsis is the involuntary constriction of the smooth muscle of the GI tract that pushes the food content in the tract. This keeps food wastes moving and helps prevent constipation. The insoluble fiber in the diet may also lessen the risk of colon cancer. Good dietary sources of insoluble fiber include cabbage, bell peppers, and grapes.

PROTEINS

Proteins are organic compounds made up of amino acids. You may think of meat and fish as major sources of dietary proteins — and they are — but there are many good plant sources as well, including soybeans (see the figure below) and other legumes. Proteins in food are broken down during digestion to provide the amino acids needed for protein synthesis. Proteins in the human body are the basis of many body structures, including muscles and skin. Proteins also function as enzymes that catalyze biochemical reactions, hormones that regulate body functions in other ways, and antibodies that help fight pathogens. Any amino acids from food that are not needed for these purposes are excreted in the urine, converted to glucose for energy, or stored as fat. One gram of protein provides 4 Calories of energy.

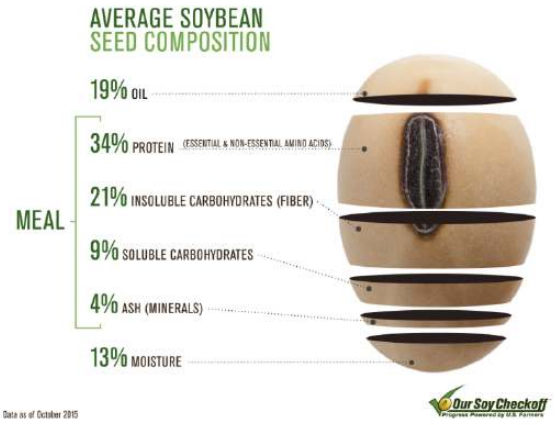


Figure **2.13.3**: Average soybean seed composition: 19% oil, 34% protein (essential and non-essential amino acids), 21% insoluble carbohydrates (fiber), 9% soluble carbohydrates, 4% ash (minerals), 13% moisture.

The most important aspect of protein structure from a nutritional standpoint is amino acid composition. About 20 amino acids are commonly found in the human body, of which about 11 are nonessential because they can be synthesized internally. The other 9 amino acids are essential amino acids that must be obtained from dietary sources. Essential amino acids are phenylalanine, valine, threonine, tryptophan, methionine, leucine, isoleucine, lysine, and histidine. Animal proteins such as meat and fish are concentrated sources of all 9 essential amino acids, whereas plant proteins may have only trace amounts of one or more essential amino acids.

LIPIDS

Lipids, commonly called fats, are organic compounds made up mainly of fatty acids. Fats in foods (Figure **2.13.4**), as well as fats in the human body, are typically triglycerides (three fatty acids attached to a molecule of glycerol). Fats provide the body with energy and serve other vital functions, including helping to make and maintain cell membranes and functioning as hormones. When used for energy, one gram of fat provides 9 Calories of energy.



Figure **2.13.4**: A variety of forms of fat are commonly used in food preparation. Fatty food sources shown here include butter, mayonnaise, vegetable oil, and salad dressing.

SATURATED VS UNSATURATED FATS

Fats are classified as either saturated or unsaturated depending on the type of bonds in their fatty acids.

- In saturated fats, carbon atoms share only single bonds, so each carbon atom is bonded to as many hydrogen atoms as possible. Saturated fats tend to be solids at room temperature. Most saturated fat in the diet comes from animal foods, such as meat and butter.
- In unsaturated fats, at least one pair of carbon atoms share a double bond, so these carbon atoms are not bonded to as many hydrogen atoms as possible. Unsaturated fats with just one double bond are called monounsaturated fats. Those with multiple double bonds are called polyunsaturated fats. Unsaturated fats tend to be liquids at room temperature. Unsaturated fats in the diet come mainly from certain fish such as salmon and from plant foods such as seeds and nuts.

ESSENTIAL FATTY ACIDS

Most fatty acids are not essential. The body can make them as needed, generally from other fatty acids, although this takes energy. Only two fatty acids are known to be essential, called omega-3 and omega-6 fatty acids. They cannot be synthesized in the body, so they must be obtained from food. The most commonly used cooking oils in processed foods are rich in omega-6 fatty acids, so most people get plenty of these fatty acids in their diet. Omega-3 fatty acids are not as prevalent in foods, and most people do not get enough of them in food. Good food sources of omega-3 fatty acids include oily fish such as salmon, walnuts, and flax seeds.

TRANS FATS

Trans fats are unsaturated fats that contain types of bonds that are rare in nature. Trans fats are typically created in an industrial process called partial hydrogenation. They may be used in a variety of processed foods (such as those shown in Figure **2.13.5**) because they tend to have a longer shelf life without going rancid. Trans fats are known to be detrimental to human health.



Figure **2.13.5**: All of the foods pictured here contain harmful trans fats.

WATER

Water is essential to life because biochemical reactions take place in water. Water is continuously lost from the body in multiple ways, including in urine and feces, during sweating, and as water vapor in exhaled breath. This constant loss of water makes water an essential nutrient that must be replenished often.

Too little water is called dehydration. It can cause weakness, dizziness, and heart palpitations. Severe dehydration can lead to death. It is easy to become dehydrated in hot weather, especially when exercising. It is more difficult to consume too much water, but overhydration is also possible. It can result in water intoxication, a serious and potentially fatal condition.

MICRONUTRIENTS

Micronutrients are nutrients the body needs in relatively small amounts. Micronutrients do not provide energy. Instead, they are necessary for the biochemical reactions of metabolism, among other vital functions. They include vitamins, minerals, and possibly phytochemicals as well.

VITAMINS

Vitamins are organic compounds that generally function as coenzymes. A coenzyme is a “helper” molecule that is required for a protein enzyme to work. In this capacity, vitamins play many roles in good health, ranging from maintaining normal vision (vitamin A) to help the blood clot (vitamin K). Some functions of these and several other vitamins are listed in the table below. Most vitamins are essential nutrients and must be obtained from food. Fruits, vegetables, meat, and fish are all high in one or more essential vitamins. There are only a few nonessential vitamins. Vitamins B_7 and K are produced by bacteria in the large intestine, and vitamin D is synthesized in the skin when it is exposed to UV light

Table **2.13.1**: Selected Vitamins and Some of Their Functions

Vitamin	Function
A	normal vision
B_1 (thiamin)	production of cellular energy from food
B_3(niacin)	cardiovascular health
B_7 (biotin)	support of carbohydrate, protein, and fat metabolism
B_9 (folic acid)	fetal health and development
B_{12}	normal nerve function and production of red blood cells
C	making connective tissue
D	healthy bones and teeth
E	normal cell membranes
K	blood clotting

MINERALS

Minerals are inorganic chemical elements that are necessary for normal body processes and good health. Because they are inorganic and not synthesized biologically, all nutrient minerals are considered essential nutrients.

Several minerals are needed in relatively large quantities (> 150 mg/day), so they are sometimes referred to as macrominerals or bulk minerals. They include:

- calcium, which is needed for bone strength, neutralizing acidity in the digestive tract, and nerve and cell membrane functions. Dairy products are good sources of calcium.
- magnesium, which is needed for strong bones, maintaining pH, processing ATP, and other functions. Green leafy vegetables, bran, and almonds are high in magnesium.
- phosphorus, which is needed for bone strength, energy processing, pH regulation, and phospholipids in cell membranes. Milk and meat are good sources of phosphorus.
- sodium, which is needed to regulate blood volume, blood pressure, water balance, and pH. Most processed foods have added sodium. A salt shaker is another common source of sodium.
- chloride, which is needed for the production of hydrochloric acid in the stomach and for cell membrane transport. Chloride in table salt added to processed foods provides plenty of chloride in most diets.
- potassium, which is needed for the proper functioning of the heart and nerves, water balance, and pH. Many fruits and vegetables are high in potassium.
- sulfur, which is needed for the synthesis of many proteins. Meat and fish are good sources of sulfur.

Other minerals are needed in much smaller quantities (≤150 mg/day), so they are often referred to as trace minerals. The table below lists several trace minerals and some of their functions. Good dietary sources of trace minerals include whole grains, seafood, fruits, vegetables, nuts, and legumes.

Table 2.13.2: Selected Trace Minerals and Some of Their Functions

Trace Mineral	Function
Cobalt	synthesis of vitamin B_{12} by gut bacteria
Copper	component of many enzymes
Chromium	metabolism of sugar
Iodine	synthesis of thyroid hormones
Iron	component of hemoglobin and many enzymes
Manganese	processing of oxygen
Molybdenum	component of several enzymes
Selenium	component of oxidases (antioxidants)
Zinc	component of several enzymes

PHYTOCHEMICALS

The naturally occurring, disease- and pest-fighting plant chemicals known as phytochemicals are commonly consumed in plant foods, particularly spices and fresh vegetables and fruits. Besides fighting attacks on plants, many phytochemicals give plants their distinctive colors and characteristic flavors and aromas. Phytochemicals are the reason that blueberries are blue (Figure 2.13.6) and that garlic has its characteristically strong, pungent taste and smell. There are known to be as many as 4,000 different phytochemicals in plants. Preliminary evidence suggests that certain phytochemicals in the diet help protect human health. For example, some phytochemicals may act as antioxidants that counter cancer-causing free radicals. Research on phytochemicals is still relatively young, so time will tell whether they will eventually be classified as micronutrients.



Figure 2.13.6: The colors of berries and other fruits are attributable to phytochemicals.

REVIEW

1. What are the nutrients?
2. List the six major classes of nutrients based on biochemical properties.
3. Compare and contrast essential and nonessential nutrients.
4. Identify macronutrients.
5. Which nutrients are classified as micronutrients? Why?
6. Describe carbohydrates, state how much energy they provide, and list good food sources of carbohydrates.
7. If fiber in food cannot be digested, why is it considered a nutrient?
8. Describe proteins, state their general uses in the human body, and identify food sources that are high in proteins. How much energy do proteins provide?
9. Describe lipids, identify how much energy they provide, and state their general uses in the human body.
10. Distinguish between saturated, unsaturated, and trans fats.
11. Water provides no energy or materials the body needs for building or controlling body processes. Why is it considered a nutrient?
12. What are vitamins? What is the general role of most vitamins? Which vitamins are not essential nutrients? Why?
13. What are the dietary minerals? Give examples of macrominerals and trace minerals.
14. What are phytochemicals? What are good food sources of phytochemicals?
15. Which of the following are inorganic substances?

    A. Vitamins
    B. Minerals
    C. All micronutrients
    D. A and B

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2.14: HEALTHY EATING

BALANCING ACT

If you practice yoga, then you know that yoga positions such as the headstand demonstrated here can help you develop a good balance. Having good balance, in turn, can reduce your risk of falls and injuries. Another kind of balance is important to ensure that you have good health and prevent disease, and that kind of balance is a balance in your diet. Achieving a dietary balance requires healthy eating.



Figure **2.14.1**: Yoga

BENEFITS OF HEALTHY EATING

It sounds like something a snake-oil salesman would say, but it's true: healthy eating is a panacea for many human ailments. A healthy diet reduces risk of obesity, cardiovascular disease, type 2 diabetes, osteoporosis, and cancer. Not surprisingly, it also extends the length of life. In fact, an unhealthy diet is one of the leading preventable causes of death. A healthy diet also has mental health benefits. It may stall or reduce the risk of dementia and have a positive effect on memory.

DIET AND NUTRITION

If you adopt healthy eating habits and get enough exercise, you are likely to have good nutrition. **Nutrition** is the process of taking in nutrients in food and using them for growth, metabolism, and repair. Good nutrition requires eating foods rich in nutrients with the right amount of food energy (Calories) to balance energy use.

NUTRIENT BALANCE AND NUTRIENT DENSITY

Eating a wide range of foods, especially fruits and vegetables, is the basis of healthy eating. This helps ensure that you are eating a wide range of nutrients. However, there is only a limited amount of food you can eat in a single day without consuming too many Calories. In order to maximize the number of nutrients you take in, you need to spend your "Calorie budget" wisely by choosing foods that have high **nutrient density.** Nutrient density refers to how much of a given nutrient is provided by a particular food, relative to the mass of the food or the number of Calories it provides. Consider vitamin K as an example. The recommended daily value of vitamin K for adults is 90 µg. Both kale and iceberg lettuce provide vitamin K. A cup of iceberg lettuce provides about 50 µg vitamin K; a cup of kale provides more than 1000 µg of vitamin K. Therefore, kale has about 20 times the nutrient density for vitamin K as lettuce. Black beans, pictured below, are another good example of nutrient-dense food.



Figure **2.14.2**: Black beans, prepared here in a salad with corn and other veggies, are nutrient-dense in both protein and fiber. One cup of cooked black beans provides about 30 percent of the protein and 60 percent of the fiber needed by a typical adult while providing virtually no fat, sodium, or sugar. Black beans are also nutrient-dense sources of many micronutrients, including folate, thiamin, manganese, magnesium, phosphorus, and iron.

ENERGY HOMEOSTASIS AND ENERGY DENSITY

Good nutrition also requires achieving energy homeostasis. **Energy homeostasis** is a balance between the energy consumed in food and the energy expended in metabolism and physical activity. If more energy is taken in as food than is used for metabolism and activity, then the extra energy is stored as fat. An extra 3,500 Calories of food energy results in the storage of almost half a kilogram (1 lb) of body fat. If less energy is taken in than is used, then stored fat may be used for energy. The human brain, particularly the hypothalamus, plays a central role in regulating energy homeostasis. Based on biochemical signals from the body, the hypothalamus generates a sense of hunger or satiation as needed to maintain energy balance.

Energy homeostasis depends on more than hunger and satiation. It also depends on dietary choices, eating habits, and activity levels. To achieve energy balance, it is important to consider the energy density of the food. **Energy density** refers to the number of Calories a food provides per gram (or ounce). Foods high in carbohydrates or proteins are generally less energy-dense than foods high in lipids. Carbohydrates and proteins provide 4 Calories of energy per gram, whereas lipids provide 9 Calories of energy per gram. However, within nutrient classes, there is considerable variation in the energy density of foods. For example, fruits are high in carbohydrates that the body uses for energy. Both casaba melons and figs are fruits and provide energy, but an ounce of casaba melon provides only about 8 Calories of energy, whereas an ounce of figs provides about 80 Calories of energy. This means that figs have 10 times the energy density of casaba melons.

MALNUTRITION

Bad nutrition is referred to as **malnutrition.** The word malnutrition may make you think of starving children in Africa who do not have

enough food to eat. This type of malnutrition is called undernutrition, and it is a major nutritional problem in developing countries. Undernutrition is typically caused by inadequate energy intake, often coupled with frequent bouts of infectious disease. It usually results in people being underweight for their height, and it commonly leads to growth failure in children.

Undernutrition is just one type of malnutrition. Excessive food intake can also cause malnutrition, in this case, overnutrition. This is the major nutritional problem in developed countries. Overnutrition is typically caused by excessive energy intake coupled with inadequate energy expenditure in physical activity. Overnutrition usually leads to people becoming overweight or obese (see Figure **2.14.3**). Obesity is associated with a host of health problems and diseases, including metabolic syndrome, cardiovascular disease, type 2 diabetes, and some types of cancer, among others.

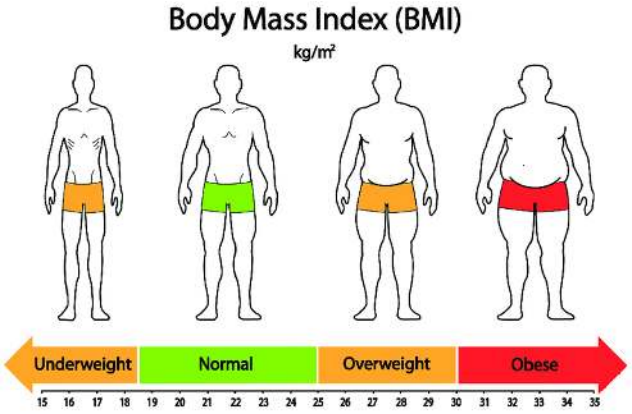


Figure **2.14.3**: Body Mass Index is a measure that can be used to help determine if a person is obese. A simple BMI scale compares height vs. weight. A BMI below 18 is generally considered to be underweight; a BMI over 25 is overweight and over 30 is obese.

Unbalanced nutrition is another type of malnutrition. In this case, the diet contains too much or not enough of specific nutrients other than energy. This type of malnutrition often occurs with undernutrition. However, a person doesn't have to be undernourished to lack specific nutrients. People with adequate food intake and even people with overnutrition may have unbalanced nutrition. Getting either too much or not enough of particular nutrients may cause diseases or other health problems. For example, inadequate vitamin A intake may cause blindness, whereas too much vitamin A can be toxic. Likewise, dietary calcium deficiency may contribute to osteoporosis, whereas too much calcium can cause kidney stones.

NUTRIENT NEEDS

The goal of healthy eating is to take in the proper amount of each nutrient to meet nutrient and energy needs. The FDA identifies the recommended adult daily values (DV) for a wide variety of nutrients, based on a 2,000 Calorie daily diet. The values in the table are average values. The exact amount of each nutrient that a given individual needs may differ, depending on factors, such as age and gender. Different stages of adulthood have different nutrient needs for several nutrients, and males have somewhat higher needs for many nutrients than do females at most ages, mainly because of gender differences in body size. Other factors that influence individual nutrient needs include health status and activity level. People in poor health may need some nutrients in greater quantities. People who are very active need to obtain more energy from macronutrients in their diet.

TOOLS AND TIPS FOR HEALTHY EATING

There are so many nutrients and daily values. Eating to meet all these nutrient needs may seem like an overwhelming challenge. Do you need to keep track of the nutrient content of everything you eat to guarantee that you are meeting your nutrient needs? Fortunately, the answer is no. Healthy eating is much easier than that. Just use MyPlate and nutrition facts labels and follow the tips below. This approach will help ensure that you are meeting your nutrient needs.

MYPLATE

One of the most useful tools for healthy eating is **MyPlate,** which is shown below. This is a visual guide to healthy eating that was developed by the United States Department of Agriculture (USDA) in 2011. MyPlate replaces the previous MyPyramid guide from the USDA and is easier to apply to daily eating. MyPlate depicts the relative proportions of different types of foods you should eat at each meal (or cumulatively by the end of the day). The foods are selected from five different food groups: vegetables, fruits, grains (such as cereal, bread, or pasta), proteins (such as meat, fish, or legumes), and dairy (such as milk, cheese, or yogurt).

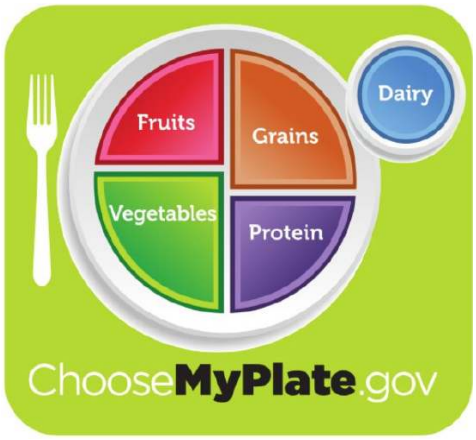


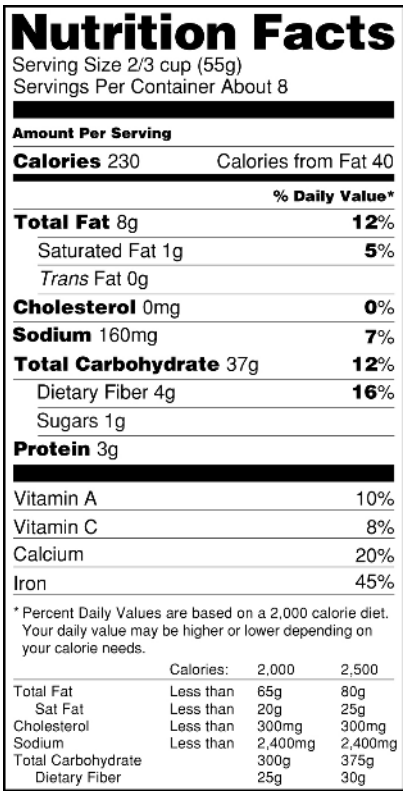
Figure **2.14.4**: MyPlate makes it relatively simple to eat balanced meals that meet nutrition needs.

According to MyPlate, about half of the food on your plate should be vegetables and fruits, and the other half should be grains and proteins. A serving of a dairy product should also accompany each meal. A meal based on MyPlate might include a serving of kale, an apple, a turkey sandwich, and a glass of milk. Think about some of your own typical meals. Do they match MyPlate? If not, how could you modify them to get the right proportions of foods from each food group?

NUTRITION FACTS LABELS

If you are like most Americans, you rely heavily on packaged and processed foods. Although limiting these foods in your diet is a good aim, in the meantime, make use of the nutrition facts labels on these

foods. A nutrition facts label, like the one shown above, gives the nutrient content and ingredients in food and makes it easy to choose the best options. A quick look at the nutrition facts can help you choose foods that are high in nutrients you are likely to need more of (such as fiber and protein) and low in nutrients you probably need less of (such as sodium and sugar). Checking the ingredients list on labels can help you choose food items that contain the most nutritious ingredients, such as whole grains instead of processed grains.



Nutrition Facts

Serving Size 2/3 cup (55g)
Servings Per Container About 8

Amount Per Serving

Calories 230	Calories from Fat 40
	% Daily Value*
Total Fat 8g	**12%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**12%**
Dietary Fiber 4g	**16%**
Sugars 1g	
Protein 3g	
Vitamin A	10%
Vitamin C	8%
Calcium	20%
Iron	45%

* Percent Daily Values are based on a 2,000 calorie diet. Your daily value may be higher or lower depending on your calorie needs.

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

Figure **2.14.5**: Nutrition facts labels like this one can help you make good food choices.

The sample nutrition label in Figure **2.14.5** indicates that a serving of this food is 55 g (with about 8 servings in the package). Each serving contains:

- 230 calories (with 40 calories from fat)
- 8 g total fat (making up 12% of the recommended fats per day)
  - 1 g of this total fat is saturated fat (making up 5% of the daily value)
  - 0 g is trans fat
- 0 mg cholesterol (0% of the daily value)
- 160 mg sodium (7% of the daily value)
- 37 g total carbohydrates (12% of daily value)
  - 4 g of that is dietary fiber (16% of daily value)
  - 1 g sugars
- 3 g proteins
- 10% of the recommended daily value of vitamin A
- 8% of the recommended daily value of vitamin C
- 20% of the recommended daily value of calcium
- 45% of the recommended daily value of Iron

TIPS FOR HEALTHY EATING

The following tips can help you attain energy homeostasis while meeting your nutrient needs.

- Eat several smaller meals throughout the day rather than a few larger meals. Eating more frequently keeps energy, blood glucose, and insulin levels stable.
- Make healthy food choices. Try to eat whole foods rather than processed foods. Whole foods have more nutrients than processed foods. Raw foods also generally retain more nutrients than cooked foods. Overall, try to eat more plant foods and fewer animal foods.
- Make healthy grain choices. Try to make at least half your grains whole grains. Choose food items with whole grains listed as the main ingredient. Avoid foods that contain mainly or only processed grains, such as white flour or white rice. Include a variety of grains, such as rice, oats, and wheat.
- Make healthy fruit and vegetable choices. Include a variety of green, yellow, red, and orange fruits and vegetables, like those pictured below. These foods are high in vitamins and phytochemicals. Consume whole fruits instead of juices. Whole fruits are higher in fiber and more filling and may also have less sugar. The highest fiber fruits include plums and prunes.
- Combine amino acids in plant foods. The right combinations, such as beans and rice, make complete proteins with all nine essential amino acids. The two foods do not have to be eaten at the same meal to be used together by the body.
- Limit sugar and salt intake. Fresh foods generally have less of these two nutrients than processed foods. For packaged foods, read nutrition facts labels and choose options that are lower in sodium and sugars. Keep in mind that sugar may come in many forms, including high fructose corn syrup. Put away the salt shaker and sugar bowl so you won't be tempted to add extra sodium or sugar at the table.
- Limit saturated fats. Eat more fish and legumes and less red meat. Use nut and vegetable oils instead of butter or other fats derived from animals.
- Always check for trans fats on nutrition facts labels. Try to avoid these harmful artificial fats completely.
- Increase omega-3 fatty acids. Foods that contain these essential fatty acids include salmon, walnuts, flax seeds, and canola oil.
- Stay hydrated. Eat foods high in water, such as fruits and vegetables. Also, try to drink 2 liters (about 8 cups) of fluids each day. Choose water or unsweetened beverages such as tea or coffee instead of sweetened beverages. Sweetened drinks such as soft drinks contain no nutrients except sugar. Frequent consumption of sweetened beverages is a major risk factor for metabolic syndrome, obesity, type 2 diabetes, and cardiovascular disease.
- Engage in at least 30 minutes of physical activity most days of the week. Besides all the other benefits of exercise to human

health, such as strong bones and muscles, exercise uses energy that helps to balance the Calories in food.

FEATURE: MY HUMAN BIOLOGY

The Zone Diet, Blood Type Diet, Paleo Diet, grapefruit diet — no doubt, you've heard of them all. Such diets — often referred to as fad diets — certainly feature prominently in the media, and many people try them. If you want to lose weight, you may be thinking about trying a fad diet yourself. And why not? Fad diets are certainly appealing. They often promise quick weight loss without exercise. They also generally spell out exactly what you can and cannot eat. This makes it easier for some people to consume less in the short term. But do fad diets really work, and are they healthy ways to lose weight?

In reality, most fad diets do not lead to significant, long-term weight loss. People may lose a lot of weight initially, but the weight loss is likely to be due to loss of water rather than fat. In addition, many fad diets are unhealthy because they are unbalanced. They typically restrict or eliminate foods — such as fruits, dairy, or whole grains — that should be the basis of a healthy eating plan because they are dense in critical nutrients. At the same time, such diets may recommend overconsumption of certain nutrients that can actually compromise health when eaten in excess. For example, high-protein diets can put a strain on the kidneys and potentially lead to kidney stones and gout. Fad diets that are restricted to certain foods also quickly become boring and difficult to stick with. They generally are not intended to become a healthy, lifetime eating plan. Once the weight is lost (if it is), dieters usually go back to their old ways of eating and regain the weight.

How can you tell if a diet is a fad diet? Ask these questions about it:

1. Does the diet promise rapid weight loss (> 2 pounds a week)?
2. Does the diet claim that the weight loss will be from certain parts of the body (such as "stubborn belly fat")?
3. Does the diet claim to work even without exercise?
4. Does the diet help sell a product, such as prepackaged meals, pills, or books?
5. Does the diet lack well-validated scientific evidence to back its claims?
6. Does the diet use "before and after" photos or testimonials from individual dieters to "prove" that the diet works?
7. Does the diet identify "bad" foods and "good" foods?
8. Does the diet require following a rigid menu or meal plan?
9. Does the diet sound too good to be true?

If you can answer "yes" to even one of these questions, then the diet is likely to be a fad diet. If you are serious about losing weight safely and permanently, avoid fad dieting. Instead, follow the general eating and physical activity recommendations made in this concept as well as the following specific tips.

- Practice portion control. This means knowing serving sizes, which are generally smaller than most people think. You can use nutrition facts labels and the table below to avoid super-sizing your food.

Table **2.14.1**: Serving Size Comparisons for Selected Types of Food

Type of Food	Serving Size Comparison
Raw leafy vegetables Baked potato	small fist
Milk or yogurt Fresh fruit	baseball
Cereal Bread	hockey puck
Meat Poultry	computer mouse
Fish	checkbook
Cheese	six stacked dice
Margarine Butter	one die

- Eat breakfast every day and do not skip meals. This will keep your metabolism fired up so you use more energy. If you go long periods without eating, your body goes into starvation mode and starts "hoarding" Calories.
- Get off the couch. Choose physical activities that you enjoy so you will do them regularly. The only exercise that works is the one you will actually do. Also, include more physical activity throughout each day. Park farther from your destination and walk the rest of the way. Take the stairs whenever you can. Wearing a pedometer may challenge you to reach the recommended 10,000 steps a day.
- Follow MyPlate but use a smaller plate. If you use a salad plate instead of a dinner plate, for example, the same-sized serving of food will look larger. You will eat less without feeling deprived.

Following the healthy-eating guidelines in this concept and the specific tips above should lead to a slow but steady weight loss of a pound or two a week. Losing weight slowly may be frustrating, but it is more likely to stay off than weight that is lost rapidly. It took you time to gain excess weight so it will take time to lose it. The only way to keep it off is to establish a healthy pattern of eating and physical activity that you can live with lifelong.

REVIEW

1. Why is healthy eating important for good health?
2. Define nutrition. What does good nutrition depend on?
3. Define malnutrition, and identify types of malnutrition.
4. Briefly describe what healthy eating means.
5. What is nutrient density? How is it related to nutritious food choices?

6. Define energy homeostasis, and identify factors that regulate or influence energy homeostasis.
7. What is energy density, and how is it related to energy homeostasis?
8. What are the recommended daily values of nutrients?
9. List factors that influence nutrient needs of individuals.
10. Describe MyPlate. What food groups is it based on?
11. What information do nutrition facts labels provide? How can the information be used to choose the most nutritious food options?
12. Give two tips for healthy eating.
13. If there are 100 Calories per 100 grams of a baked potato, and 5.5 Calories per 1 gram of potato chips, which has a higher energy density — a baked potato or potato chips? Explain your answer.
14. When comparing two multivitamins in the store, you see that one has 500% of the daily value for a particular vitamin, while the other has 100% of the daily value for that vitamin. Is the one with 500% of the daily value necessarily better for your health? Explain your answer.
15. Explain why it is better for your health to eat whole fruits instead of drinking fruit juices.

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2.15: CASE STUDY CONCLUSION- DIET AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: DIET DILEMMA

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



Figure **2.15.1**: Fruits and yogurt

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

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

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

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

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

CHAPTER SUMMARY

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

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

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

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

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

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

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

CHAPTER SUMMARY REVIEW

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

digestion if the pH is raised significantly?

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

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CHAPTER OVERVIEW

3: CELLS

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

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

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3.1: CASE STUDY- THE IMPORTANCE OF CELLS

CASE STUDY: MORE THAN JUST TIRED

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



Figure **3.1.1**: Exhausted

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

CHAPTER OVERVIEW: CELLS

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

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

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

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

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3.2: DISCOVERY OF CELLS AND CELL THEORY

A BIG BLUE CELL

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

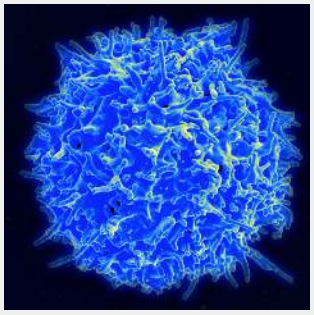


Figure **3.2.1**: Healthy human T-cell

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

DISCOVERY OF CELLS

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

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

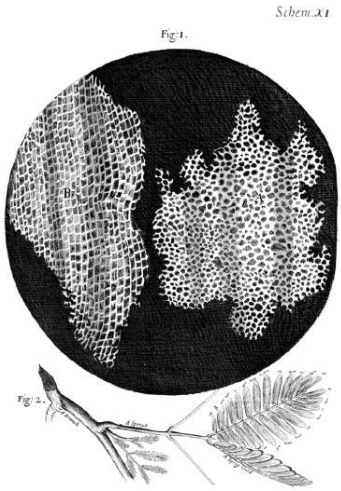


Figure **3.2.2**: Robert Hooke sketched these cork cells as they appeared under a simple light microscope.

CELL THEORY

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

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

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

SEEING INSIDE CELLS

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

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

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

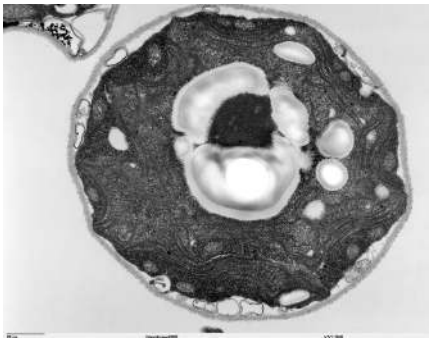


Figure **3.2.3**: An electron microscope produced this image of the structures inside a cell.

STRUCTURES SHARED BY ALL CELLS

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

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

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

REVIEW

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

EXPLORE MORE

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3.3: VARIATION IN CELLS

BACTERIA ATTACK!

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



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

EXPLAINING CELL SIZE

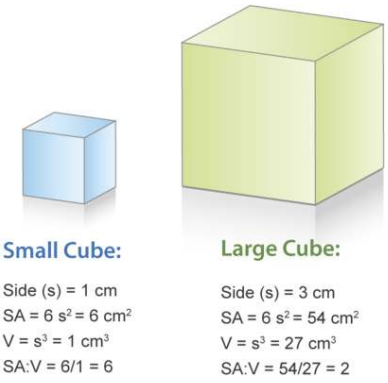


Figure **3.3.2**: Surface Area to Volume Comparison. A larger cube has a smaller surface area (SA) to volume (V) ratio than a smaller cube. This also holds true for cells and limits how large they can be.

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

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

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

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

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

CELL FORM AND FUNCTION

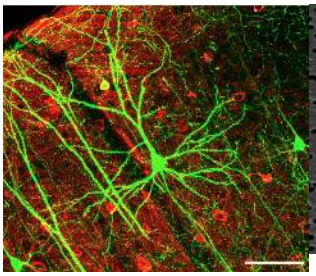


Figure **3.3.3**: Human nerve cell

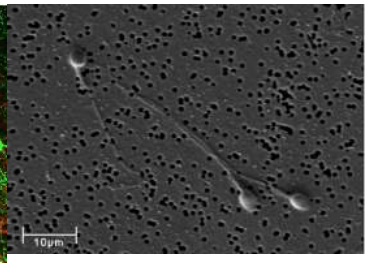


Figure **3.3.4**: Human sperm cells

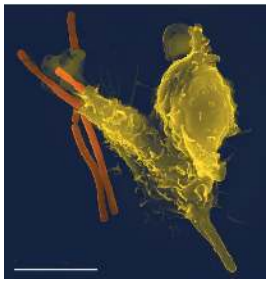


Figure **3.3.5**: Human white blood cell

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

CELLS WITH AND WITHOUT A NUCLEUS

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

PROKARYOTIC CELLS

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

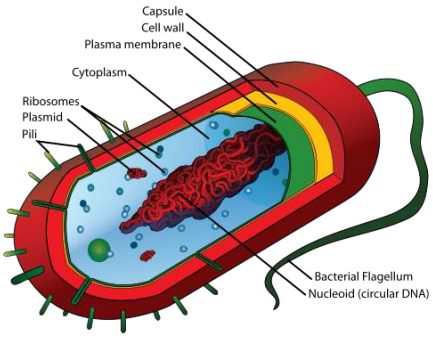


Figure **3.3.6**: Prokaryotic Cell. This diagram shows the structure of a typical prokaryotic cell, a bacterium. Like other prokaryotic cells, this bacterial cell lacks a nucleus but has other cell parts, including a plasma membrane, cytoplasm, ribosomes, and DNA.

Table **3.3.2**: Prokaryotic cell structures

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

EUKARYOTIC CELLS

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

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

Table **3.3.3**: Eukaryotic cell structures

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

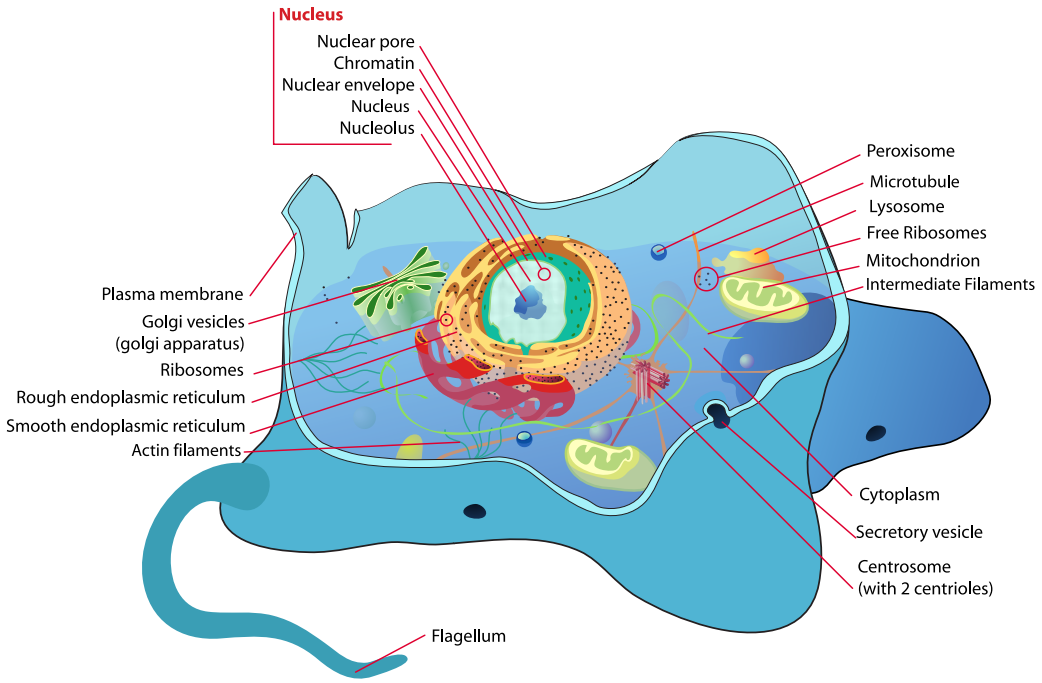


Figure **3.3.7**: Eukaryotic Cell. Compare and contrast the eukaryotic cell shown here with the prokaryotic cell. What similarities and differences can you identify?

REVIEW

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

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3.4: PLASMA MEMBRANE

A BAG FULL OF JELL-O

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



Figure **3.4.1**: Animal cell model

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

PHOSPHOLIPID BILAYER

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

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

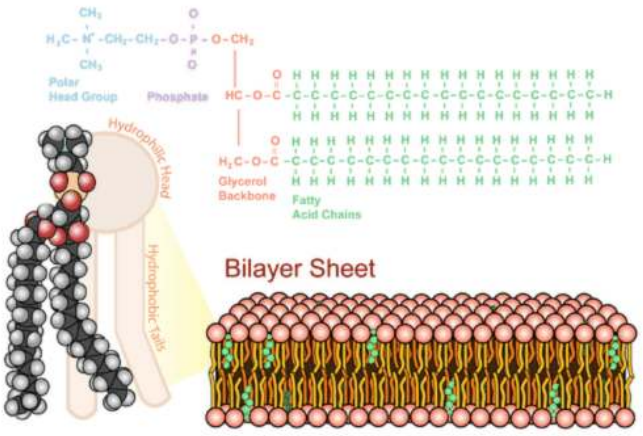


Figure **3.4.2**: Phospholipid and a phospholipid Bilayer.

OTHER MOLECULES IN THE PLASMA MEMBRANE

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

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

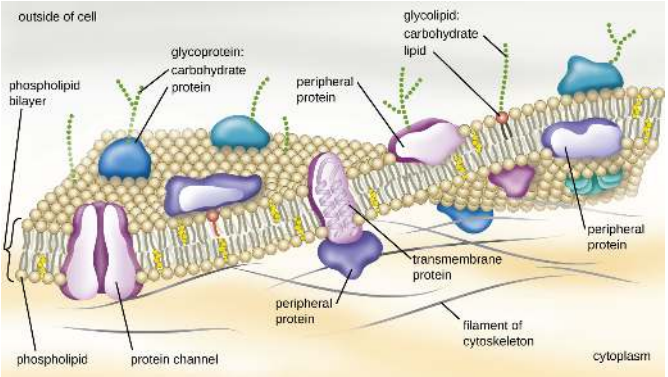


Figure **3.4.3**: The figure illustrates the major components of the phospholipid bilayer.

ADDITIONAL FUNCTIONS OF THE PLASMA MEMBRANE

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

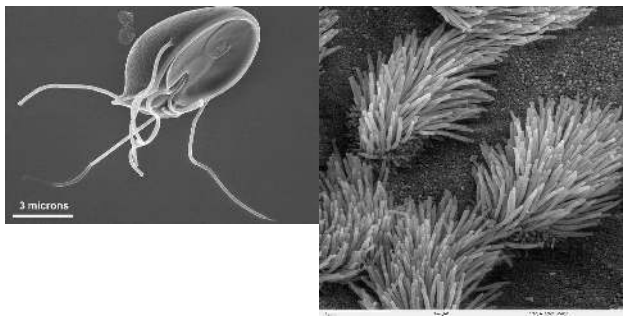


Figure **3.4.4**: Flagella of Giardia (left) and cilia of human respiratory mucosa (right). Flagella and cilia are extensions of the plasma membrane of many cells.

FEATURE: MY HUMAN BODY

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

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

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

REVIEW

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

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3.5: CYTOPLASM AND CYTOSKELETON

A PEEK INSIDE THE CELL

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

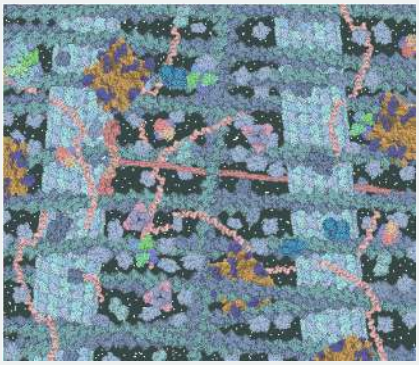


Figure **3.5.1**: Picture of cytosol, showing microtubules (light blue), actin filaments (dark blue), ribosomes (yellow and purple), soluble proteins (light blue), kinesin (red), small molecules (white) and RNA (pink).

CYTOPLASM

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

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

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

CYTOSKELETON

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

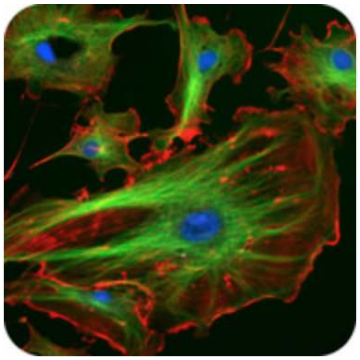


Figure **3.5.2**: Cytoskeleton. The cytoskeleton gives the cell an internal structure, like the frame of a house. In this photograph, actin filaments and tubules of the cytoskeleton are green and red, respectively. The blue dots are cell nuclei.

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

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

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

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

Table **3.5.1**: Cytoskeleton Structure

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

FEATURE: HUMAN BIOLOGY IN THE NEWS

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

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

REVIEW

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

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3.6: CELL ORGANELLES

RIBOSOME REVIEW

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

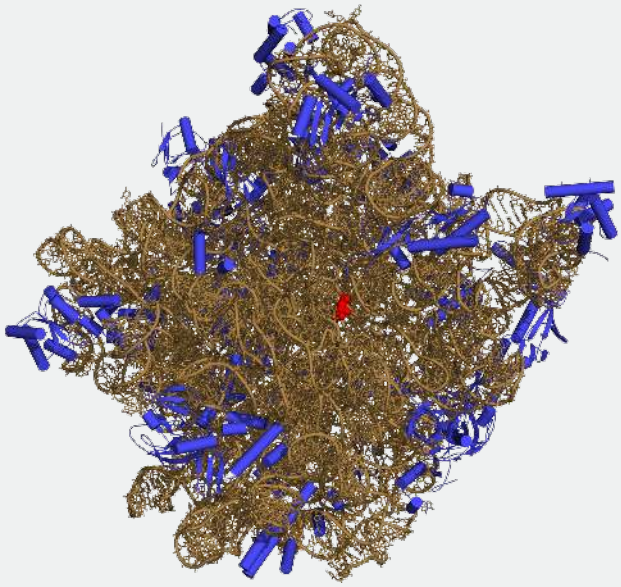


Figure **3.6.1**: Ribosomal subunit

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

THE NUCLEUS

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

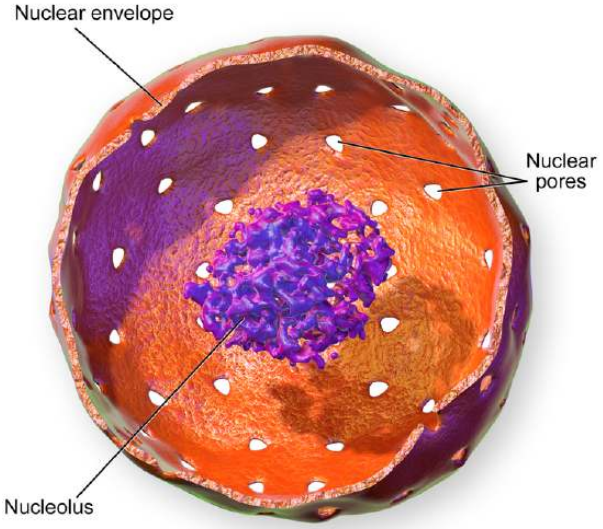


Figure **3.6.2**: This closeup of a cell nucleus shows that it is surrounded by a structure called the nuclear envelope, which contains tiny perforations, or pores. The nucleus also contains a dense center called the nucleolus.

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

MITOCHONDRIA

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

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

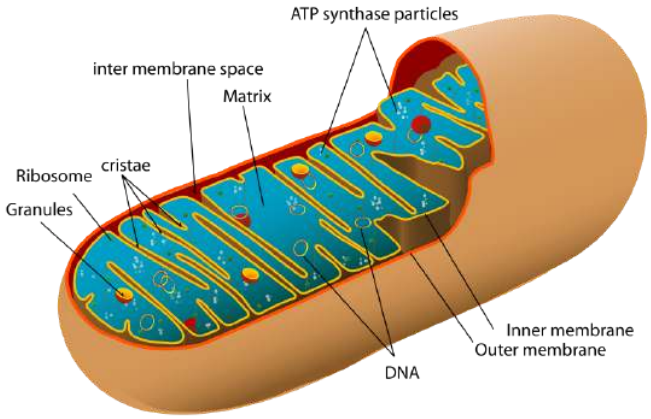


Figure **3.6.3**: Mitochondria, organelles specialized to carry out aerobic respiration, contain an inner membrane folded into cristae, which form two separate compartments: the inner membrane space and the matrix. The Krebs Cycle takes place in the matrix. The electron transport chain is embedded in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

MITOCHONDRIAL COMPARTMENTS

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

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

ENDOPLASMIC RETICULUM

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

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

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

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

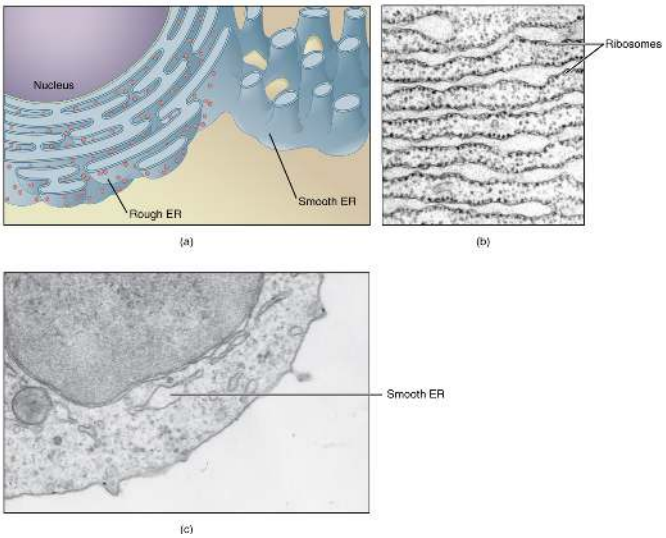


Figure **3.6.4**: The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function (source: mouse tissue). (b) Rough ER is studded with numerous ribosomes, which are sites of protein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

GOLGI APPARATUS

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

The Golgi apparatus manipulates products from the Rough Endoplasmic Reticulum (ER) and also produces new organelles called lysosomes. Proteins and other products of the ER are sent to the Golgi apparatus, which organizes, modifies, packages, and tags them. Some of these products are transported to other areas of the cell and some are exported from the cell through exocytosis. Enzymatic proteins are packaged as new lysosomes.

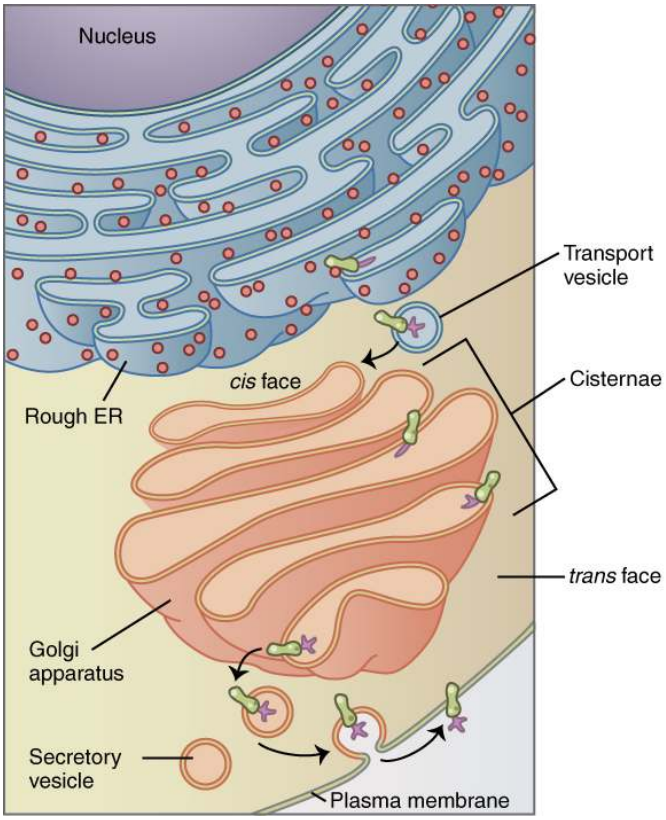


Figure **3.6.5**: The rough ER is continuous with the nuclear envelope and has ribosomes on it's surface. The ribosomes produce proteins such as the one shown which remains bound to the membrane of the rough ER. The membrane of the rough ER pinches off to form a transport vesicle containing the protein.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

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

VESICLES AND VACUOLES

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

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

CENTRIOLES

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

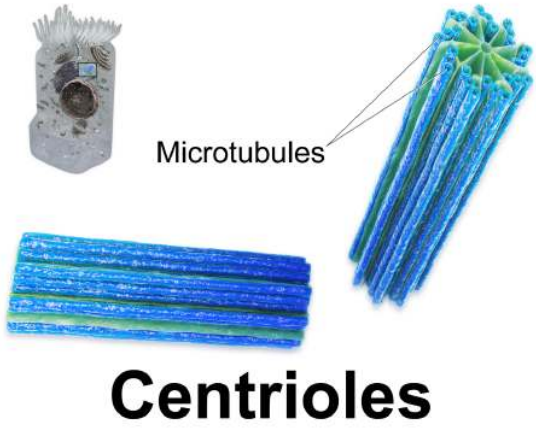


Figure **3.6.6**: Centrioles are tiny cylinders near the nucleus, enlarged here to show their tubular structure.

RIBOSOMES

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

REVIEW

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

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3.7: CELL TRANSPORT

LETTING IN THE LIGHT

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



Figure **3.7.1**: A house with windows

TRANSPORT ACROSS MEMBRANES

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

TRANSPORT WITHOUT ENERGY

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

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

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

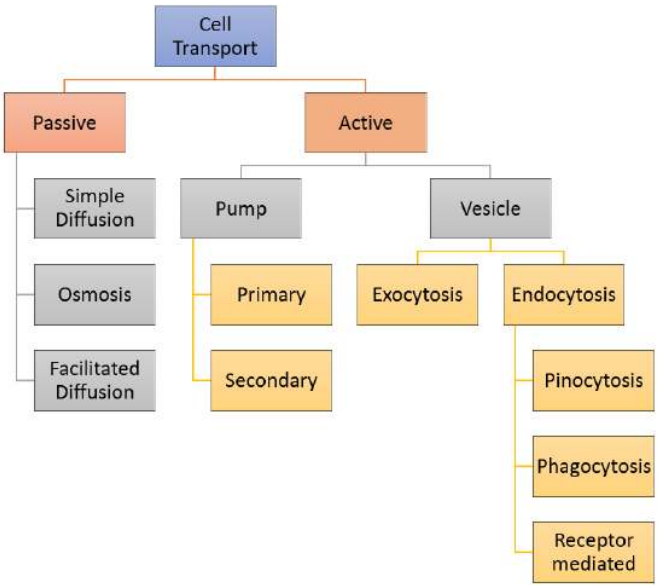


Figure **3.7.2**: The Cell Transport Concept Map illustrates various types of cell transports that happen at the plasma membrane

SIMPLE DIFFUSION

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

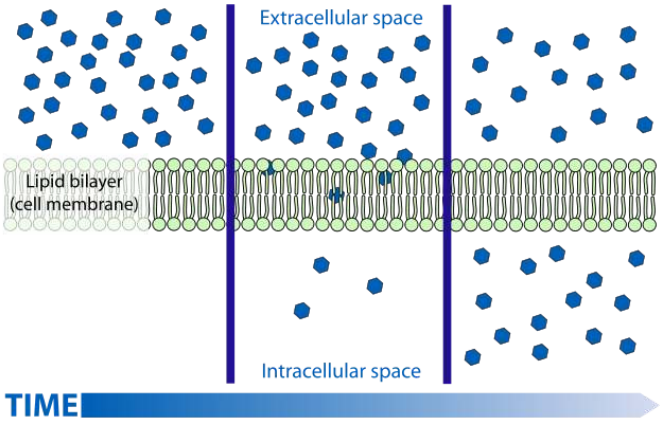


Figure **3.7.3**. Simple diffusion shows as a timeline with the outside of the cell (extracellular space) separated from the inside of the cell (intracellular space) by the cell membrane. In the beginning of the timeline there are many molecules outside of the cell and none inside. Over time, they diffuse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

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

OSMOSIS

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

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

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

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

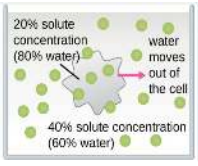


Figure **3.7.4.*A***: **Hypertonic solution.** A solution that has a higher solute concentration than another solution. Water particles will move out of the cell, causing crenation.

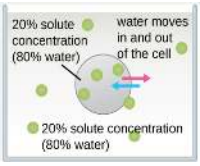


Figure **3.7.4.*B***: **Isotonic solution.** A solution that has the same solute concentration as another solution. There is no net movement of water particles, and the overall concentration on both sides of the cell membrane remains constant.

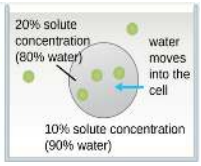


Figure **3.7.4.*C***: **Hypotonic solution.** A solution that has a lower solute concentration than another solution. Water particles will move into the cell, causing the cell to expand and eventually lyse.

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

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

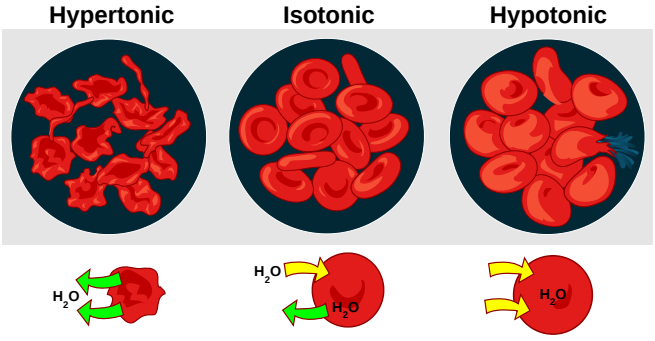


Figure **3.7.5**: Osmosis demonstration with Red Blood cells places in a hypertonic, isotonic, and hypotonic solution.

FACILITATED DIFFUSION

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

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

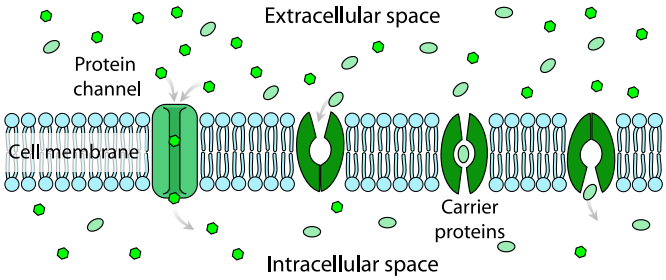


Figure **3.7.6**: Facilitated Diffusion Across a Cell Membrane. Channel proteins and carrier proteins help substances diffuse across a cell membrane. In this diagram, the channel and carrier proteins are helping substances move into the cell (from the extracellular space to the intracellular space).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

REVIEW

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

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3.8: ACTIVE TRANSPORT AND HOMEOSTASIS

LIKE PUSHING A HUMVEE UPHILL

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



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

WHAT IS ACTIVE TRANSPORT?

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

PUMP

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

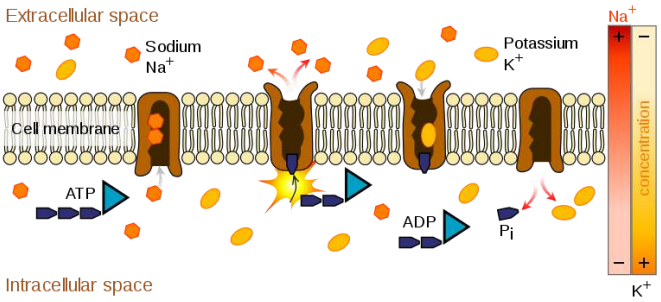


Figure **3.8.2**: The sodium-potassium pump. The sodium-potassium pump moves sodium ions (Na^+) out of the cell and potassium ions (K^+) into the cell. First, three sodium ions bind with a carrier protein in the cell membrane. Then, the carrier protein receives a phosphate group from ATP. When ATP loses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

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

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

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

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

VESICLE TRANSPORT

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

ENDOCYTOSIS

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

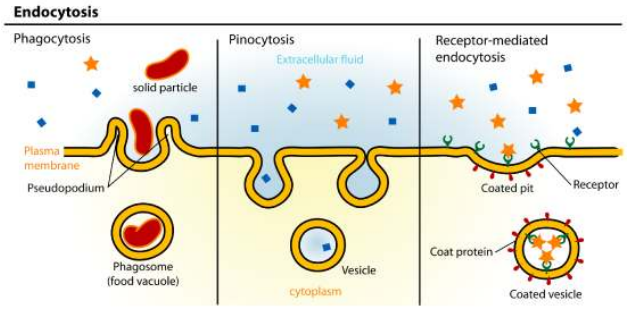


Figure **3.8.3**: (On the right) Phagocytosis is when the plasma membrane wraps around a solid particle outside the cell using projections called pseudopodia. The membrane then pinches off to form a phagosome (food vacuole). (Middle)Pinocytosis is when the membrane folds to form a vesicle that carries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

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

EXOCYTOSIS

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

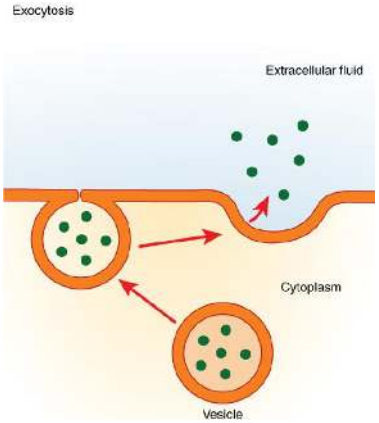


Figure **3.8.4**: Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

HOMEOSTASIS AND CELL FUNCTION

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

FEATURE:FEATURE: MY HUMAN BODY

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

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

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

REVIEW

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

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3.9: CELLULAR RESPIRATION

BRING ON THE S'MORES!

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



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

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

WHERE DO ORGANISMS GET ENERGY FROM?

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

WHAT IS ATP?

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

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

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

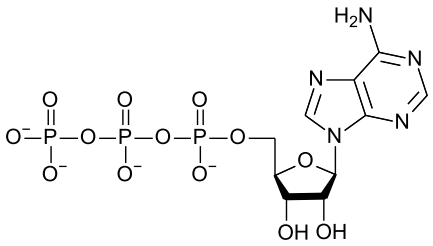


Figure **3.9.2**: Chemical structure of ATP consists of a 5-carbon sugar (ribose) attached to a nitrogenous base (adenine) and three phosphates. When the covalent bond between the terminal phosphate group and the middle phosphate group breaks, energy is released which is used by the cells to do work.

WHAT IS CELLULAR RESPIRATION?

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

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

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

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

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

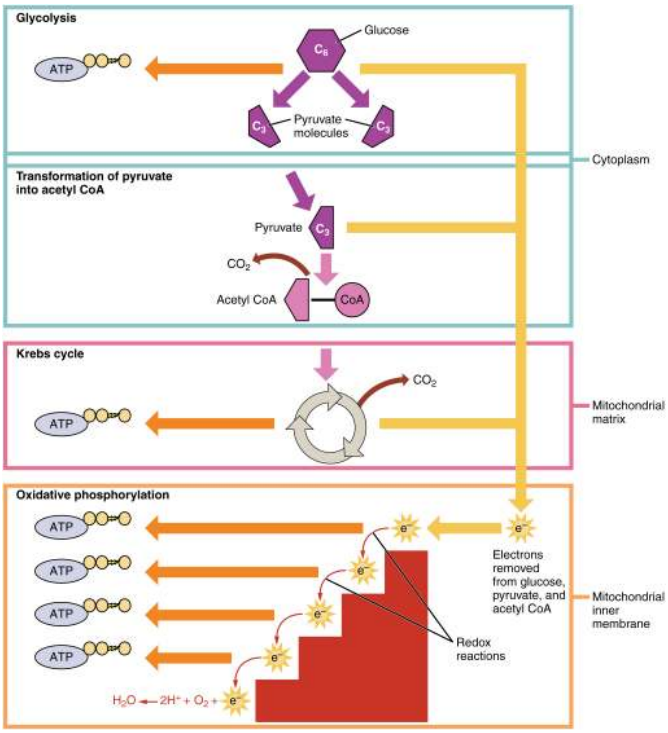


Figure 3.9.3: Cellular respiration takes place in the stages shown here. The process begins with Glycolysis. In this first step, a molecule of glucose, which has six carbon atoms, is split into two three-carbon molecules. The three-carbon molecule is called pyruvate. Pyruvate is oxidized and converted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

GLYCOLYSIS

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

SPLITTING GLUCOSE

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

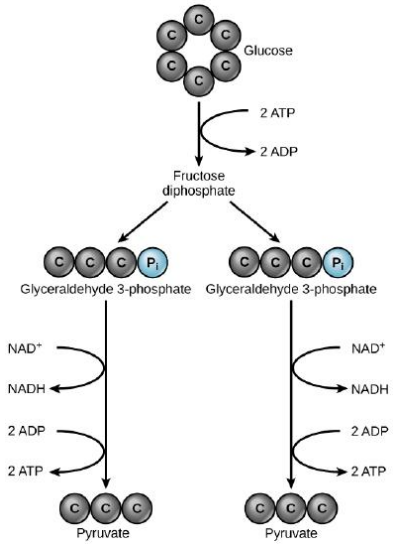


Figure 3.9.4: In glycolysis, a glucose molecule is converted into two pyruvate molecules.

RESULTS OF GLYCOLYSIS

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

- 2 molecules of NADH
- 2 net molecules of ATP

TRANSFORMATION OF PYRUVATE INTO ACETYL-COA

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

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

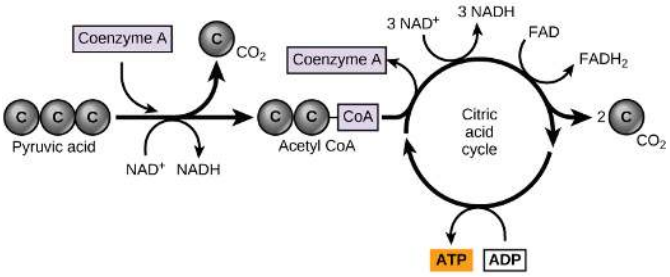


Figure **3.9.5**: Pyruvate is converted into acetyl-CoA before entering the Citric Acid Cycle (Krebs cycle)

CITRIC ACID CYCLE

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

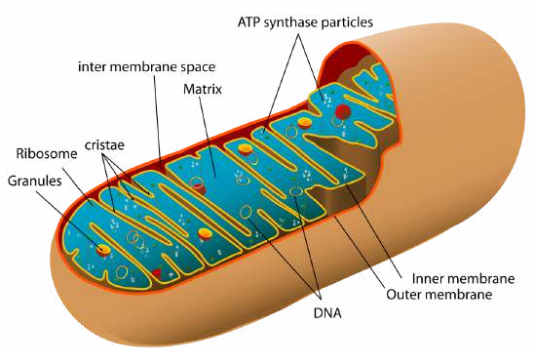


Figure **3.9.6**: The structure of a mitochondrion is defined by an inner and outer membrane. The space inside the inner membrane is full of fluid, enzymes, ribosomes, and mitochondrial DNA. This space is called a matrix. The inner membrane has a larger surface area as compared to the outer membrane.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

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

STEPS OF THE CITRIC ACID (KREBS) CYCLE

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

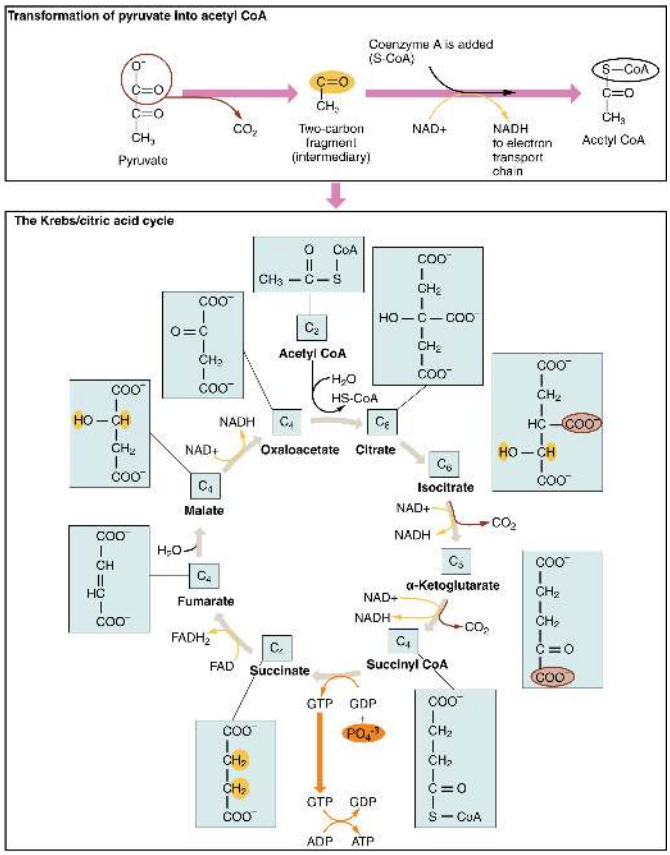


Figure **3.9.7**: In the Citric Acid Cycle, the acetyl group from acetyl CoA is attached to a four-carbon oxaloacetate molecule to form a six-carbon citrate molecule. Through a series of steps, citrate is oxidized, releasing two carbon dioxide molecules for each acetyl group fed into the cycle. In the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

RESULTS OF THE CITRIC ACID CYCLE

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

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

OXIDATIVE PHOSPHORYLATION

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

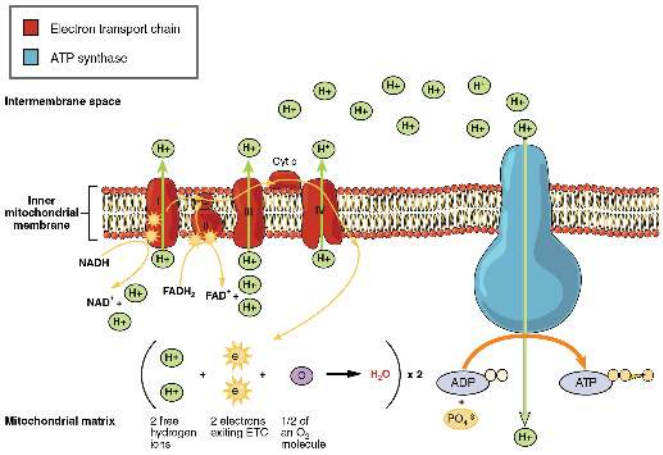


Figure **3.9.8**: Oxidative Phosphorylation: Electron Transport chain and Chemiosmosis.

ELECTRON TRANSPORT CHAIN (ETC)

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

CHEMIOSMOSIS

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

HOW MUCH ATP?

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

REVIEW

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

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3.10: FERMENTATION

FAST AND FURIOUS

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



Figure **3.10.1**: Sprinter on the field

MAKING ATP WITHOUT OXYGEN

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

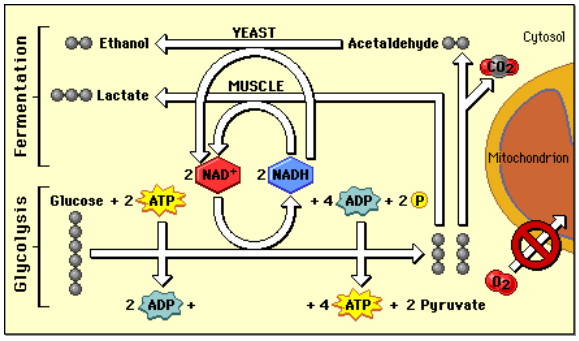


Figure **3.10.2**. The picture shows glycolysis and fermentation. There are two types of fermentation, alcoholic and lactic acid. Fermentation follows glycolysis in the absence of oxygen. Alcoholic fermentation produces ethanol, carbon dioxide, and NAD^+. Lactic acid fermentation produces lactic acid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

FERMENTATION

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

ALCOHOLIC FERMENTATION

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

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



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

LACTIC ACID FERMENTATION

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

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

PROS AND CONS OF FERMENTATION

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

FEATURE: MYTH VS. REALITY

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

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

REVIEW

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

EXPLORE MORE

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3.11: CASE STUDY CONCLUSION- TIRED AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: MORE THAN JUST TIRED

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

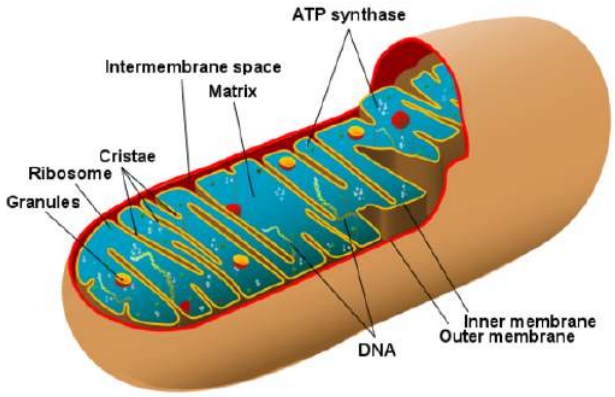


Figure **3.11.1**: Mitochondrial structures. You can see the outer membrane, the inner membrane with cristae, intermembrane space, and matrix with granules, ribosomes, and mitochondrial DNA. ATP synthase is located in the inner membrane.

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

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

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

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

CHAPTER SUMMARY

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

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

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

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

CHAPTER SUMMARY REVIEW

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

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CHAPTER OVERVIEW

4: INTRODUCTION TO THE HUMAN BODY

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

4.1: Case Study- Getting to Know Your Body
4.2: Organization of the Body
4.3: Human Cells and Tissues
4.4: Human Organs and Organ Systems
4.5: Human Body Cavities
4.6: Interaction of Organ Systems
4.7: Homeostasis and Feedback
4.8: Case Study Conclusion- Pressure and Chapter Summary

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4.1: CASE STUDY- GETTING TO KNOW YOUR BODY

CASE STUDY: UNDER PRESSURE

Looking at the photo of a football game in Figure **4.1.1**, you can see why it is so important that the players wear helmets because players may fall on their heads or on top of each other's heads. Football often involves forceful impact to the head as players tackle each other. This can cause damage to the brain — either temporarily as in the case of a concussion, or long-term and more severe types of damage. Helmets are critical to reducing the incidence of traumatic brain injuries (TBIs), but they do not fully prevent them.



Figure **4.1.1**:Football players

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

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

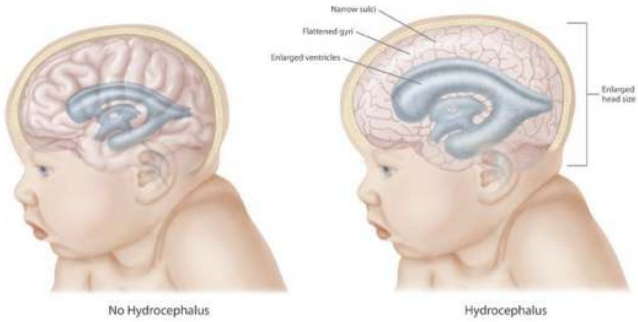


Figure **4.1.2**. Comparison of an infant with (on the right) and without hydrocephalus (on the left). The ventricles (shown in blue-gray) are located inside of the brain (shown in pink). Ventricles are enlarged in the infant with hydrocephalus.

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

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

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

CHAPTER OVERVIEW: INTRODUCTION TO THE HUMAN BODY

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

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

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

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

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

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4.2: ORGANIZATION OF THE BODY

A FANTASTIC MACHINE

This six-legged robot in Figure **4.2.1** was created for research, but it looks like it might be fun to play with. It's obviously a complex machine. Think about some other, more familiar machines, such as power drills, washing machines, and lawnmowers. Each machine consists of many parts, and each part does a specific job, yet all the parts work together to perform certain functions. Many people have compared the human body to a machine, albeit an extremely complex one. Like real machines, the human body also consists of many parts that work together to perform certain functions, which in the case of the human body include keeping the organism alive. The human body may be the most fantastic machine on Earth, as you will discover when you learn more about it in this concept.



Figure **4.2.1**: Six-legged walking robot LAURON IV

WHAT THE HUMAN MACHINE CAN DO

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

ORGANIZATION OF THE HUMAN BODY

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

The organization of the human body can be seen as a hierarchy of increasing size and complexity, starting at the level of atoms and molecules and ending at the level of the entire organism, which is an individual living thing. You can see the intervening levels of organization in Figure **4.2.2** and read about them in the figure and the sections that follow.

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

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

The cellular level is considered when a variety of molecules combine to form the fluid and organelles of a body cell. A cell is the smallest independently functioning unit of a living organism. Even bacteria, which are extremely small, independently living organisms, have a cellular structure. Each bacterium is a single cell. All living structures of human anatomy contain cells, and almost all functions of human physiology are performed in cells or are initiated by cells. A human cell, such as a smooth muscle cell, typically consists of flexible membranes that enclose cytoplasm, a water-based cellular fluid together with a variety of tiny functioning units called organelles.

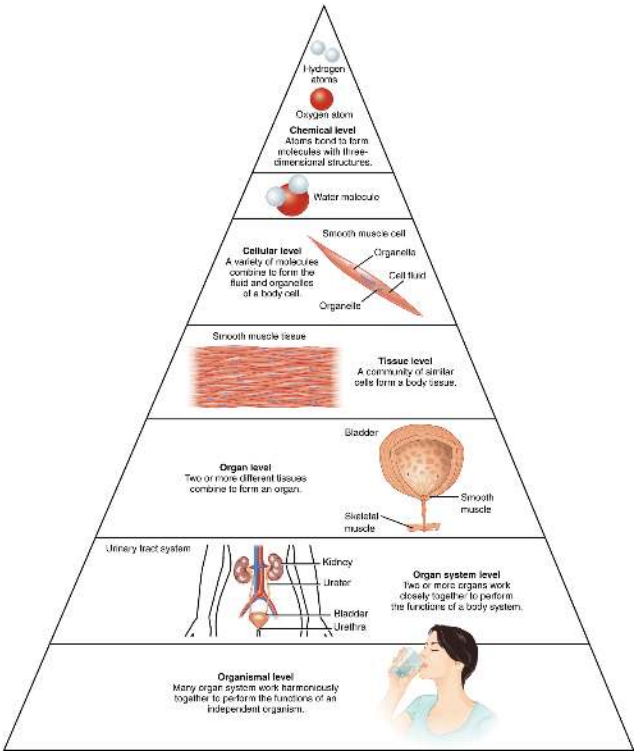


Figure **4.2.2**: This diagram shows the levels of organization of the human body, from atoms to the whole organism.

The tissue level can be studied when a community of similar cells forms a body tissue. A tissue is a group of many similar cells (though sometimes composed of a few related types) that work together to perform a specific function. For example, when many smooth muscle cells come together both structurally and functionally, these cells collectively form a layer of smooth muscle tissue.

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

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

CELLS

The basic units of structure and function of the human body, as in all living things, are cells — an amazing 37 trillion of them by the time the average person reaches adulthood! Each cell carries out basic life processes that allow the body to survive. In addition, most human cells are specialized in structure and function to carry out other specific roles. In fact, the human body may consist of as many as 200 different types of cells, each of which has a special job to do. Just a few of these different human cell types are pictured in Figure **4.2.3**. The cells in the figure have obvious differences in structure that reflect their different functions. For example, nerve cells have long projections sticking out from the body of the cell. These projections help them carry electrical messages to other cells.

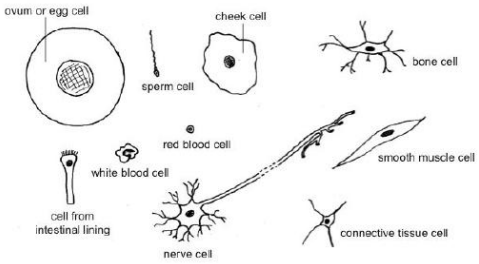


Figure **4.2.3**: A few of the many different types of cells in the human body are illustrated here. Each type of cell is specialized for a particular role in the body.

TISSUES

After the cell, the tissue is the next level of organization in the human body. A **tissue** is a group of connected cells that have a similar function. There are four basic types of human tissues: connective, epithelial, muscle, and nervous tissues. These four tissue types, which are shown in Figure **4.2.4**, make up all the organs of the human body. Connective tissue is composed of cells that are suspended in a matrix. Epithelial tissue is mostly composed of cells that are tightly packed together in sheets. Muscle tissue is also composed of tightly packed cells and some types of muscle, such as the skeletal muscle shown in Figure **4.2.4** contains striation due to the organization of muscle fibers. Nervous tissue is composed of cells with long extensions.

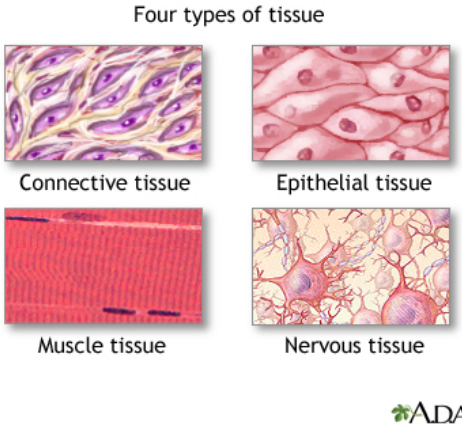


Figure **4.2.4**: Four types of tissues: Connective tissue, Epithelial tissue, Muscle tissue, Nervous tissue

ORGANS AND ORGAN SYSTEMS

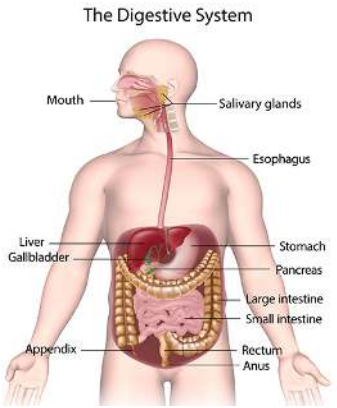


Figure **4.2.5**: A sample organ system (the digestive system) showing the organs within the system (mouth, salivary glands, esophagus, stomach, pancreas, large intestine, small intestine, liver, gallbladder, appendix, rectum, anus).

After tissues, organs are the next level of the organization of the human body. An organ is a structure that consists of two or more types of tissues that work together to do the same job. Examples of human organs include the heart, brain, lungs, skin, and kidneys. Human organs are organized into organ systems; the digestive system is shown in figure Figure **4.2.5**. An organ system is a group of organs that work together to carry out a complex overall function. Each organ of the system does part of the larger job.

A WELL-OILED MACHINE

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

REVIEW

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

EXPLORE MORE

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4.3: HUMAN CELLS AND TISSUES

DUST MOP

This photo in Figure **4.3.1** looks like a close-up of an old-fashioned dust mop, and the object it shows has a somewhat similar function. However, the object is greatly enlarged in the photo. Can you guess what it is? The answer may surprise you. It is a scanning electron micrograph of human epithelial cells that line the bronchial passages. The floppy, dust-mop-like extensions are actually microscopic structures called cilia projecting from the outer surface of the epithelial cells. The function of the cilia is to trap dust, pathogens, and other particles in the air before it enters the lungs. The cilia also sway back and forth to sweep the trapped particles upward toward the throat, from which they can be expelled from the body.

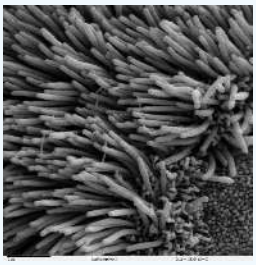


Figure **4.3.1**: Scanning electron microscope image of lung trachea epithelium. There are both ciliated and on-ciliated cells in this epithelium. Note the difference in size between the cilia and the microvilli (on the non-ciliated cell surface)

HUMAN CELLS

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

VARIATION IN HUMAN CELLS

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

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

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

DIFFERENT BUT IDENTICAL

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

EXAMPLES OF HUMAN CELL TYPES

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

BONE CELLS

There are four main subtypes of bone cells, as shown in Figure **4.3.2**. Each type has a different form and function:

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

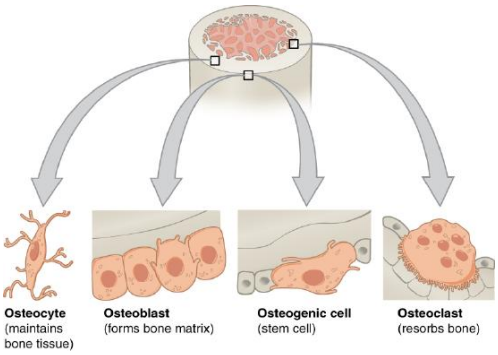


Figure **4.3.2**: Four sub-types of bone cells in the human skeletal system: Osteocytes (maintain bone tissues), Osteoblast (form bone matrix), Osteogenic cells (stem cell), Osteoclasts (reabsorb bone)

WHITE BLOOD CELLS

White blood cells (also called leukocytes) are even more variable than bone cells. Five subtypes of white blood cells are shown in Figure **4.3.3**. All of them are immune system cells involved in defending the body, but each subtype has a different function. They also differ in the normal proportion of all leukocytes they make up.

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

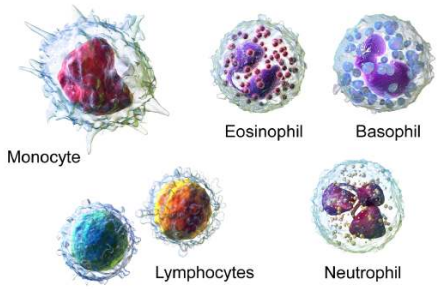


Figure **4.3.3**: Five sub-types of human white blood cells in the human immune system: monocyte, eosinophil, basophil, lymphocyte, neutrophil

TISSUES

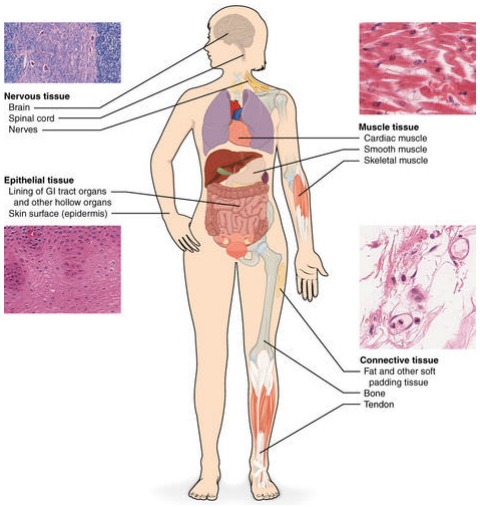


Figure **4.3.4**: There are 4 different types of tissues in our body. Nervous tissue is found in the brain, spinal cord, and nerves. Muscular tissue such as cardiac, smooth, and skeletal muscle. Epithelial tissue lines the GI tract organs and other hollow organs and is found on the skin surface (epidermis). Connective tissue such as fat and other soft padding tissue, bone, and tendon.

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

CONNECTIVE TISSUE

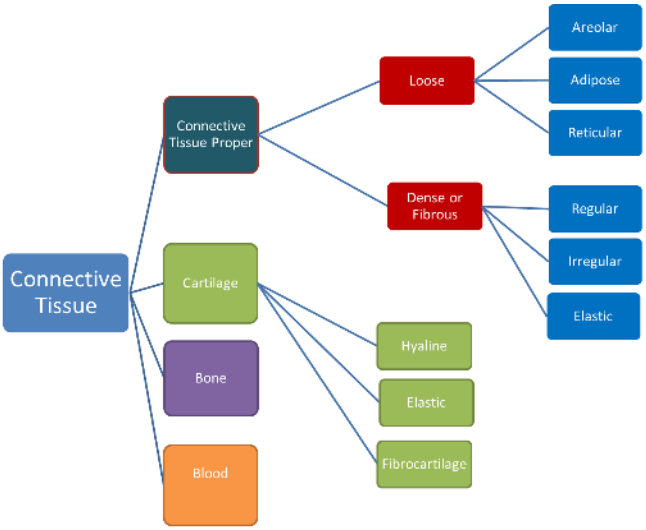


Figure **4.3.5**: The image summarizes the various categories of connective tissues found in the human body. Connective tissue can be classified as connective tissue proper, cartilage, bone, or blood. Cartilage can be classified as hyaline cartilage, elastic cartilage, or fibrocartilage. Connective tissue proper can be classified as loose and dense or fibrous. Loose connective tissue can be classified as areolar, adipose, or reticular. Dense or fibrous connective tissue can be classified as regular, irregular, and elastic.

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

ground substance) is secreted by the connective tissue cells and determines the characteristics of the connective tissue. It is the consistency of the matrix that determines the function of the connective tissue. The matrix can be liquid, gel-like or solid, all depending on the type of connective tissue. For example, the extracellular matrix of bone is a rigid mineral framework. The extracellular matrix of blood is liquid plasma. Connective tissues such as bone and cartilage generally form the body's structure. There are many sub-types of the four major types of tissues in a human body, see the flow chart in Figure **4.3.5**.

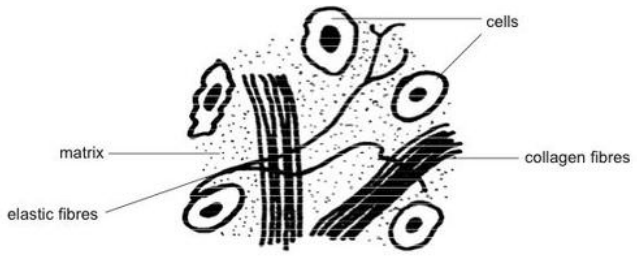


Figure **4.3.6**: General features of connective tissues. The Matrix of most connective tissues is made up of ground substance and protein fibers. There are cells suspended in the matrix.

CONNECTIVE TISSUE PROPER

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

LOOSE CONNECTIVE TISSUE

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

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

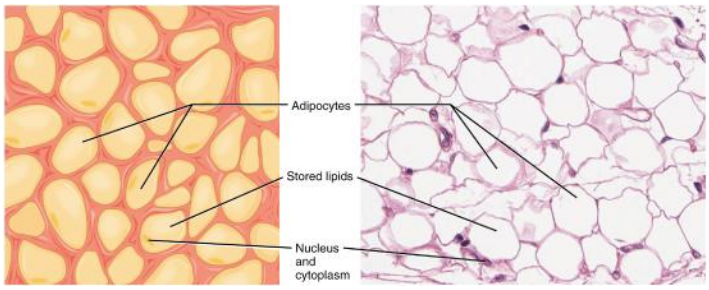


Figure **4.3.7**: Adipose Connective Tissue consists of fat cells (adipocytes with a nucleus and stored lipids in their cytoplasm) with a little extracellular matrix. It stores fat for energy and provides insulation.

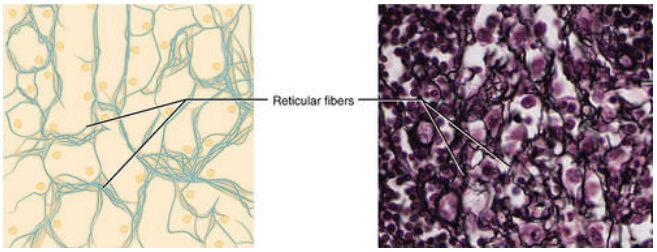


Figure **4.3.8**: Reticular Connective Tissue. This is a loose connective tissue made up of a network of reticular fibers that provides a supportive framework for soft organs

DENSE CONNECTIVE TISSUE PROPER

This tissue consists of three categories, dense regular connective tissue, dense irregular connective tissue, and elastic connective tissue. These tissues differ on the arrangement and composition of the fibrous elements of the extracellular matrix.

1. **Dense regular connective tissue** has extracellular fibers that all run in the same direction and plane. Muscle tendons are a type of dense regular connective tissue.
2. **Dense irregular connective tissue** contains collagen and elastic fibers which are found running in all different directions and planes. The dermis of the skin is composed of dense irregular connective tissue.
3. **Elastic connective tissue**: Made up of freely branching elastic fibers with fibroblasts in the spaces between the fibers, this tissue allows the kind of stretch that is found in the walls of arteries.

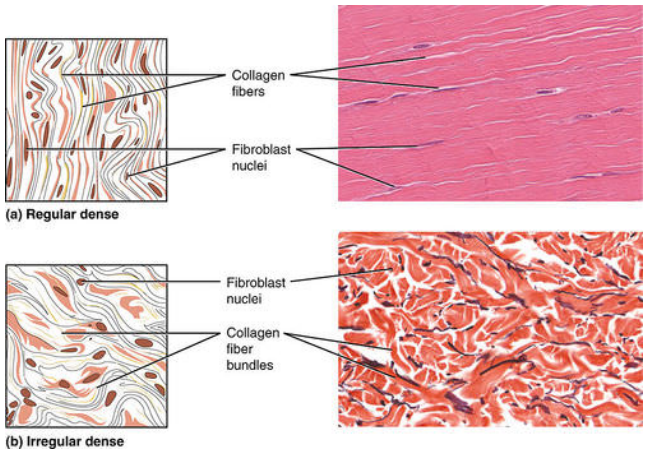


Figure 4.3.9: (a) Dense regular connective tissue consists of collagen fibers packed into parallel bundles. (b) Dense irregular connective tissue consists of collagen fibers interwoven into a mesh-like network..

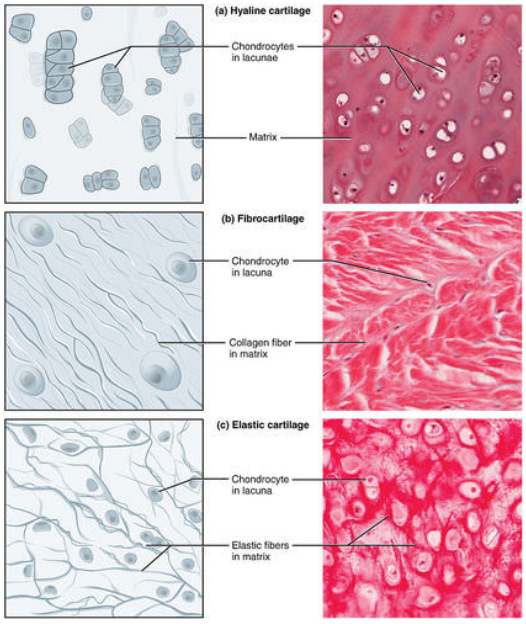


Figure 4.3.10: Cartilage is a connective tissue consisting of collagenous fibers embedded in a firm matrix of chondroitin sulfates. (a) Hyaline cartilage has chondrocytes in lacunae within a matrix. (b) Fibrocartilage has chondrocytes in lacunae within collage fibers in a matrix. (c) Elastic cartilage has chondrocytes in lacunae within elastic fibers in a matrix.

CARTILAGE

This connective tissue is relatively solid and is a non-vascularized tissue (does not have a blood supply). The matrix is produced by cells called chondroblasts. When these cells slow down, they reside is small spaces called lacunae. These mature cells in the lacunae are called chondrocytes. There are three types of cartilage: hyaline cartilage, elastic cartilage, and fibrocartilage.

1. **Hyaline cartilage** is the most common type of cartilage, contains many collagen fibers and is found in many places including the nose, between the ribs and the sternum and in the rings of the trachea.
2. **Elastic cartilage** has many elastic fibers in the matrix and supports the shape of the ears and forms part of the larynx.
3. **Fibrocartilage** is tough and contains many collagen fibers and is responsible for cushioning the knee joint and for forming the disks between the vertebrae.

BONE

Bone is a hard, mineralized tissue found in the skeleton. The bone matrix contains many collagen fibers as well as inorganic mineral salts, calcium carbonate, and calcium phosphate, all features that make it a very rigid structure. Bone cells, called **osteoblasts**, secrete the osteoid substance that eventually hardens around the cells to form an ossified matrix. The **osteon** forms the basic unit of compact bone. Within the

osteon, the osteocytes (mature bone cells) are located in lacunae. Because the bone matrix is very dense, the osteocytes get their nutrition from the central canal via tiny canals called canaliculi.

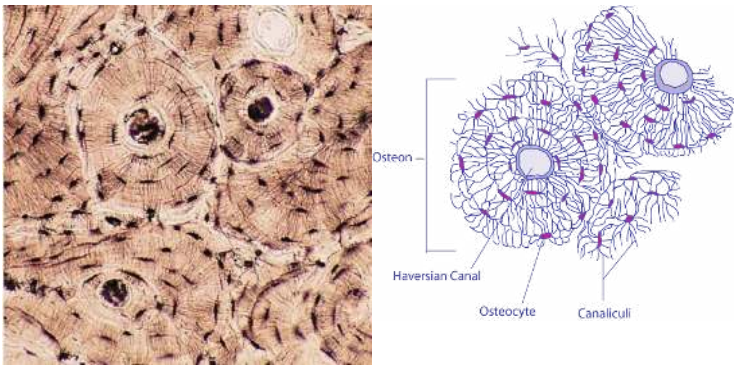


Figure **4.3.11**: The image shows a micrograph as well as an illustration of the cross-section of the compact bone tissue. The osteons are concentric structures that are composed of osteocytes in the lacunae and central (Haversian) canal. The small tunnels, canaliculi, connect osteocytes in the different layers of an osteon.

BLOOD

Blood is considered a type of fluid connective tissue because the matrix of blood is not solid. The fluid matrix is called plasma, and formed elements of this tissue include white blood cells, red blood cells, and platelets. Read more about the composition and function of blood in the cardiovascular system chapter.

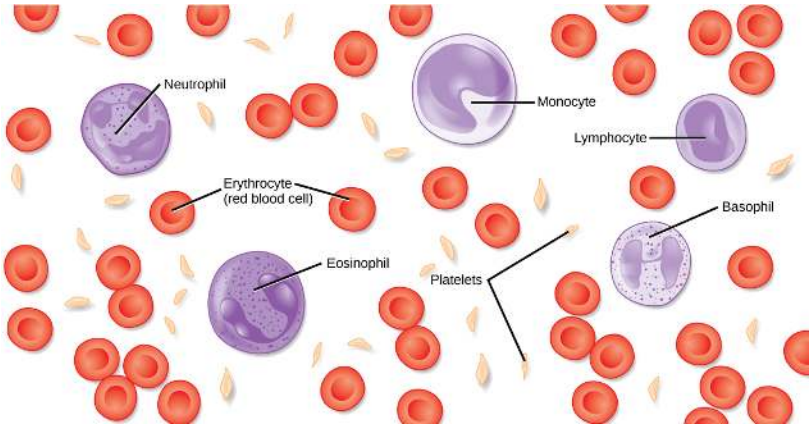


Figure **4.3.12**: The cells and cellular components of human blood are shown. Red blood cells deliver oxygen to the cells and remove carbon dioxide. White blood cells (including neutrophils, monocytes, lymphocytes, eosinophils, and basophils) are involved in the immune response. Platelets form clots that prevent blood loss after injury.

EPITHELIAL TISSUE

Epithelial tissue is made up of cells that line inner and outer body surfaces, such as the skin and the inner surface of the digestive tract. Epithelial tissue that lines inner body surfaces and body openings is called **mucous membrane.** This type of epithelial tissue produces **mucus**, a slimy substance that coats mucous membranes and traps pathogens, particles, and debris. Epithelial tissue protects the body and its internal organs, secretes substances such as hormones in addition to mucus, and absorbs substances such as nutrients.

EPITHELIAL CELL CLASSIFICATION

Most epithelial tissue is described with two names. The first name describes the number of cell layers present and the second describes the shape of the cells. One layer of epithelial cells is called simple and more than one layer of epithelial cells is called stratified. There are three basic shapes of epithelial cells, squamous, cuboidal, and columnar. Squamous cells are thin and flat; cuboidal cells have a shape of a cube; columnar cells have a shape of a pillar. For example, simple squamous epithelial tissue describes a single layer of cells that are flat and scale-like in shape.

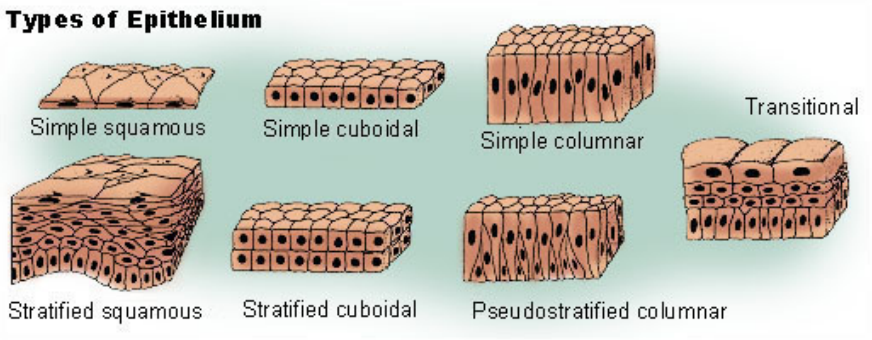


Figure **4.3.13**: Classification of Epithelial Tissues

LOCATIONS AND FUNCTIONS OF EPITHELIAL TISSUES

These tissues are found at various locations in our body and they have many functions. Some locations and functions are listed below:

- Simple squamous epithelium: This tissue is located in the sacs of the lungs and kidney where the exchange of nutrients and gas is essential.
- Simple cuboidal epithelium: This tissue is located in the glands and their ducts and kidneys. The main function of this tissue is secretion.
- Simple Columnar epithelium: This tissue lines the Gastrointestinal tract. The main function of this tissue is absorption and secretion.
- Pseudostratified epithelium: This is a simple tissue with the appearance of stratification. This tissue is located in the respiratory tract. This tissue may contain cilia to move mucus.
- Stratified squamous epithelium: This tissue is located where protection is needed such as skin.
- Stratified cuboidal epithelium: This tissue is located in the sweat glands for protection.
- Stratified columnar epithelium: This tissue is located in some sweat glands. The main function is to protect and secrete sweat components.
- Transitional epithelium: This tissue lines bladder, urethra, and ureters. The tissue allows the urinary organs to expand and stretch.

MUSCLE TISSUE

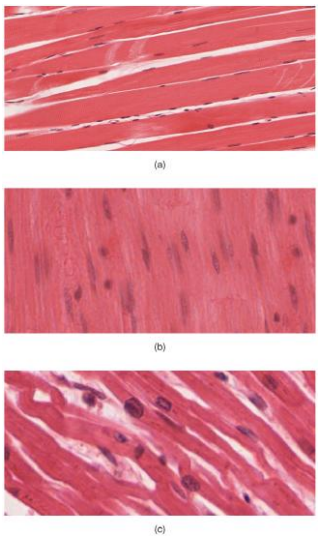


Figure **4.3.14**: The body contains three types of muscle tissue: (a) skeletal muscle, (b) smooth muscle, and (c) cardiac muscle.

Muscle tissue is made up of cells that have the unique ability to contract or become shorter. There are three major types of muscle tissue, as pictured in Figure **4.3.14**: skeletal, smooth, and cardiac muscle tissues.

1. **Skeletal muscles** are striated, or striped in appearance, because of their internal structure. Skeletal muscles are attached to bones, and when they pull on the bones, they enable the body to move. Skeletal muscles are under voluntary control.
2. **Smooth muscles** are nonstriated muscles. They are found in the walls of blood vessels and in the reproductive, gastrointestinal, and respiratory tracts. Smooth muscles are not under voluntary control.
3. **Cardiac muscles** are striated and found only in the heart. Their contractions cause the heart to beat. Cardiac muscles are not under voluntary control.

NERVOUS TISSUE

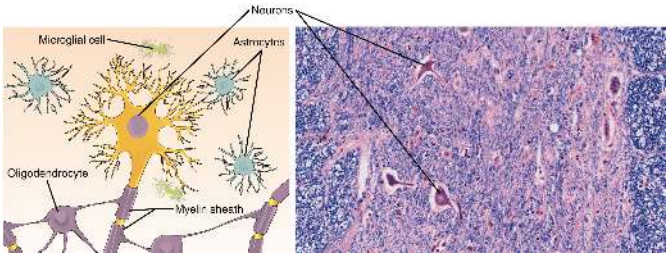


Figure **4.3.15**. This diagram shows some of the cell types that make up nervous tissues.

Nervous tissue is made up of neurons and other types of cells generally called glial cells (Figure **4.3.15**). Neurons are composed of cell body and extensions. The cell body contains the nucleus and the extensions make connections with the other tissues and neurons. Neurons transmit electrical messages and the glial cells play supporting roles. Nervous tissue makes up the central nervous system (mainly the brain and spinal cord) and peripheral nervous system (the network of nerves that runs throughout the rest of the body).

FEATURE: MY HUMAN BODY

If you are a blood donor, then you have donated tissue. Blood is a tissue that you can donate when you are alive. You may have indicated on your driver's license application that you wish to be a tissue donor in the event of your death. Deceased people can donate many different tissues, including skin, bone, heart valves, and the corneas of the eyes. If you are not already registered as a tissue donor, the information below may help you decide if you would like to register.

Each year, approximately 30,000 people donate tissues, which supply tissues for up to 1 million tissue transplants. One tissue donor can enhance or save the life of more than 50 people! Unlike organs, which generally must be transplanted immediately after the donor dies, donated tissues can be processed and stored for a long time for later use. Donated tissues can be used to replace burned skin and damaged bone and to repair ligaments. Corneal tissues can be used for corneal transplants that restore sight in blind people. In fact, each year 48,000 patients have their sight restored with corneal transplants. Unfortunately, there are not enough tissues to go around, and the need for donated tissues keeps rising.

REVIEW

1. Give an example of cells that function individually and move freely, and give an example of cells that act together and are attached to other cells of the same type.
2. What are examples of cells that can readily divide and cells that can divide only under rare circumstances?
3. Identify a type of cell that secretes an important substance and name the substance it secretes.
4. Explain how different cell types come about when all the cells in an individual human being are genetically identical.
5. Compare and contrast four subtypes of human bone cells.
6. Identify three types of human white blood cells, and state their functions.
7. Why are bone and blood both classified as connective tissues?
8. Name another type of connective tissue, and describe its role in the human body.
9. Based on the information in the table above of types of epithelial tissues, list four general functions of this type of tissue in the human body.
10. Compare and contrast the three types of muscle tissues.
11. Identify the four types of nervous tissues, where each type is found, and its basic function.
12. Of the main types of human tissue, name two that can secrete hormones.
13. Cells in a particular tissue:
    A. Are all of the same type
    B. Have different genes from cells in other tissues
    C. Work together to carry out a function
    D. Are always connected physically to each other
14. Why are mucous membranes often located in regions that interface between the body and the outside world?
15. Skin is a type of _____ tissue.
16. Body fat is a type of _____ tissue.

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4.4: HUMAN ORGANS AND ORGAN SYSTEMS

"ACHY BREAKY HEART"

Billy Ray Cyrus's song "Achy Breaky Heart" has lyrics suc as: Heartache, heartbreak...it all has to do with love. Did you ever wonder why the heart is associated with love? The heart was once thought to be the center of all thought processes, as well as the site of all emotions. This notion may have stemmed from very early anatomical dissections that found many nerves can be traced to the region of the heart. The fact that the heart may start racing when one is excited or otherwise emotionally aroused may have contributed to this idea as well. In fact, the heart is not the organ that controls thoughts or emotions. The organ that controls those functions is the brain. In this concept, you'll be introduced to the heart, brain, and other major organs of the human body.



Figure **4.4.1**: Twemoji

HUMAN ORGANS

An organ is a collection of tissues joined in a structural unit to serve a common function. Organs exist in most multicellular organisms, including not only humans and other animals but also plants. In single-celled organisms such as bacteria, the functional equivalent of an organ is an organelle.

TISSUES IN ORGANS

Although organs consist of multiple tissue types, many organs are composed of the main tissue that is associated with the organ's major function and other tissues that play supporting roles. The main tissue may be unique to that specific organ. For example, the main tissue of the heart is the cardiac muscle, which performs the heart's major function of pumping blood and is found only in the heart. The heart also includes nervous and connective tissues that are required for it to perform its major function. For example, nervous tissues control the beating of the heart, and connective tissues make up heart valves that keep blood flowing in just one direction through the heart.

VITAL ORGANS

The human body contains five organs that are considered vital for survival. They are the heart, brain, kidneys, liver, and lungs. The locations of these five organs and several other internal organs are shown in Figure **4.4.2**. If any of the five vital organs stops functioning, the death of the organism is imminent without medical intervention.

1. The heart is located in the center of the chest, and its function is to keep blood flowing through the body. Blood carries substances to cells that they need and also carries away wastes from cells.
2. The brain is located in the head and functions as the body's control center. It is the seat of all thoughts, memories, perceptions, and feelings.
3. The two kidneys are located in the back of the abdomen on either side of the body. Their function is to filter blood and form urine, which is excreted from the body.
4. The liver is located on the right side of the abdomen. It has many functions, including filtering blood, secreting bile that is needed for digestion, and producing proteins necessary for blood clotting.
5. The two lungs are located on either side of the upper chest. Their main function is exchanging oxygen and carbon dioxide with the blood.

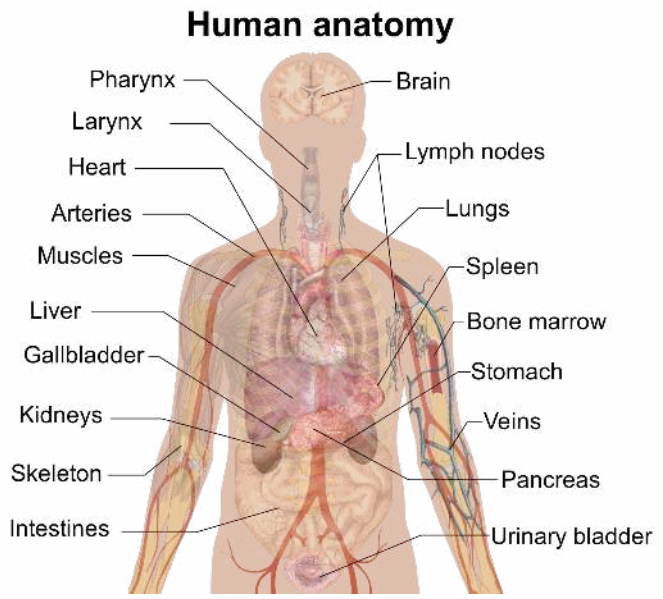


Figure **4.4.2**: Use this shadow diagram of human anatomy to locate the five organs described above: heart, brain, kidneys, liver, and lungs. Do you know the functions of any of the other organs in the diagram?

HUMAN ORGAN SYSTEMS

Functionally related organs often cooperate to form whole organ systems. Figure **4.4.3** and Figure **4.4.4** show 11 human organ systems, including separate diagrams for the male and female reproductive systems. Some of the organs and functions of the organ systems are identified in the figure. Each system is also described in more detail in the text that follows. Most of these human organ systems are also the subject of separate chapters in this book.

INTEGUMENTARY SYSTEM

Organs of the integumentary system include the skin, hair, and nails. The skin is the largest organ in the body. It encloses and protects the body and is the site of many sensory receptors. The skin is the body's first defense against pathogens, and it also helps regulate body temperature and eliminate wastes in sweat.

SKELETAL SYSTEM

The skeletal system consists of bones, joints, teeth. The bones of the skeletal system are connected by tendons, ligaments, and cartilage. Functions of the skeletal system include supporting the body and giving it shape. Along with the muscular system, the skeletal system enables the body to move. The bones of the skeletal system also protect internal organs, store calcium, and produce red and white blood cells.

MUSCULAR SYSTEM

The muscular system consists of three different types of muscles, including skeletal muscles, which are attached to bones by tendons and allow for voluntary movements of the body. Smooth muscle tissues control the involuntary movements of internal organs, such as the organs of the digestive system, allowing food to move through the system. Smooth muscles in blood vessels allow vasoconstriction and vasodilation and thereby help regulate body temperature. Cardiac muscle tissues control the involuntary beating of the heart, allowing it to pump blood through the blood vessels of the cardiovascular system.

NERVOUS SYSTEM

The nervous system includes the brain and spinal cord, which make up the central nervous system, and nerves that run throughout the rest of the body, which make up the peripheral nervous system. The nervous system controls both voluntary and involuntary responses of the human organism and also detects and processes sensory information.

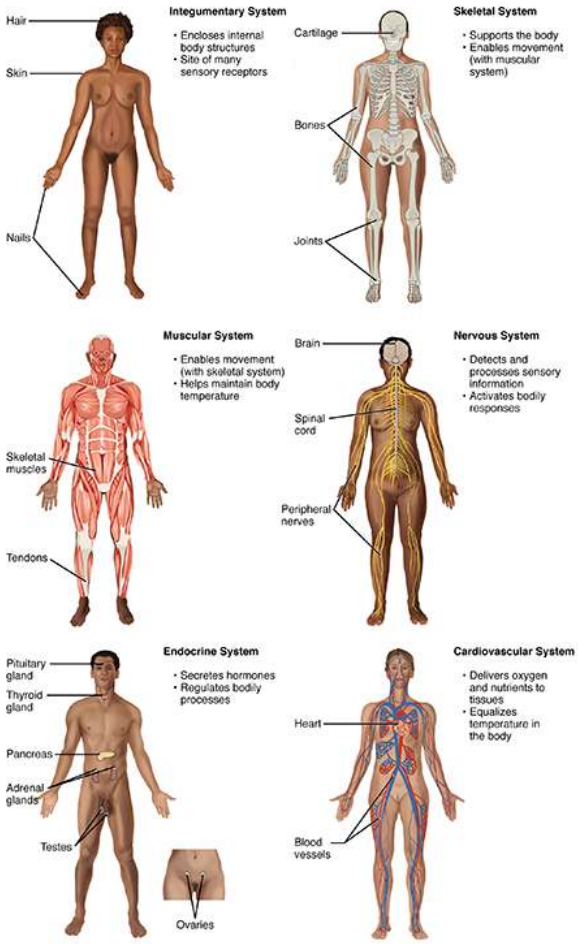


Figure **4.4.3**: Organ systems: Integumentary, Skeletal, Muscular, Nervous, Endocrine, and Cardiovascular

ENDOCRINE SYSTEM

The endocrine system is made up of glands that secrete hormones into the blood, which carries the hormones throughout the body. Endocrine hormones are chemical messengers that control many body functions, including metabolism, growth, and sexual development. The master gland of the endocrine system is the pituitary gland, which produces hormones that control other endocrine glands. Some of the other endocrine glands include the pancreas, thyroid gland, and adrenal glands.

CARDIOVASCULAR SYSTEM

The cardiovascular system (also called the circulatory system) includes the heart, blood, and three types of blood vessels: arteries, veins, and capillaries. The heart pumps blood, which travels through the blood vessels. The main function of the cardiovascular system is transport. Oxygen from the lungs and nutrients from the digestive system are transported to cells throughout the body. Carbon dioxide and other waste materials are picked up from the cells and transported to organs such as the lungs and kidneys for elimination from the body. The cardiovascular system also equalizes body

temperature and transports endocrine hormones to cells in the body where they are needed.

URINARY SYSTEM

The urinary system includes the pair of kidneys, which filter excess water and a waste product called urea from the blood and form urine. Two tubes called ureters carry the urine from the kidneys to the urinary bladder, which stores the urine until it is excreted from the body through another tube named the urethra. The kidneys also produce an enzyme called renin and a variety of hormones. These substances help regulate blood pressure, the production of red blood cells, and the balance of calcium and phosphorus in the body.

RESPIRATORY SYSTEM

Organs and other structures of the respiratory system include the nasal passages, lungs, and a long tube called the trachea, which carries air between the nasal passages and lungs. The main function of the respiratory system is to deliver oxygen to the blood and remove carbon dioxide from the body. Gases are exchanged between the lungs and blood across the walls of capillaries lining tiny air sacs (alveoli) in the lungs.

LYMPHATIC SYSTEM

The lymphatic system is sometimes considered to be part of the immune system. It consists of a network of lymph vessels and ducts that collect excess fluid (called lymph) from extracellular spaces in tissues and transport the fluid to the bloodstream. The lymphatic system also includes many small collections of tissue, called lymph nodes, and an organ called the spleen, both of which remove pathogens and cellular debris from the lymph or blood. In addition, the thymus gland in the lymphatic system produces some types of white blood cells (lymphocytes) that fight infections.

DIGESTIVE SYSTEM

The digestive system consists of several main organs — including the mouth, esophagus, stomach, and small and large intestines — that form a long tube called the gastrointestinal (GI) tract. Food moves through this tract where it is digested, its nutrients absorbed, and its waste products excreted. The digestive system also includes accessory organs (such as the pancreas and liver) that produce enzymes and other substances needed for digestion but through which food does not actually pass.

MALE AND FEMALE REPRODUCTIVE SYSTEMS

The reproductive system is the only body system that differs substantially between individuals. There is a range of Biological sex, but most books divide them into male and female. We will discuss the Biology of sex in detail in the reproductive and development chapters.

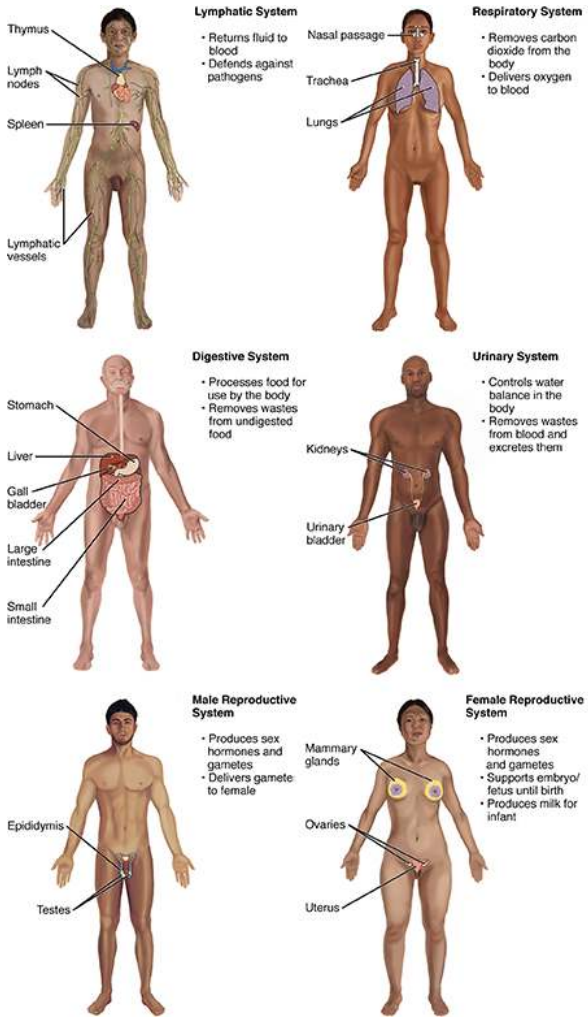


Figure **4.4.4**: Organ Systems: Lymphatic, Respiratory, Digestive, Urinary, male and female reproductive

FEATURE: HUMAN BIOLOGY IN THE NEWS

Organ transplantation has been performed by surgeons for more than six decades, and you've no doubt heard of people receiving heart, lung, and kidney transplants. However, you may have never heard of a penis transplant. The first U.S. penis transplant was performed in May of 2016 at Massachusetts General Hospital in Boston. The 15-hour procedure involved a team of more than 50 physicians, surgeons, and nurses. The patient was a 64-year-old man who had lost his penis to cancer in 2012. The surgical milestone involved grafting microscopic blood vessels and nerves of the donor organ to those of the recipient. As with most transplant patients, this patient will have to take immunosuppressing drugs for the rest of his life so his immune system will not reject the organ. The transplant team said that their success with this transplant "holds promise for patients with devastating genitourinary injuries and disease." They also hope their experiences will be helpful for gender reassignment surgery.

REVIEW

1. What is the main tissue in the heart, and what is its role?
2. What non-muscle tissues are found in the heart? What are their functions?
3. Identify two vital organs in the human body. Identify their locations and functions.
4. List three human organ systems. For each organ system, identify some of its organs and functions.
5. Compare and contrast the male and female reproductive systems.
6. For each of the following pairs of organ systems, describe one way in which they work together and/or overlap.
   A. Skeletal system and muscular system
   B. Muscular system and digestive system
   C. Endocrine system and reproductive system
   D. Cardiovascular system and urinary system
7. What is the largest organ of the human body?
8. What are the three organ systems involved in regulating human body temperature?
9. Teeth are part of which system?
   A. Integumentary
   B. Skeletal
   C. Nervous
   D. A and B
10. Hair is part of which organ system?
11. *True or False.* Organs only exist in animals.
12. *True or False.* The respiratory system helps to remove wastes from the body.

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4.5: HUMAN BODY CAVITIES

CONTAIN THE BRAIN

The brain is a delicate organ that regulates the physiology of the whole body. Figure **4.5.1** shows the brain with its superficial structures. Brain coverings and the skull provide protection to the brain. The space where the brain is located in the skull is called the cranial cavity.

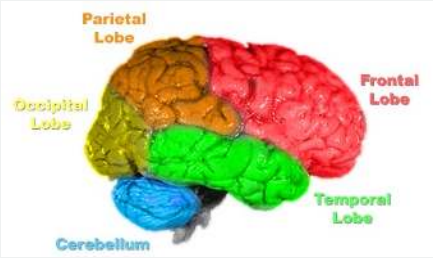


Figure **4.5.1**: Human Brain lateral view

WHAT ARE BODY CAVITIES?

The human body, like that of many other multicellular organisms, is divided into a number of body cavities. A **body cavity** is a fluid-filled space inside the body that holds and protects internal organs. Human body cavities are separated by membranes and other structures. The two largest human body cavities are the ventral cavity and the dorsal cavity. These two body cavities are subdivided into smaller body cavities. Both the dorsal and ventral cavities and their subdivisions are shown in Figure **4.5.2**.

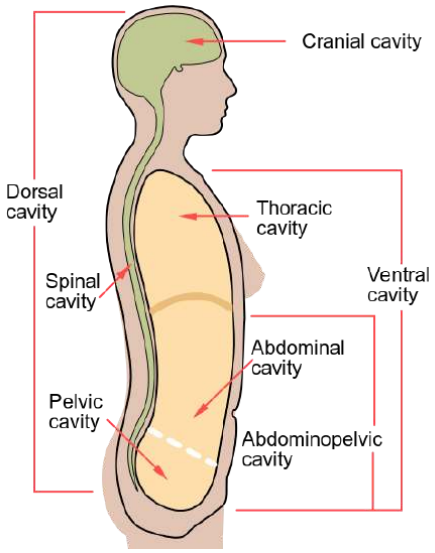


Figure **4.5.2**: The ventral cavity includes the thoracic and abdominopelvic cavities and their subdivisions. The abdominopelvic cavity is further divided into abdominal and pelvic cavities. The dorsal cavity includes the cranial and spinal cavities.

VENTRAL CAVITY

The **ventral cavity** is at the anterior, or front, of the trunk. Organs contained within this body cavity include the lungs, heart, stomach, intestines, and reproductive organs. You can see some of the organs in the ventral cavity in Figure **4.5.3**. The ventral cavity allows for considerable changes in the size and shape of the organs within it as they perform their functions. For example, organs such as the lungs, stomach, or uterus can expand or contract without distorting other tissues or disrupting the activities of nearby organs.

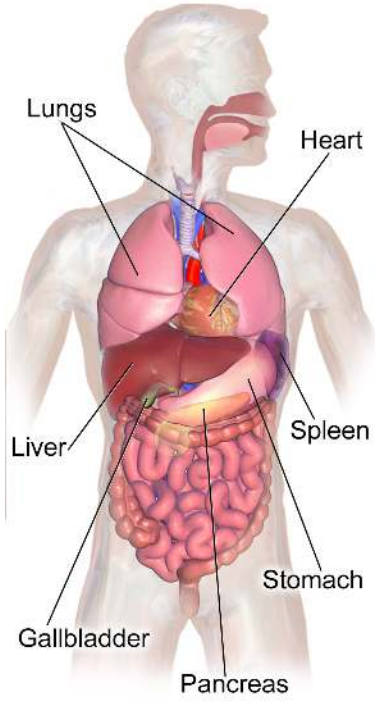


Figure **4.5.3**: Some of the major organs such as the spleen, stomach, pancreas, gallbladder, liver, lungs, and heart inside the ventral cavity of the human body

The ventral cavity is subdivided into the thoracic and abdominopelvic cavities.

- The **thoracic cavity** fills the chest and is subdivided into two pleural cavities and the pericardial cavity. The pleural cavities hold the lungs, and the pericardial cavity holds the heart.
- The **abdominopelvic cavity** fills the lower half of the trunk and is subdivided into the abdominal cavity and the pelvic cavity. The abdominal cavity holds digestive organs and the kidneys, and the pelvic cavity holds reproductive organs and organs of excretion.

DORSAL CAVITY

The **dorsal cavity** is at the posterior, or back, of the body, including both the head and the back of the trunk. The dorsal cavity is subdivided into the cranial and spinal cavities.

- The **cranial cavity** fills most of the upper part of the skull and contains the brain.
- The **spinal cavity** is a very long, narrow cavity inside the vertebral column. It runs the length of the trunk and contains the spinal cord.

The brain and spinal cord are protected by the bones of the skull and the vertebrae of the spine. They are further protected by the **meninges,** a three-layer membrane that encloses the brain and spinal cord. A thin layer of **cerebrospinal fluid** is maintained between two of the meningeal layers. This clear fluid is produced by the brain, and it provides extra protection and cushioning for the brain and spinal cord.

FEATURE: MY HUMAN BODY

The meninges membranes that protect the brain and spinal cord inside their cavities may become inflamed, generally due to a bacterial or viral infection. This condition is called meningitis. Meningitis can lead to serious long-term consequences such as deafness, epilepsy, or cognitive deficits, especially if not treated quickly. Meningitis can also rapidly become life-threatening, so it is classified as a medical emergency.

Learning the symptoms of meningitis may help you or a loved one get prompt medical attention if you ever develop the disease. Common symptoms include fever, headache, and neck stiffness. Other symptoms may include confusion or altered consciousness, vomiting, and an inability to tolerate light or loud noises. Young children often exhibit less specific symptoms, such as irritability, drowsiness, or poor feeding.

Meningitis is diagnosed with a lumbar puncture (commonly known as a "spinal tap"), in which a needle is inserted into the spinal canal to collect a sample of cerebrospinal fluid. The fluid is analyzed for the presence of pathogens in a medical lab. If meningitis is diagnosed, treatment consists of antibiotics and sometimes antiviral drugs. Corticosteroids may also be administered to reduce inflammation and the risk of complications such as brain damage. Supportive measures such as IV fluids may also be provided.

Some types of meningitis can be prevented with a vaccine. Ask your health care professional whether you have had the vaccine or should get it. Giving antibiotics to people who have had significant exposure to certain types of meningitis may reduce their risk of developing the disease. If someone you know is diagnosed with meningitis, see your doctor for advice if you are concerned about contracting the disease.

REVIEW

1. What is a body cavity?
2. Compare and contrast ventral and dorsal body cavities.
3. Identify the subdivisions of the ventral cavity and the organs each contains.
4. Describe the subdivisions of the dorsal cavity and its contents.
5. Identify and describe all the tissues that protect the brain and spinal cord.
6. What do you think might happen if fluid were to build up excessively in one of the body cavities?
7. Explain why a woman's body can accommodate a full-term fetus during pregnancy, without damage to her internal organs.
8. Which body cavity does the needle enter in a lumbar puncture?
9. What are the names given to the three body cavity divisions where the heart is located?
10. What are the names given to the three body cavity divisions where the kidneys are located?
11. *True or False.* The stomach is located in the dorsal cavity.
12. *True or False.* A body cavity must open to the outside world.
13. *True or False.* The vertebral column surrounds the spinal cavity.
14. The _____ cavity is directly below the thoracic cavity.
15. What is the name of the fluid that protects the brain and spinal cord?

    A. meningeal
    B. cerebrospinal
    C. lumbar
    D. cranial

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4.6: INTERACTION OF ORGAN SYSTEMS

TEAMWORK

Every player on a softball team has a special job to perform. Each of the orange team's players in Figure **4.6.1** has his part of the infield or outfield covered if the ball comes his way. Other players on the orange team cover other parts of the field or pitch or catch the ball. Playing softball clearly requires teamwork. The human body is like a softball team in that regard. All the organ systems of the human body must work together as a team to keep the body alive and well. Teamwork within the body begins with communication.



Figure **4.6.1**: Softball

COMMUNICATION AMONG ORGAN SYSTEMS

Communication among organ systems is vital if they are to work together as a team. They must be able to respond to each other and change their responses as needed to keep the body in balance. Communication among organ systems is controlled mainly by the autonomic nervous system and the endocrine system.

The autonomic nervous system is the part of the nervous system that controls involuntary functions. For example, the autonomic nervous system controls heart rate, blood flow, and digestion. You don't have to tell your heart to beat faster or to consciously squeeze muscles to push food through the digestive system. In fact, you don't have to even think about these functions at all. The autonomic nervous system orchestrates all the signals needed to control them. It sends messages between parts of the nervous system and between the nervous system and other organ systems via chemical messengers called neurotransmitters.

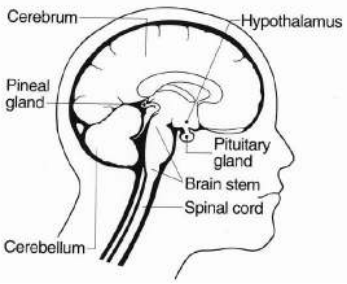


Figure **4.6.2**: The figure illustrates the hypothalamus, pituitary gland, brain stem, spinal cord, cerebellum, pineal gland, and cerebrum.

The endocrine system is the system of glands that secrete hormones directly into the bloodstream. Once in the blood, endocrine hormones circulate to cells everywhere in the body. The endocrine system is under the control of the hypothalamus, a part of the brain. The hypothalamus secretes hormones that travel directly to cells of the pituitary gland, which is located beneath it. The pituitary gland is the master gland of the endocrine system. Most of its hormones either turn on or turn off other endocrine glands. For example, if the pituitary gland secretes thyroid stimulating hormone, the hormone travels through the circulation to the thyroid gland, which is stimulated to secrete thyroid hormone. Thyroid hormone then travels to cells throughout the body, where it increases their metabolism.

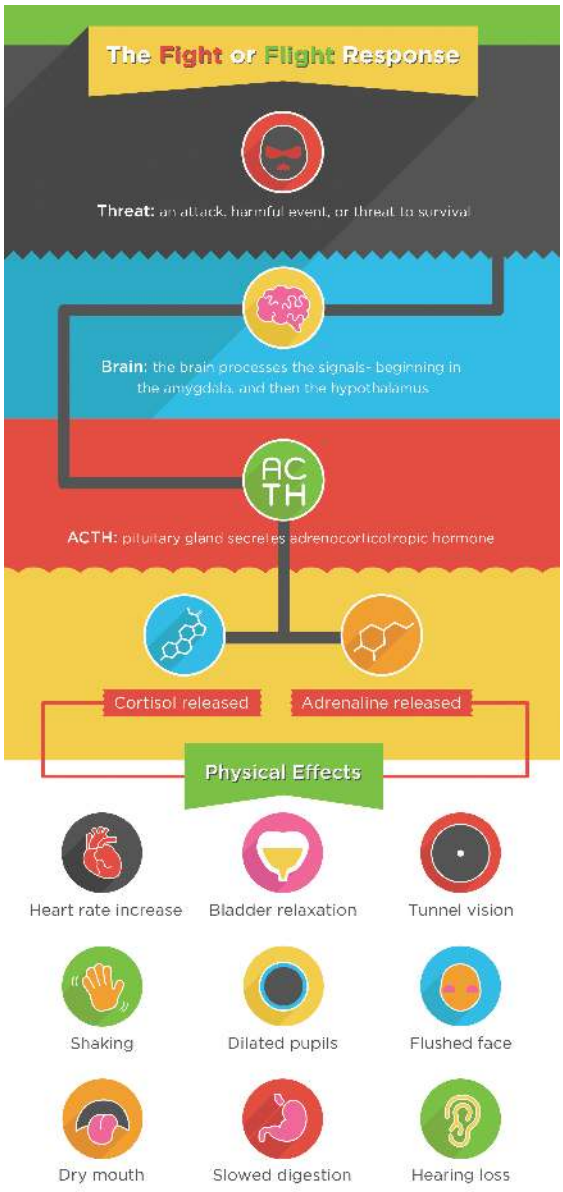


Figure **4.6.3**: The image shows a concept map of how the fight-or-flight response occurs. A treat (an attack, harmful event, or threat to survive) leads to the brain processing the signals - beginning in the amygdala, and then the hypothalamus. ACTH (adrenocorticotropic hormone) is released by the pituitary gland. This causes cortisol and adrenaline to be released. The physical effects include heart rate increase, bladder relaxation, tunnel vision, shaking, dilated pupils, flushed face, dry mouth, slowed digestion, and hearing loss.

EXAMPLES OF ORGAN SYSTEM INTERACTIONS

An increase in cellular metabolism requires more cellular respiration. Cellular respiration is a good example of organ system interactions because it is a basic life process that occurs in all living cells.

CELLULAR RESPIRATION

Cellular respiration is the intracellular process that breaks down glucose with oxygen to produce carbon dioxide and energy in the form of ATP molecules. It is the process by which cells obtain usable energy to power other cellular processes. Which organ systems are involved in cellular respiration? The glucose needed for cellular respiration comes from the digestive system via the cardiovascular system. The oxygen needed for cellular respiration comes from the respiratory system also via the cardiovascular system. The carbon dioxide produced in cellular respiration leaves the body by the opposite route. In short, cellular respiration requires at a minimum the digestive, cardiovascular, and respiratory systems.

FIGHT-OR-FLIGHT RESPONSE

The well-known **fight-or-flight response** is a good example of how the nervous and endocrine systems control other organ system responses. The fight-or-flight response begins when the nervous system perceives sudden danger, as shown in Figure **4.6.2**. The brain sends a message to the endocrine system (via the pituitary gland) for the adrenal glands to secrete their hormones cortisol and adrenaline. These hormones flood the circulation and affect other organ systems throughout the body, including the cardiovascular, urinary, sensory, and digestive systems. Specific responses include increased heart rate, bladder relaxation, tunnel vision, and a shunting of blood away from the digestive system and toward the muscles, brain, and other vital organs needed to fight or flee.

DIGESTING FOOD

Digesting food requires teamwork between the digestive system and several other organ systems, including the nervous, cardiovascular, and muscular systems. When you eat a meal, the organs of the digestive system need more blood to perform their digestive functions. Food entering the digestive systems causes nerve impulses to be sent to the brain; in response, the brain sends messages to the cardiovascular system to increase heart rate and dilate blood vessels in the digestive organs. Food passes through the organs of the digestive tract by rhythmic contractions of smooth muscles in the walls of the organs, so the muscular system is also needed for digestion. After food is digested, nutrients from the food are absorbed into the blood of the vessels lining the small intestine. Any remaining food waste is excreted through the large intestine.

PLAYING SOFTBALL

The men playing softball in Figure **4.6.1** are using multiple organ systems in this voluntary activity. Their nervous systems are focused on observing and preparing to respond to the next play. Their other systems are being controlled by the autonomic nervous system. Organ systems they are using include the muscular, skeletal, respiratory, and cardiovascular systems. Can you explain how each of these organ systems is involved in playing softball?

FEATURE: RELIABLE SOURCES

Teamwork among organ systems allows the human organism to work like a finely tuned machine. Or at least it does until one of the organ systems fails. When that happens, other organ systems interacting in the same overall process will also be affected. This is especially likely if the system affected plays a controlling role in the process. An example is type 1 diabetes.

This disorder occurs when the pancreas does not secrete the endocrine hormone insulin. Insulin normally is secreted in response to an increasing level of glucose in the blood, and it brings the level of glucose back to normal by stimulating body cells to take up insulin from the blood.

Learn more about type 1 diabetes. Use several reliable Internet sources to answer the following questions:

1. What causes the endocrine system to fail to produce insulin in type 1 diabetes?
2. Which organ systems are affected by high blood glucose levels if type 1 diabetes is not controlled? What are some of the specific effects?
3. How can blood glucose levels be controlled in patients with type 1 diabetes?

REVIEW

1. What is the autonomic nervous system?
2. How do the autonomic nervous system and endocrine system communicate with other organ systems so the systems can interact?
3. Explain how the brain communicates with the endocrine system.
4. What is the role of the pituitary gland in the endocrine system?
5. Identify organ systems that play a role in cellular respiration.
6. How does the hormone adrenaline prepare the body to fight or flee? What specific physiological changes does it bring about?
7. Explain the role of the muscular system in the digestion of food.
8. Describe how three different organ systems are involved when a player makes a particular play in softball, such as catching a fly ball.
9. *True or False*. The autonomic nervous system controls conscious movements.
10. *True or False*. Hormones travel throughout the body.
11. *True or False*. The pituitary gland directly secretes thyroid hormone.
12. What are two types of molecules that the body uses to communicate between organ systems?
13. Explain why hormones can have such a wide variety of effects on the body.
14. Heart rate can be affected by:
    A. Hormones
    B. Neurotransmitters
    C. The fight-or-flight response
    D. All of the above
15. Which gland secretes the hormone cortisol?

EXPLORE MORE

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4.7: HOMEOSTASIS AND FEEDBACK

STEADY AS SHE GOES

This device looks simple, but it controls a complex system that keeps a home at a steady temperature. The device is an old-fashioned thermostat. The dial shows the current temperature in the room and also allows the occupant to set the thermostat to the desired temperature. A thermostat is a commonly cited model of how living systems, including the human body, maintain a steady state called homeostasis.



Figure **4.7.1**: Thermostat for a building

WHAT IS HOMEOSTASIS?

Homeostasis is the condition in which a system such as the human body is maintained in a more-or-less steady state. It is the job of cells, tissues, organs, and organ systems throughout the body to maintain many different variables within narrow ranges that are compatible with life. Keeping a stable internal environment requires continuous monitoring of the internal environment and constantly making adjustments to keep things in balance.

SETPOINT AND NORMAL RANGE

For any given variable, such as body temperature or blood glucose level, there is a particular **setpoint** that is the physiological optimum value. For example, the setpoint for human body temperature is about 37 ºC (98.6 ºF). As the body works to maintain homeostasis for temperature or any other internal variable, the value typically fluctuates around the set point. Such fluctuations are normal as long as they do not become too extreme. The spread of values within which such fluctuations are considered insignificant is called the **normal range**. In the case of body temperature, for example, the normal range for an adult is about 36.5 to 37.5 ºC (97.7 to 99.5 ºF).

MAINTAINING HOMEOSTASIS

Homeostasis is normally maintained in the human body by an extremely complex balancing act. Regardless of the variable being kept within its normal range, maintaining homeostasis requires at least four interacting components: stimulus, sensor, control center, and effector.

1. The **stimulus** is provided by the variable that is being regulated. Generally, the stimulus indicates that the value of the variable has moved away from the set point or has left the normal range.
2. The **sensor** monitors the values of the variable and sends data on it to the control center.
3. The **control center** matches the data with normal values. If the value is not at the set point or is outside the normal range, the control center sends a signal to the effector.
4. The **effector** is an organ, gland, muscle, or other structure that acts on the signal from the control center to move the variable back toward the set point.

Each of these components is illustrated in Figure **4.7.2**. The diagram on the left is a general model showing how the components interact to maintain homeostasis. The stimulus activates the sensor. The sensor activates the control system that regulates the effector. The diagram on the right shows the example of body temperature. From the diagrams, you can see that maintaining homeostasis involves feedback, which is data that feeds back to control a response. High body temperature may stimulate the temperature regulatory center of the brain to activate the sweat glands to bring the body temperature down. When body temperature reaches normal range, it acts as negative feedback to stop the process. Feedback may be negative or positive. All the feedback mechanisms that maintain homeostasis use negative feedback. Biological examples of positive feedback are much less common.

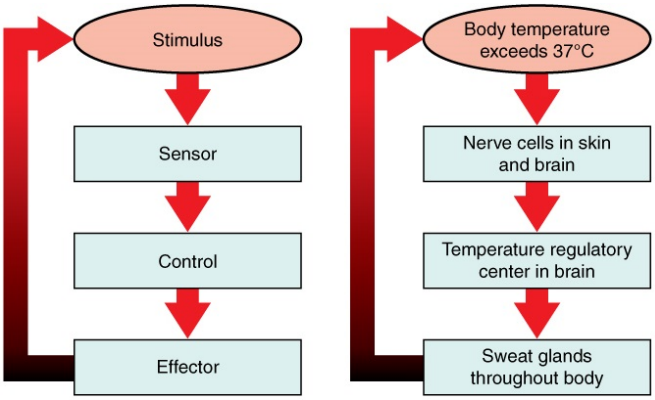


Figure **4.7.2**: Maintaining homeostasis through feedback requires a stimulus, sensor, control center, and effector

NEGATIVE FEEDBACK

In a **negative feedback loop**, feedback serves to reduce an excessive response and keep a variable within the normal range. Examples of processes controlled by negative feedback include body temperature regulation and control of blood glucose.

BODY TEMPERATURE

Body temperature regulation involves negative feedback whether it lowers the temperature or raises it (Figure **4.7.3**).

COOLING DOWN

The human body's temperature regulatory center is the hypothalamus in the brain. When the hypothalamus receives data from sensors in the skin and brain that body temperature is higher than the setpoint, it sets into motion the following responses:

- Blood vessels in the skin dilate (vasodilation) to allow more blood from the warm body core to flow close to the surface of the body, so heat can be radiated into the environment.
- As blood flow to the skin increases, sweat glands in the skin are activated to increase their output of sweat (diaphoresis). When the sweat evaporates from the skin surface into the surrounding air, it takes the heat with it.
- Breathing becomes deeper, and the person may breathe through the mouth instead of the nasal passages. This increases heat loss from the lungs.

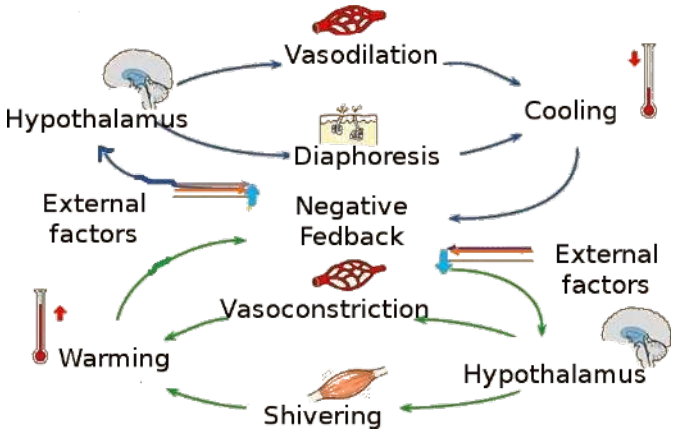


Figure **4.7.3**: The hypothalamus plays a major role in temperature regulation

HEATING UP

When the brain's temperature regulatory center receives data that body temperature is lower than the setpoint, it sets into motion the following responses:

- Blood vessels in the skin contract (vasoconstriction) to prevent blood from flowing close to the surface of the body. This reduces heat loss from the surface.
- As the temperature falls lower, random signals to skeletal muscles are triggered, causing them to contract. This causes shivering, which generates a small amount of heat.
- The thyroid gland may be stimulated by the brain (via the pituitary gland) to secrete more thyroid hormones. This hormone increases metabolic activity and heat production in cells throughout the body.
- The adrenal glands may also be stimulated to secrete the hormone adrenaline. This hormone causes the breakdown of glycogen (the carbohydrate used for energy storage in animals) to glucose, which can be used as an energy source. This catabolic chemical process is exothermic, or heat producing.

BLOOD GLUCOSE

In the control of the blood glucose level, certain endocrine cells in the pancreas called alpha and beta cells, detect the level of glucose in the blood. Then they respond appropriately to keep the level of blood glucose within the normal range.

- If the blood glucose level rises above the normal range, pancreatic beta cells release the hormone insulin into the bloodstream. Insulin signals cells to take up the excess glucose from the blood until the level of blood glucose decreases to the normal range.
- If the blood glucose level falls below the normal range, pancreatic alpha cells release the hormone **glucagon** into the bloodstream. Glucagon signals cells to break down stored glycogen to glucose and release the glucose into the blood until the level of blood glucose increases to the normal range.

POSITIVE FEEDBACK

In a **positive feedback loop**, feedback serves to intensify a response until an endpoint is reached. Examples of processes controlled by positive feedback in the human body include blood clotting and childbirth.

BLOOD CLOTTING

When a wound causes bleeding, the body responds with a positive feedback loop to clot the blood and stop blood loss. Substances released by the injured blood vessel wall begin the process of blood clotting. Platelets in the blood start to cling to the injured site and release chemicals that attract additional platelets. As the platelets continue to amass, more of the chemicals are released and more platelets are attracted to the site of the clot. The positive feedback accelerates the process of clotting until the clot is large enough to stop the bleeding.

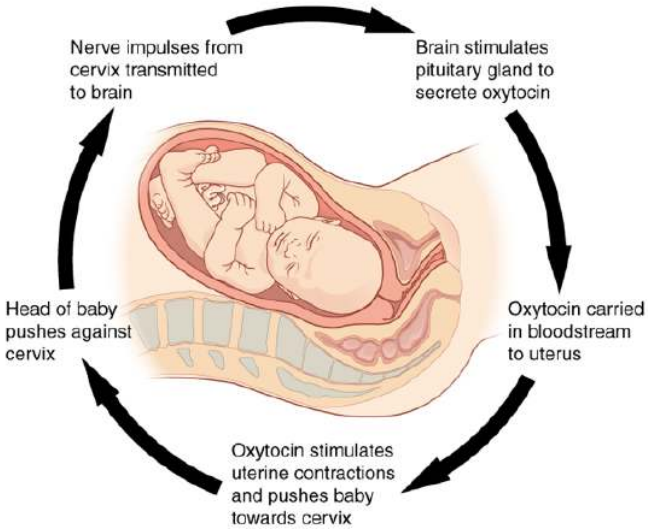


Figure **4.7.4**: Normal childbirth is driven by a positive feedback loop. Positive feedback causes an increasing deviation from the normal state to a fixed endpoint rather than a return to a normal set point as in homeostasis

CHILDBIRTH

Figure **4.7.4** shows the positive feedback loop that controls childbirth. The process normally begins when the head of the infant pushes against the cervix. This stimulates nerve impulses, which travel from the cervix to the hypothalamus in the brain. In response, the hypothalamus sends the hormone **oxytocin** to the pituitary gland, which secretes it into the bloodstream so it can be carried to the uterus. Oxytocin stimulates uterine contractions, which push the baby harder against the cervix. In response, the cervix starts to dilate in preparation for the passage of the baby. This cycle of positive feedback continues, with increasing levels of oxytocin, stronger uterine contractions, and wider dilation of the cervix until the baby is pushed through the birth canal and out of the body. At that point, the cervix is no longer stimulated to send nerve impulses to the brain, and the entire process stops.

WHEN HOMEOSTASIS FAILS

Homeostatic mechanisms work continuously to maintain stable conditions in the human body. Sometimes, however, the mechanisms fail. When they do, **homeostatic imbalance** may result, in which cells may not get everything they need or toxic wastes may accumulate in the body. If homeostasis is not restored, the imbalance may lead to disease or even death. Diabetes is an example of a disease caused by homeostatic imbalance. In the case of diabetes, blood glucose levels are no longer regulated and may be dangerously high. Medical intervention can help restore homeostasis and possibly prevent permanent damage to the organism.

FEATURE: MY HUMAN BODY

Diabetes is diagnosed in people who have abnormally high levels of blood glucose after fasting for at least 12 hours. A fasting level of blood glucose below 100 is normal. A level between 100 and 125 places you in the pre-diabetes category, and a level higher than 125 results in a diagnosis of diabetes.

Of the two types of diabetes, type 2 diabetes is the most common, accounting for about 90 percent of all cases of diabetes in the United States. Type 2 diabetes typically starts after the age of 40. However, because of the dramatic increase in recent decades in obesity in younger people, the age at which type 2 diabetes is diagnosed has fallen. Even children are now being diagnosed with type 2 diabetes. Today, about 30 million Americans have type 2 diabetes, and another 90 million have pre-diabetes.

You are likely to have your blood glucose level tested during a routine medical exam. If your blood glucose level indicates that you have diabetes, it may come as a shock to you because you may not have any symptoms of the disease. You are not alone, because as many as one in four diabetics does not know they have the disease. Once the diagnosis of diabetes sinks in, you may be devastated by the news. Diabetes can lead to heart attacks, strokes, blindness, kidney failure, and loss of toes or feet. The risk of death in adults with diabetes is 50 percent greater than it is in adults without diabetes, and diabetes is the seventh leading cause of death in adults. In addition, controlling diabetes usually requires frequent blood glucose testing, watching what and when you eat and taking medications or even insulin injections. All of this may seem overwhelming.

The good news is that changing your lifestyle may stop the progression of type 2 diabetes or even reverse it. Here's how:

- Lose weight. Any weight loss is beneficial. Losing as little as seven percent of your weight may be all that is needed to stop diabetes in its tracks. It is especially important to eliminate excess weight around your waist.
- Exercise regularly. You should try to exercise five days a week for at least 30 minutes. This will not only lower your blood sugar and help your insulin work better; it will also lower your blood pressure and improve your heart health. Another bonus of exercise is that it will help you lose weight by increasing your basal metabolic rate.
- Adopt a healthy diet. Decrease your consumption of refined carbohydrates such as sweets and sugary drinks. Increase your intake of fiber-rich foods such as fruits, vegetables, and whole grains. About a quarter of each meal should consist of high-protein foods, such as fish, chicken, dairy products, legumes, or nuts.
- Control stress. Stress can increase your blood glucose and also raise your blood pressure and risk of heart disease. When you feel stressed out, do breathing exercises or take a brisk walk or jog. Also, try to replace stressful thoughts with more calming ones.
- Establish a support system. Enlist the help and support of loved ones as well as medical professionals such as a nutritionist and diabetes educator. Having a support system will help ensure that you are on the path to wellness and that you can stick to your plan.

REVIEW

1. What is homeostasis?
2. Define the setpoint and normal range for physiological measures.
3. Identify and define the four interacting components that maintain homeostasis in feedback loops.
4. Compare and contrast negative and positive feedback loops.
5. Explain how negative feedback controls body temperature.
6. Give two examples of physiological processes that are controlled by positive feedback loops.
7. A negative feedback loop:
   A. brings a variable's level back to a normal range
   B. can lower, but not raise, body temperature
   C. is the type of feedback involved in blood clotting
   D. A and B
8. During breastfeeding, the stimulus of the baby sucking on the nipple increases the amount of milk produced by the mother. The more sucking, the more milk is usually produced.

A. Is this an example of negative or positive feedback? Explain your answer.
B. What do you think might be the evolutionary benefit of the milk production regulation mechanism described in part a?

9. Explain why homeostasis is regulated by negative feedback loops, rather than positive feedback loops.
10. A setpoint is usually:
    A. the top of a normal range
    B. the bottom of a normal range
    C. in the middle of a normal range
    D. the point at which changes can no longer occur
11. The level of a sex hormone, testosterone (T), is controlled by negative feedback. Another hormone, gonadotropin-releasing hormone (GnRH), is released by the hypothalamus of the brain, which triggers the pituitary gland to release luteinizing hormone (LH). LH stimulates the gonads to produce T. When there is too much T in the bloodstream, it feeds back on the hypothalamus, causing it to produce less GnRH. While this does not describe all the feedback loops involved in regulating T, answer the following questions about this particular feedback loop.
    A. What is the stimulus in this system? Explain your answer.
    B. What is the control center in this system? Explain your answer.
    C. What is the pituitary considered in this system: stimulus, sensor, control center, or effector? Explain your answer.

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4.8: CASE STUDY CONCLUSION- PRESSURE AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: UNDER PRESSURE

As you learned in this chapter, the human body consists of many complex systems that normally work together efficiently like a well-oiled machine to carry out life's functions. For example, Figure 4.8.1 illustrates how the brain and spinal cord are protected by layers of membrane called meninges and fluid that flows between the meninges and in spaces called ventricles inside the brain. This fluid is called **cerebrospinal fluid (CSF)** and as you have learned, one of its important functions is to cushion and protect the brain and spinal cord, which make up most of the central nervous system (CNS). CSF additionally circulates nutrients and removes waste products from the CNS. CSF is produced continually in the ventricles, circulates throughout the CNS, and then is reabsorbed by the bloodstream. If too much CSF is produced, its flow blocked, or if not enough is reabsorbed, the system becomes out of balance, and CSF can build up in the ventricles. This causes an enlargement of the ventricles called hydrocephalus that can put pressure on the brain, resulting in the types of neurological problems that former professional football player, Dayo, described at the beginning of this chapter, is suffering from.

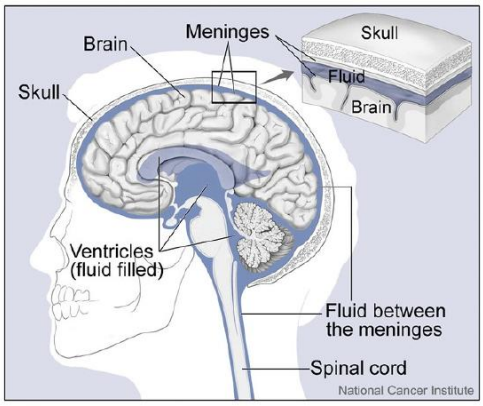


Figure 4.8.1: The brain and nearby structures (including the skull, meninges, ventricles, and spinal cord). An enlarged inset shows the skull, fluid, and brain.

Recall that Dayo's symptoms included loss of bladder control, memory loss, and difficulty walking. The cause of their symptoms was not immediately clear, although their doctors suspected that it related to the nervous system since the nervous system acts as the control center of the body, controlling and regulating many other organ systems. Dayo's memory loss directly implicated the involvement of the brain, since that is the site of thoughts and memory. The urinary system is also controlled in part by the nervous system, and the inability to hold urine appropriately can be a sign of a neurological issue. Dayo's trouble walking involved the muscular system, which works alongside the skeletal system to enable movement of the limbs. In turn, the contraction of muscles is regulated by the nervous system. You can see why a problem in the nervous system can cause a variety of different symptoms by affecting multiple organ systems in the human body.

To try to find the exact cause of Dayo's symptoms, their doctors performed a lumbar puncture, or spinal tap, which is the removal of some CSF through a needle inserted into the lower part of the spinal canal. Doctors then analyzed Dayo's CSF for the presence of pathogens such as bacteria to determine whether an infection was the cause of their neurological symptoms. When no evidence of infection was found, Doctors used an MRI to observe the structures of Dayo's brain. This is when Doctors discovered Dayo's enlarged ventricles, which are a hallmark of hydrocephalus.

To treat Dayo's hydrocephalus, a surgeon implanted a device called a shunt in Dayo's brain to remove the excess fluid (Figure 4.8.2). One side of the shunt consists of a small tube, called a **catheter**, which was inserted into Dayo's ventricles. Excess CSF is then drained through a one-way valve to the other end of the shunt, which was threaded under their skin to their abdominal cavity, where the CSF is released and can be reabsorbed by the bloodstream.

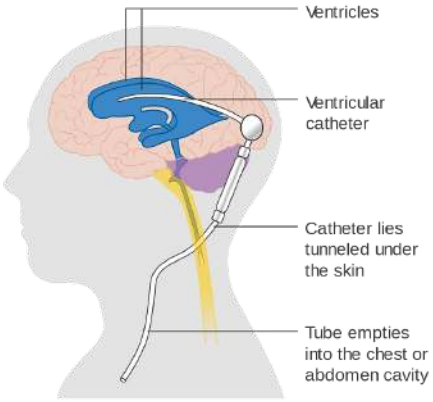


Figure 4.8.2: Tube empties CSF into the abdominal cavity.

Implantation of a shunt is the most common way to treat hydrocephalus, and for some people, it can allow them to recover almost completely. However, there can be complications associated with a brain shunt. The shunt can have mechanical problems or cause an infection. Also, the rate of draining must be carefully monitored and adjusted to balance the rate of removal of CSF with the rate of its production. If it is drained too fast, it is called overdraining, and if it is drained too slowly, it is called **underdraining**. In the case of underdraining, the pressure on the brain and associated neurological symptoms will persist. In the case of overdraining, the ventricles can collapse, which can cause serious problems such as the tearing of blood vessels and hemorrhaging. To avoid these problems, some shunts have an adjustable pressure valve where the rate of draining can be adjusted by placing a special magnet over the scalp. You can see how the proper balance between CSF production and removal is so critical – both in the causes of hydrocephalus and in its treatment.

In what other ways does your body regulate balance, or maintain a state of homeostasis? In this chapter, you learned about the feedback loops that keep body temperature and blood glucose within normal

ranges. Other important examples of homeostasis in the human body are the regulation of the pH in the blood and the balance of water in the body. You will learn more about homeostasis in different body systems in the coming chapters.

Thanks to Dayo's shunt, their symptoms are starting to improve, but they have not fully recovered. Time may tell whether the removal of the excess CSF from their ventricles will eventually allow them to recover normal functioning or whether permanent damage to their nervous system has already been done. The flow of CSF might seem simple but when it gets out of balance, it can easily wreak havoc on multiple organ systems because of the intricate interconnectedness of the systems within the human "machine."

CHAPTER SUMMARY

This chapter provided an overview of the organization and functioning of the human body. You learned that:

- The human body consists of multiple parts that function together to maintain life. The biology of the human body incorporates the body's structure, or anatomy, and the body's functioning, or physiology.
- The organization of the human body is a hierarchy of increasing size and complexity, starting at the level of atoms and molecules and ending at the level of the entire organism.
- Cells are the level of organization above atoms and molecules, and they are the basic units of structure and function of the human body. Each cell carries out basic life functions as well as other specific roles. Cells of the human body show a lot of variation.
  - Variations in cell function are generally reflected in variations in cell structure.
  - Some cells are unattached to other cells and can move freely; others are attached to each other and cannot move freely. Some cells can divide readily and form new cells; others can divide only under exceptional circumstances. Many cells are specialized to produce and secrete particular substances.
  - All the different cell types within an individual have the same genes. Cells can vary because different genes are expressed depending on the cell type.
  - Many common types of human cells consist of several subtypes of cells, each of which has a special structure and function. For example, subtypes of bone cells include osteocytes, osteoblasts, osteogenic cells, and osteoclasts.
- A tissue is a group of connected cells that have a similar function. There are four basic types of human tissues that make up all the organs of the human body: epithelial, muscle, nervous, and connective tissues.
  - Connective tissues, such as bone and blood, are made up of cells that are separated by non-living material, called the extracellular matrix.
  - Epithelial tissues, such as skin and mucous membranes, protect the body and its internal organs and secrete or absorb substances.
  - Muscle tissues are made up of cells that have the unique ability to contract. They include skeletal, smooth, and cardiac muscle tissues.
  - Nervous tissues are made up of neurons, which transmit electrical messages, and glial cells of various types, which play supporting roles. Types of nervous tissues include gray matter, white matter, nerves, and ganglia.
- An organ is a structure that consists of two or more types of tissues that work together to do the same job. Examples include the brain and heart.
  - Many organs are composed of a major tissue that performs the organ's main function, as well as other tissues that play supporting roles.
  - The human body contains five organs that are considered vital for survival. They are the heart, brain, kidneys, liver, and lungs. If any of these five organs stops functioning, the death of the organism is imminent without medical intervention.
- An organ system is a group of organs that work together to carry out a complex overall function. For example, the skeletal system provides structure to the body and protects internal organs.
  - There are 11 major organ systems in the human organism. They are the integumentary, skeletal, muscular, nervous, endocrine, cardiovascular, lymphatic, respiratory, digestive, urinary, and reproductive systems. Only the reproductive system varies significantly between males and females.
- The human body is divided into a number of body cavities. A body cavity is a fluid-filled space in the body that holds and protects internal organs. The two largest human body cavities are the ventral cavity and the dorsal cavity.
  - The ventral cavity is at the anterior, or front, of the trunk. It is subdivided into the thoracic cavity and abdominopelvic cavity.
  - The dorsal cavity is at the posterior, or back, of the body, and includes the head and the back of the trunk. It is subdivided into the cranial cavity and spinal cavity.
- Organ systems of the human body must work together to keep the body alive and functioning normally. This requires communication among organ systems. This is controlled by the autonomic nervous system and endocrine system. The autonomic nervous controls involuntary body functions, such as heart rate and digestion. The endocrine system secretes hormones into the blood that travel to body cells and influence their activities.
  - Cellular respiration is a good example of organ system interactions because it is a basic life process that occurs in all living cells. It is the intracellular process that breaks down glucose with oxygen to produce carbon dioxide and energy. Cellular respiration requires the interaction of the digestive, cardiovascular, and respiratory systems.
  - The fight-or-flight response is a good example of how the nervous and endocrine systems control other organ system responses. It is triggered by a message from the brain to the endocrine system and prepares the body for flight or a fight.

Many organ systems are stimulated to respond, including the cardiovascular, respiratory, and digestive systems.
    - Digesting food requires teamwork between the digestive system and several other organ systems, including the nervous, cardiovascular, and muscular systems.
    - Playing softball or doing other voluntary physical activities may involve the interaction of nervous, muscular, skeletal, respiratory, and cardiovascular systems.
- Homeostasis is the condition in which a system such as the human body is maintained in a more-or-less steady state. It is the job of cells, tissues, organs, and organ systems throughout the body to maintain homeostasis.
    - For any given variable, such as body temperature, there is a particular set point that is the physiological optimum value. The spread of values around the setpoint that is considered insignificant is called the normal range.
    - Homeostasis is generally maintained by a negative feedback loop that includes a stimulus, sensor, control center, and effector. Negative feedback serves to reduce an excessive response and to keep a variable within the normal range. Negative feedback loops control body temperature and blood glucose level.
    - Sometimes homeostatic mechanisms fail, resulting in homeostatic imbalance. Diabetes is an example of a disease caused by homeostatic imbalance. Aging can bring about a reduction in the efficiency of the body's control system, making the elderly more susceptible to disease.
- Positive feedback loops are not common in biological systems. Positive feedback serves to intensify a response until an endpoint is reached. Positive feedback loops control blood clotting and childbirth.

The severe and broad impact of hydrocephalus on the body's systems highlights the importance of the nervous system and its role as the master control system of the body. In the next chapter, you will learn much more about the structures and functioning of this fascinating and important system.

CHAPTER SUMMARY REVIEW

1. Compare and contrast tissues and organs.
2. Osteocyte cells are part of which type of tissue and organ system?
3. Adipose tissue, or body fat, is the same general type of tissue as:
    A. mucous membranes
    B. gray matter
    C. skin
    D. blood
4. Which type of tissue lines the inner and outer surfaces of the body?
5. *True or False.* The extracellular matrix that surrounds cells is always solid.
6. *True or False.* Skin is an organ.
7. What is a vital organ? What happens if a vital organ stops working?
8. Name three organ systems that transport or remove wastes from the body.
9. Name two types of tissue in the digestive system.
10. For each of the following body functions, choose the organ system that is most associated with the function. Organ systems: integumentary; skeletal; muscular; nervous; endocrine; cardiovascular; lymphatic; respiratory; digestive; urinary; reproductive
    A. Processes sensory information
    B. Secretes hormones
    C. Releases carbon dioxide from the body to the outside world
    D. Produces gametes
    E. Controls water balance in the body
11. The spleen is part of which organ system?
    A. Digestive
    B. Lymphatic
    C. Integumentary
    D. Urinary
12. Describe one way in which the integumentary and cardiovascular systems work together to regulate homeostasis in the human body.
13. Name the two largest body cavities in humans and describe their general locations.
14. What are the names given to the three body cavity divisions where the reproductive organs are located?
15. *True or False.* There are two pleural cavities.
16. *True or False.* Body cavities are filled with air.
17. The pituitary gland is in which organ system? Describe how the pituitary gland increases metabolism.
18. When the level of thyroid hormone in the body gets too high, it acts on other cells to reduce the production of more thyroid hormone. What type of feedback loop does this represent?
19. Hypothetical organ A is the control center in a feedback loop that helps maintain homeostasis. It secretes molecule A1 which reaches organ B, causing organ B to secrete molecule B1. B1 negatively feeds back onto organ A, reducing the production of A1 when the level of B1 gets too high.
    A. What is the stimulus in this feedback loop?
    B. If the level of B1 falls significantly below the setpoint, what do you think happens to the production of A1? Why?
    C. What is the effector in this feedback loop?
    D. If organs A and B are part of the endocrine system, what type of molecules do you think A1 and B1 are likely to be?
20. What are the two main systems that allow various organ systems to communicate with each other?
21. The hypothalamus is part of the:
    A. spinal cord
    B. thoracic cavity
    C. kidneys
    D. brain

22. What are two functions of the hypothalamus that you learned about in this chapter?

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CHAPTER OVERVIEW

5: CARDIOVASCULAR SYSTEM

This chapter provides a detailed description of the heart, blood vessels, and blood. It explains how they function together to transport substances throughout the body and maintain homeostasis. The chapter also describes several diseases of the cardiovascular system and lifestyle choices that can help prevent most of them.

5.1: Case Study- Your Body's Transportation System

5.2: Introduction to the Cardiovascular System

5.3: Heart

5.4: Blood Vessels

5.5: Blood

5.6: Blood Types

5.7: Cardiovascular Disease

5.8: Case Study Conclusion- Flight and Chapter Summary

Thumbnail: Flow of blood through the cardiac chambers. (Public Domain; Josinho8).

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5.1: CASE STUDY- YOUR BODY'S TRANSPORTATION SYSTEM

CASE STUDY: FLIGHT RISK

Nineteen-year-old Antônio is about to take his first plane flight. Shortly after he boards the plane and sits down, a man in his late sixties sits next to him in the aisle seat. About half an hour after the plane takes off, the pilot announces that she is turning the seat belt light off and that "it is now safe to move about the cabin."



Figure **5.1.1**: Airplane aisle

The man in the aisle seat, who has introduced himself to Antônio as Ahaya, immediately unbuckles his seat belt and paces up and down the aisle a few times before returning to his seat. After about forty-five minutes, Ahaya gets up again, walks some more, then sits back down and does some foot and leg exercises. After the third time, Ahaya gets up and paces the aisles, Antônio asks him whether he is walking so much to accumulate steps on a pedometer or fitness tracking device. Ahaya laughs and says no, he is trying to do something even more important for his health—prevent a blood clot from forming in his legs.

Ahaya explains that he has a chronic condition called heart failure. Although it sounds scary, his condition is currently well-managed and he is able to lead a relatively normal lifestyle. However, it does put him at risk of developing other serious health conditions such as deep vein thrombosis (DVT), which is when a blood clot occurs in the deep veins, usually in the legs. Air travel, or other situations where a person has to sit for a long period of time, increases the risk of DVT. Ahaya's doctor said that he was healthy enough to fly, but that he should walk frequently and do leg exercises to help avoid a blood clot.

As you read this chapter, you will learn about the heart, blood vessels, and blood that make up the cardiovascular system, as well as disorders of the cardiovascular system such as heart failure. At the end of the chapter, you will learn more about why DVT occurs, why Ahaya has to take extra precautions when he flies, and what can be done to lower the risk of DVT and its potentially deadly consequences.

CHAPTER OVERVIEW: CARDIOVASCULAR SYSTEM

In this chapter, you will learn about the cardiovascular system, which transports substances throughout the body. Specifically, you will learn about:

- The major components of the cardiovascular system: the heart, blood vessels, and blood.
- The functions of the cardiovascular system, including transporting needed substances such as oxygen and nutrients to the cells of the body and picking up waste products.
- How blood is oxygenated through the pulmonary circulation, which transports blood between the heart and lungs.
- How blood is circulated throughout the body through the systemic circulation.
- The components of blood, including plasma, red blood cells, white blood cells, and platelets, and their specific functions.
- Types of blood vessels, including arteries, veins, and capillaries, and their functions, similarities, and differences.
- The structure of the heart, how it pumps blood, and how contractions of the heart are controlled.
- What blood pressure is and how it is regulated.
- Blood types: A, B, AB, and O
- Blood disorders, including anemia, HIV, and leukemia.
- Cardiovascular diseases including heart attack, stroke, and angina, and the risk factors and precursors, such as high blood pressure and atherosclerosis, which contribute to them.

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

1. What is heart failure? How do you think it increases the risk of DVT?
2. What is a blood clot? What are the possible health consequences of blood clots?
3. Why do you think sitting for long periods of time increases the risk of DVT and why does walking and exercising the legs help reduce this risk?

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5.2: INTRODUCTION TO THE CARDIOVASCULAR SYSTEM

ANT HILL OR PLUMBING SYSTEM?

What do you think Figure **5.2.1** shows? Does it show a maze of underground passageways in an anthill? A network of interconnected pipes in a complex plumbing system? The picture actually shows something that, like ant tunnels and plumbing pipes, functions as a transportation system. It shows a network of blood vessels. Blood vessels are part of the cardiovascular system.

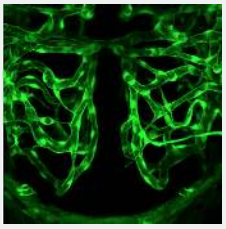


Figure **5.2.1**: Blood Vessels

WHAT IS THE CARDIOVASCULAR SYSTEM?

The **cardiovascular system**, also called the circulatory system, is the organ system that transports materials to and from all the cells of the body. The materials carried by the cardiovascular system include oxygen from the lungs, nutrients from the digestive system, hormones from glands of the endocrine system, and waste materials from cells throughout the body. Transport of these and many other materials is necessary to maintain homeostasis of the body. The main components of the cardiovascular system are the heart, blood vessels, and blood. Each of these components is shown in Figure **5.2.2** and introduced in the text.

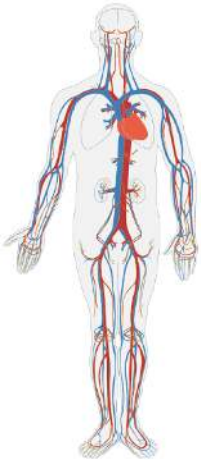


Figure **5.2.2**: This simplified drawing of the cardiovascular system shows its main structures. The heart is shown in the chest in red. Blood vessels called arteries are also shown in red, and blood vessels called veins are shown in blue.

HEART

The heart is a muscular organ in the chest. It consists mainly of cardiac muscle tissue and pumps blood through blood vessels by repeated, rhythmic contractions. As shown in Figure **5.2.3**, the heart has four inner chambers: a right atrium and ventricle and a left atrium and ventricle. On each side of the heart, blood is pumped from the atrium to the ventricle below it and from the ventricle out of the heart. The heart also contains several valves that allow blood to flow only in the proper direction through the heart.

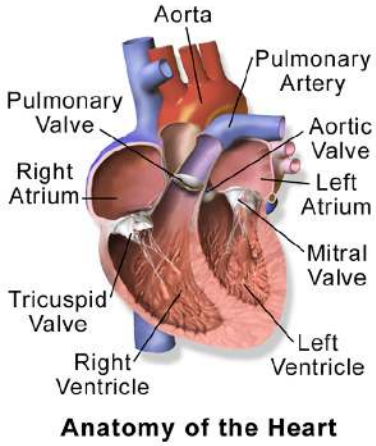


Figure **5.2.3**: The right side of the heart includes the right atrium and right ventricle. The left side includes the left atrium and left ventricle. The valves between the chambers and the major vessels are also visible

Unlike skeletal muscle, cardiac muscle routinely contracts without stimulation by the nervous system. Specialized cardiac muscle cells send out electrical impulses that stimulate the contractions. As a result, the atria and ventricles normally contract with just the right timing to keep blood pumping efficiently through the heart.

BLOOD VESSELS

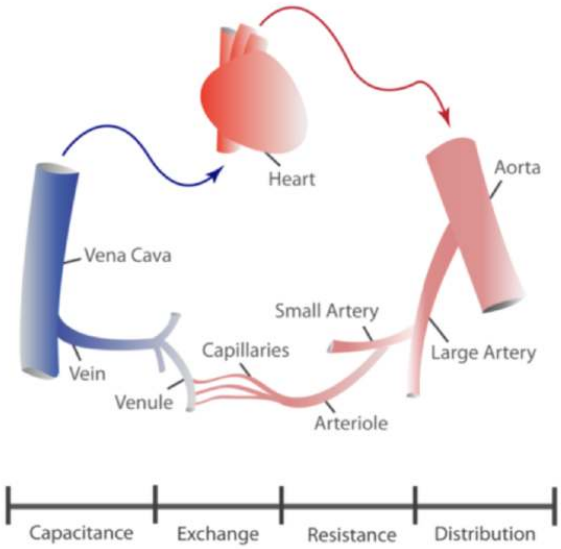


Figure **5.2.4**: This diagram represents the structure and functions of the different types of blood vessels in the cardiovascular system. Arteries carry blood from the heart and to capillaries. Veins carry blood from the capillaries back to the heart.

The blood vessels of the cardiovascular system are like a network of interconnected, one-way roads that range from superhighways to back alleys. Like a network of roads, the blood vessels have the job of allowing the transport of materials from one place to another. There are three major types of blood vessels: arteries, veins, and capillaries. They are illustrated in Figure 5.2.4.

- Arteries are blood vessels that carry blood away from the heart (except for the arteries that actually supply blood to the heart muscle). Most arteries carry oxygen-rich blood, and one of their main functions is distributing oxygen to tissues throughout the body. The smallest arteries are called arterioles.
- Veins are blood vessels that carry blood toward the heart. Most veins carry deoxygenated blood. The smallest veins are called venules.
- Capillaries are the smallest blood vessels. They connect arterioles and venules. As they pass through tissues, they exchange substances including oxygen with cells.

TWO CIRCULATIONS

Cells throughout the body need a constant supply of oxygen. They get oxygen from capillaries in the systemic circulation. The systemic circulation is just one of two interconnected circulations that make up the human cardiovascular system. The other circulation is the pulmonary system. This is where the blood picks up oxygen to carry to cells. It takes blood about 20 seconds to make one complete transit through both circulations.

PULMONARY CIRCULATION

The **pulmonary circulation** involves only the heart and lungs and the major blood vessels that connect them. It is illustrated in Figure 5.2.5. Blood moves through the pulmonary circulation from the heart to the lungs, and back to the heart again, becoming oxygenated in the process. Specifically, the right ventricle of the heart pumps deoxygenated blood into the right and left pulmonary arteries. These arteries carry the blood to the right and left lungs, respectively. Oxygenated blood then returns from the right and left lungs through the two right and two left pulmonary veins. All four pulmonary veins enter the left atrium of the heart.

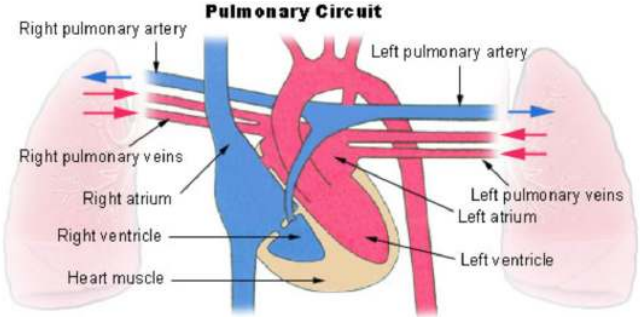


Figure 5.2.5: This diagram shows the heart, lungs, and major vessels that make up the pulmonary circulation. The colored arrows indicate the direction of blood flow. Oxygenated blood (in red) flows from the lungs to the left side of the heart. Deoxygenated blood (in blue) flows from the right side of the heart to the lungs.

What happens to the blood while it is in the lungs? It passes through increasingly smaller arteries and finally through capillary networks surrounding the alveoli (Figure 5.2.6). This is where gas exchange takes place. The deoxygenated blood in the capillaries picks up oxygen from the alveoli and gives up carbon dioxide to the alveoli. As a result, the blood returning to the heart in the pulmonary veins is almost completely saturated with oxygen.

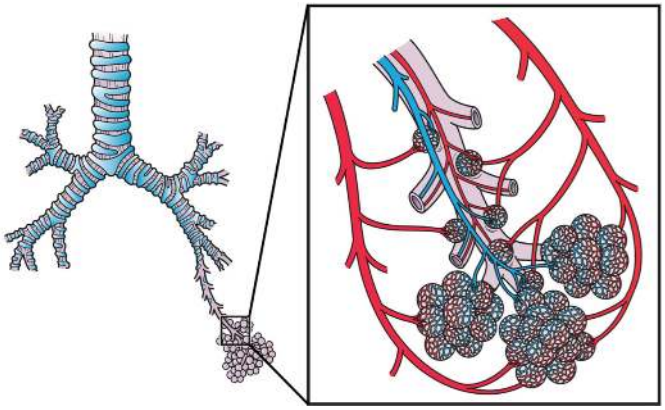


Figure 5.2.6: This diagram illustrates clusters of alveoli in the lungs where gas exchange takes place with blood in capillaries as it passes through the pulmonary circulation.

SYSTEMIC CIRCULATION

The oxygenated blood that enters the left atrium of the heart in the pulmonary circulation then passes into the **systemic circulation.** This is the part of the cardiovascular system that transports blood to and from all of the tissues of the body to provide oxygen and nutrients and pick up wastes. It consists of the heart and blood vessels that supply the metabolic needs of all the cells in the body, including those of the heart and lungs.

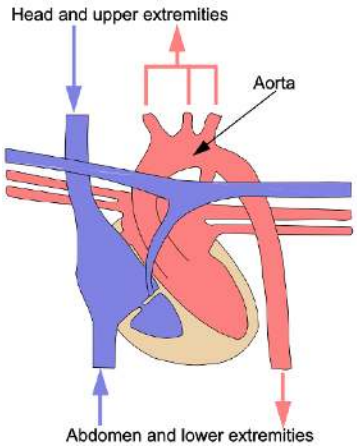


Figure 5.2.7: The systemic circulation includes the aorta (red), which carries oxygenated blood away from the heart to the rest of the body; and the inferior and superior venae cavae (blue), which return deoxygenated blood to the heart from the body. The colored arrows in the diagram indicate the direction of blood flow, red for oxygenated and blue for deoxygenated.

As shown in Figure 5.2.7, in the systemic circulation, the left atrium pumps oxygenated blood to the left ventricle, which pumps the blood directly into the aorta, the body's largest artery. Major arteries branching off the aorta carry the blood to the head and upper

extremities. The aorta continues down through the abdomen and carries blood to the abdomen and lower extremities. The blood then returns to the heart through the network of increasingly larger veins of the systemic circulation. All of the returning blood eventually collects in the superior vena cava (upper body) and inferior vena cava (lower body), which empty directly into the right atrium of the heart.

BLOOD

Blood is a fluid connective tissue that circulates throughout the body in blood vessels by the pumping action of the heart. Blood carries oxygen and nutrients to all the body's cells, and it carries carbon dioxide and other wastes away from the cells to be excreted. Blood also transports many other substances, defends the body against infection, repairs body tissues, and controls the body's pH, among other functions.

The fluid part of blood is called plasma. It is a yellowish, watery liquid that contains many dissolved substances and blood cells. Types of blood cells in plasma include red blood cells, white blood cells, and platelets, all of which are illustrated in Figure **5.2.8** and explained in the text.

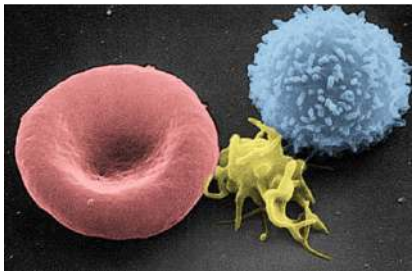


Figure **5.2.8**: The three types of cells in the blood are pictured here: red blood cell (left), platelet (center), and white blood cell (right).

- Red blood cells have the main function of carrying oxygen in the blood. Red blood cells consist mostly of hemoglobin, a protein containing iron that binds with oxygen.
- White blood cells are far fewer in number than red blood cells. They defend the body in various ways. For example, white blood cells called phagocytes swallow and destroy pathogens, dead cells, and other debris in the blood.
- Platelets are cell fragments involved in blood clotting. They stick to tears in blood vessels and to each other, forming a plug at the site of injury. They also release chemicals that are needed for clotting to occur.

REVIEW

1. What is the cardiovascular system? What are its main components?
2. Describe the heart and how it functions.
3. List the three major types of blood vessels and their basic functions.
4. Compare and contrast the pulmonary and systemic circulations.
5. What is blood? What are its chief constituents?
6. *True or False.* The circulatory system brings blood to and from the body, while the cardiovascular system brings blood to and from the lungs only.
7. *True or False.* Arteries carry mainly oxygenated blood.
8. Name three different types of substances that are transported by the cardiovascular system.
9. Describe where and how the pulmonary and systemic circulation systems meet.
10. Which of the following carries blood to the lungs? Choose all that apply.

    A. Left pulmonary artery

    B. Left pulmonary vein

    C. Right pulmonary artery

    D. Right pulmonary vein

11. Put the following structures in order of how blood flows from the heart out to the body and back again.

    capillaries; venules; aorta; veins; arteries

12. Explain why the heart and lungs need blood from the systemic circulation.
13. *Choose one.* Blood vessels carrying deoxygenated blood from the body back to the heart get increasingly (larger/smaller).
14. Blood becomes oxygenated in the lungs through gas exchange into:

    A. Arterioles

    B. Capillaries

    C. Venules

    D. Bronchioles

15. Which type of blood cell carries oxygen?

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5.3: HEART

LUB DUB

Lub dub, lub dub, lub dub... That's how the sound of a beating heart is typically described. In a normal, healthy heart, those are the only two sounds that should be audible when listening to the heart through a stethoscope. If a physician assistant hears something different from the normal lub dub sounds, it's a sign of a possible heart abnormality. What causes the heart to produce the characteristic lub dub sounds? Read on to find out.



Figure **5.3.1**: Listening to a heartbeat

The **heart** is a muscular organ behind the sternum (breastbone), slightly to the left of the center of the chest. A normal adult heart is about the size of a fist. The function of the heart is to pump blood through the blood vessels of the cardiovascular system. The continuous flow of blood through the system is necessary to provide all the cells of the body with oxygen and nutrients and to remove their metabolic wastes.

STRUCTURE OF THE HEART

The heart has a thick muscular wall that consists of several layers of tissue. Internally, the heart is divided into four chambers through which blood flows. Blood flows in just one direction through the chambers due to heart valves.

HEART WALL

As shown in Figure **5.3.2**, the wall of the heart is made up of three layers, called the endocardium, myocardium, and pericardium.

- The endocardium is the innermost layer of the heart wall. It is made up primarily of simple epithelial cells. It covers the heart chambers and valves. A thin layer of connective tissue joins the endocardium to the myocardium.
- The myocardium is the middle and thickest layer of the heart wall. It consists of cardiac muscle surrounded by a framework of collagen. There are two types of cardiac muscle cells in the myocardium: cardiomyocytes, which have the ability to contract easily; and pacemaker cells, which conduct electrical impulses that cause the cardiomyocytes to contract. About 99 percent of cardiac muscle cells are cardiomyocytes, and the remaining 1 percent are pacemaker cells. The myocardium is supplied with blood vessels and nerve fibers via the pericardium.
- The epicardium is the third layer which is a part of the pericardium, a protective sac that encloses and protects the heart. The pericardium consists of two membranes (visceral pericardium called epicardium and parietal pericardium), between which there is a fluid-filled cavity. The fluid helps to cushion the heart and also lubricates its outer surface.

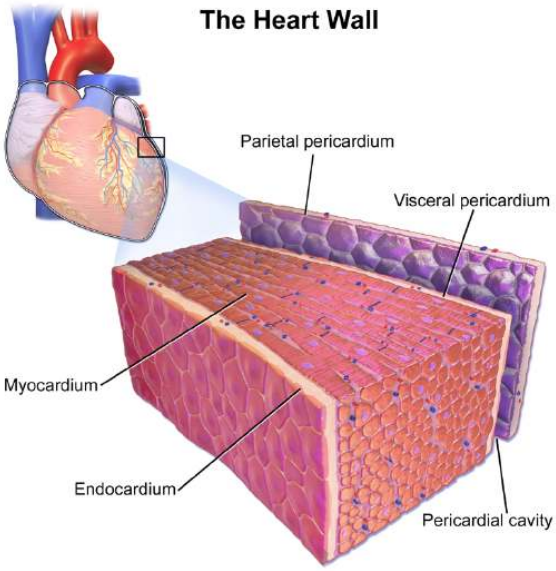


Figure **5.3.2**: The wall of the heart is made up mainly of the myocardium, which consists largely of cardiac muscle.

HEART CHAMBERS

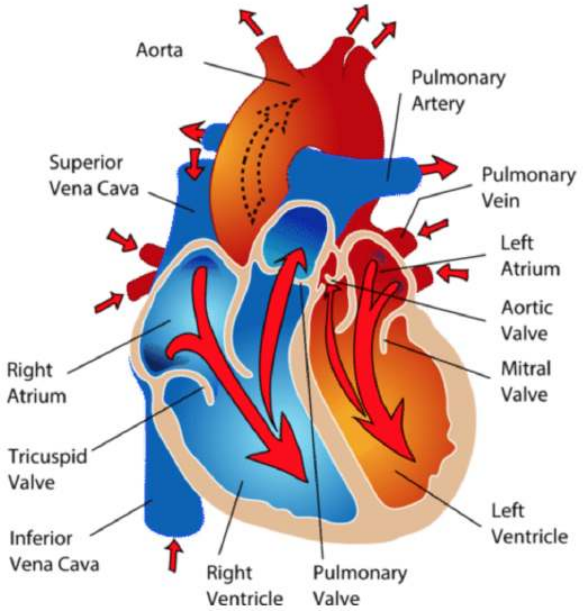


Figure **5.3.3**: This cross-sectional diagram of the heart shows its four chambers and four valves. The red arrows indicate the direction of blood flow through the heart chambers.

As shown in Figure 5.3.3, the four chambers of the heart include two upper chambers called **atria (singular, atrium)** and two lower chambers called ventricles. The atria are also referred to as receiving chambers because blood coming into the heart first enters these two chambers. The right atrium receives blood from the upper and lower body through the superior vena cava and inferior vena cava, respectively; and the left atrium receives blood from the lungs through the pulmonary veins. The **ventricles** are also referred to as discharging chambers because the blood leaving the heart passes out through these two chambers. The right ventricle discharges blood to the lungs through the pulmonary artery, and the left ventricle discharges blood to the rest of the body through the aorta. The four chambers are separated from each other by dense connective tissue consisting mainly of collagen.

HEART VALVES

Figure 5.3.3 also shows the location of the four valves of the heart. The heart valves allow blood to flow from the atria to the ventricles and from the ventricles to the pulmonary artery and aorta. The valves are constructed in such a way that blood can flow through them in only one direction, thus preventing the backflow of blood. The four valves are the:

1. tricuspid valve, which allows blood to flow from the right atrium to the right ventricle.
2. the mitral valve, which allows blood to flow from the left atrium to the left ventricle.
3. pulmonary valve, which allows blood to flow from the right ventricle to the pulmonary artery.
4. the aortic valve, which allows blood to flow from the left ventricle to the aorta.

The tricuspid and mitral valves are also called atrioventricular (or AV) valves because they are found between the atrium and the ventricle. The pulmonary and aortic valves are also called semilunar valves because they are shaped like half-moons.

CORONARY CIRCULATION

The cardiomyocytes of the muscular walls of the heart are very active cells because they are responsible for the constant beating of the heart. These cells need a continuous supply of oxygen and nutrients. The carbon dioxide and waste products they produce also must be continuously removed. The blood vessels that carry blood to and from the heart muscle cells make up the coronary circulation. Note that the blood vessels of the coronary circulation supply heart tissues with blood and are different from the blood vessels that carry blood to and from the chambers of the heart as part of the general circulation. **Coronary arteries** supply oxygen-rich blood to the heart muscle cells. Coronary veins remove deoxygenated blood from the heart muscle cells.

- There are two coronary arteries: a right coronary artery that supplies the right side of the heart and a left coronary artery that supplies the left side of the heart. These arteries branch repeatedly into smaller and smaller arteries and finally into capillaries, which exchange gases, nutrients, and waste products with cardiomyocytes.
- At the back of the heart, small cardiac veins drain into larger veins and finally into the great cardiac vein, which empties into the right atrium. At the front of the heart, small cardiac veins drain directly into the right atrium.

BLOOD CIRCULATION THROUGH THE HEART

Figure 5.3.4 shows how blood circulates through the chambers of the heart. The right atrium collects blood from two large veins, the superior vena cava (from the upper body) and the inferior vena cava (from the lower body). The blood that collects in the right atrium is pumped through the tricuspid valve into the right ventricle. From the right ventricle, the blood is pumped through the pulmonary valve into the pulmonary artery. The pulmonary artery carries the blood to the lungs, where it enters the pulmonary circulation, gives up carbon dioxide, and picks up oxygen. The oxygenated blood travels back from the lungs through the pulmonary veins (of which there are four) and enters the left atrium of the heart. From the left atrium, the blood is pumped through the mitral valve into the left ventricle. From the left ventricle, the blood is pumped through the aortic valve into the aorta, which subsequently branches into smaller arteries that carry the blood throughout the rest of the body. After passing through capillaries and exchanging substances with cells, the blood returns to the right atrium via the superior vena cava and inferior vena cava, and the process begins anew.

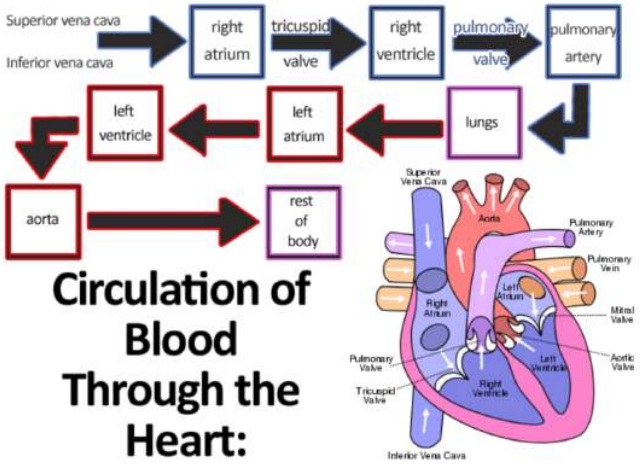


Figure 5.3.4: The flow chart in this diagram summarizes the pathway blood takes as it flows into, through, and out of the heart. Trace the path of blood flow in the diagram of the heart as you follow it through the flow chart.

CARDIAC CYCLE

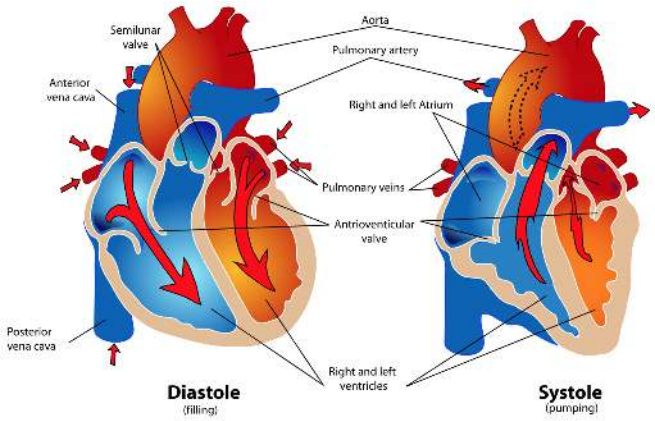


Figure **5.3.5**: Diastole is referred to as the filling stage because this is when the ventricles fill with blood. Systole is referred to as the pumping stage because this is when the ventricles pump blood out of the heart.

The cardiac cycle refers to a single complete heartbeat, which includes one iteration of the lub and dub sounds heard through a stethoscope. During the cardiac cycle, the atria and ventricles work in a coordinated fashion so that blood is pumped efficiently through and out of the heart. The cardiac cycle includes two parts, called diastole and systole, which are illustrated in Figure **5.3.5**.

- During **diastole,** the atria contract and pump blood into the ventricles, while the ventricles relax and fill with blood from the atria.
- During **systole,** the atria relax and collect blood from the lungs and body, while the ventricles contract and pump blood out of the heart.

ELECTRICAL STIMULATION OF THE HEART

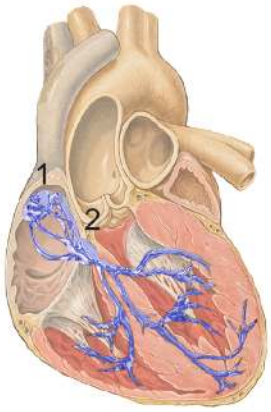


Figure **5.3.6**: In this drawing of the heart, the numbers refer to (1) the sinoatrial node and (2) the atrioventricular node. The blue lines in the drawing indicate the path of transmission of electrical signals through the heart.

The normal, rhythmical beating of the heart is called **sinus rhythm.** It is established by the heart's **pacemaker** cells, which are located in an area of the heart called the sinoatrial node (Figure **5.3.6**). The pacemaker cells create electrical signals by the movement of electrolytes (sodium, potassium, and calcium ions) into and out of the cells. For each cardiac cycle, an electrical signal rapidly travels first from the sinoatrial node to the right and left atria so they contract together. Then the signal travels to another node, called the atrioventricular node (also shown in Figure **5.3.6**), and from there to the right and left ventricles, which also contract together, just a split second after the atria contract.

The normal sinus rhythm of the heart is influenced by the autonomic nervous system through sympathetic and parasympathetic nerves. These nerves arise from two paired cardiovascular centers in the medulla of the brainstem. The parasympathetic nerves act to decrease the heart rate, and the sympathetic nerves act to increase the heart rate. Parasympathetic input normally predominates. Without it, the pacemaker cells of the heart would generate a resting heart rate of about 100 beats per minute, instead of a normal resting heart rate of about 72 beats per minute. The cardiovascular centers receive input from receptors throughout the body and act through the sympathetic nerves to increase the heart rate as needed. For example, increased physical activity is detected by receptors in muscles, joints, and tendons. These receptors send nerve impulses to the cardiovascular centers, causing sympathetic nerves to increase the heart rate. This allows more blood to flow to the muscles.

Besides the autonomic nervous system, other factors can also affect the heart rate. For example, thyroid hormones and adrenal hormones such as epinephrine can stimulate the heart to beat faster. The heart rate also increases when blood pressure drops or the body is dehydrated or overheated. On the other hand, cooling of the body and relaxation, among other factors, can contribute to a decrease in the heart rate.

FEATURE: HUMAN BIOLOGY IN THE NEWS

When a patient's heart is too diseased or damaged to sustain life, a heart transplant is likely to be the only long-term solution. The first successful heart transplant was undertaken in South Africa in 1967. For the past two decades in the United States, about 2,400 hearts were transplanted each year. The problem is that far too few hearts are available for transplant, and many patients die each year waiting for a life-saving heart to become available.

Hearts for transplant have to be used within four hours of the death of the donor. In addition, hearts can only come from brain-dead individuals whose hearts are removed while they are still healthy. Then the hearts are placed on ice inside picnic coolers to be transported to a waiting recipient. The four-hour window means that traffic jams, bad weather, or other unforeseen delays often result in a heart being in less than optimal condition by the time it arrives at its destination. Unfortunately, there is no way to know if the heart will start up again after it is transplanted until it is actually placed in the recipient's body. In up to seven percent of cases, a transplanted heart does not work and has to be removed.

A medical device company in Massachusetts named TransMedic was featured in many news stories when it developed the Organ Care System, commonly referred to as "heart in a box." The system takes a new approach to maintain

donated hearts until they are transplanted. The box is heated and contains a device that pumps oxygenated blood through the heart while it is being transported to the recipient. This extends the time up to 12 hours that the heart can remain healthy and usable. It also allows the heart to be monitored so it is kept in optimal condition while it is on the route. The end result, ideally, is that the recipient gets a healthier heart with less chance of failure of the new organ and a lower risk of death.

As of mid-2016, the heart-in-a-box system had already been used for several successful heart transplants in other countries. At that time, the system was also undergoing clinical trials in the United States to assess its effectiveness in promoting positive recipient outcomes. Developers of the heart-in-a-box predict that the system could increase the number of usable donor hearts by as much as 30 percent, thus greatly increasing the number of patients who are saved from death due to heart failure.

REVIEW

1. What is the heart, where is located, and what is its function?
2. Outline the structure of the heart.
3. Describe the coronary circulation.
4. Summarize how blood flows into, through, and out of the heart.
5. Define the cardiac cycle, and identify its two parts.
6. Explain what controls the beating of the heart.
7. a. What are the two types of cardiac muscle cells in the myocardium?

   b. What are the differences between these two types of cells?
8. Match each of the three layers of the walls of the heart (endocardium, myocardium, and pericardium) with the description that best matches it below.

   a. Protects the heart

   b. Covers the heart valves

   c. Responsible for the beating of the heart
9. Is the blood flowing through the mitral valve oxygenated or deoxygenated? Explain your reasoning.
10. *True or False.* The coronary arteries carry blood to the heart.
11. *True or False.* Systole is when the heart is contracting, diastole is when the heart is fully relaxed.
12. Explain why the blood from the cardiac veins empties into the right atrium of the heart. Focus on function rather than anatomy in your answer.

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5.4: BLOOD VESSELS

BULGING VEINS

Why do bodybuilders have such prominent veins? Bulging muscles push surface veins closer to the skin. Couple that with a virtual lack of subcutaneous fat, and you have bulging veins as well as bulging muscles. Veins are one of three major types of blood vessels in the cardiovascular system.



Figure **5.4.1**: 2012 Hong Kong Bodybuilding Championship participant

TYPES OF BLOOD VESSELS

Blood vessels are part of the cardiovascular system that transports blood throughout the human body. There are three major types of blood vessels: veins, arteries, and capillaries.

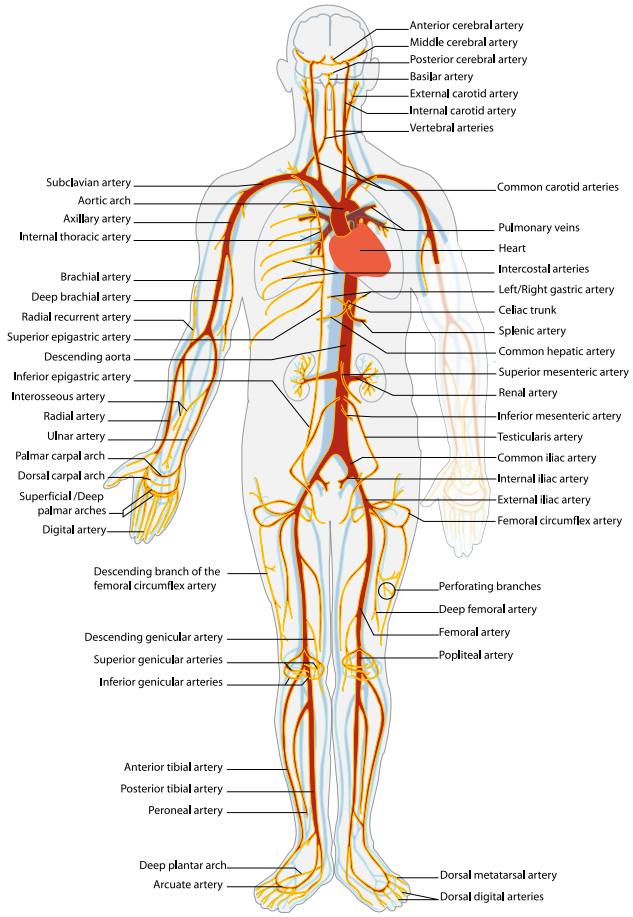


Figure **5.4.2**: This figure shows the heart and the major arteries of the cardiovascular system. The pulmonary veins are included in the diagram because, like arteries, they carry oxygenated blood.

Arteries are defined as blood vessels that carry blood away from the heart. Blood flows through arteries largely because it is under pressure from the pumping action of the heart. It should be noted that coronary arteries, which supply heart muscle cells with blood, travel toward the heart but not as part of the blood flow that travels through the chambers of the heart. Most arteries, including coronary arteries, carry oxygenated blood, but there are a few exceptions, most notably the pulmonary artery. This artery carries deoxygenated blood from the heart to the lungs, where it picks up oxygen and releases carbon dioxide. In virtually all other arteries, the hemoglobin in red blood cells is highly saturated with oxygen (95-100 percent). These arteries distribute oxygenated blood to tissues throughout the body.

The largest artery in the body is the aorta, which is connected to the heart and extends down into the abdomen (Figure **5.4.2**). The aorta has high-pressure, oxygenated blood pumped directly into it from the left ventricle of the heart. The aorta has many branches, and the branches subdivide repeatedly, with the subdivisions growing smaller and smaller in diameter. The smallest arteries are called arterioles.

VEINS

Veins are defined as blood vessels that carry blood toward the heart. Blood traveling through veins is not under pressure from the beating heart. It gets help moving along by the squeezing action of skeletal muscles, for example, when you walk or breathe. It is also prevented from flowing backward by valves in the larger veins, as illustrated in Figure 5.4.3. Veins are called capacitance blood vessels because the majority (about 60 percent) of the body's total volume of blood is contained within veins.

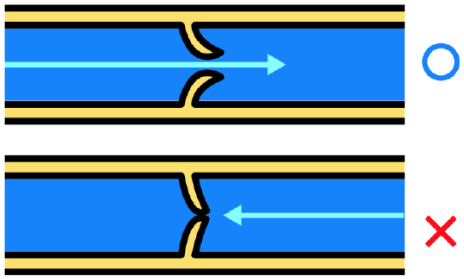


Figure 5.4.3: The two flaps that make up a venous valve can open in just one direction, so blood can flow in only one direction through the vein.

Most veins carry deoxygenated blood, but there are a few exceptions, including the four pulmonary veins. These veins carry oxygenated blood from the lungs to the heart, which then pumps the blood to the rest of the body. In virtually all other veins, hemoglobin is relatively unsaturated with oxygen (about 75 percent).

The two largest veins in the body are the **superior vena cava**, which carries blood from the upper body directly to the right atrium of the heart, and the **inferior vena cava**, which carries blood from the lower body directly to the right atrium. The inferior vena cava is labeled in the figure below. The superior vena cava is not labeled in Figure 5.4.4 but is clearly visible entering the right atrium of the heart. Like arteries, veins form a complex, branching system of larger and smaller vessels. The smallest veins are called venules. They receive blood from capillaries and transport it to larger veins. Each venule receives blood from multiple capillaries.

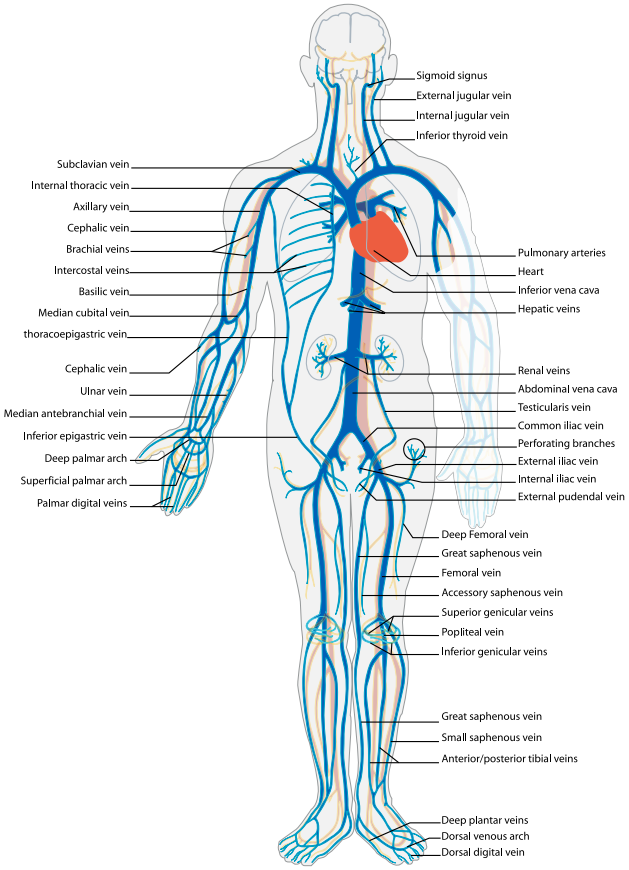


Figure 5.4.4: This diagram shows the heart and major veins of the cardiovascular system. The pulmonary arteries are included in the diagram because, like veins, they carry deoxygenated blood.

CAPILLARIES

Capillaries are the smallest blood vessels in the cardiovascular system. They are so small that only one red blood cell at a time can squeeze through a capillary, and then only if the red blood cell deforms. Capillaries connect arterioles and venules, as shown in Figure 5.4.5. Capillaries generally form a branching network of vessels, called a capillary bed, that provides a large surface area for the exchange of substances between the blood and surrounding tissues.

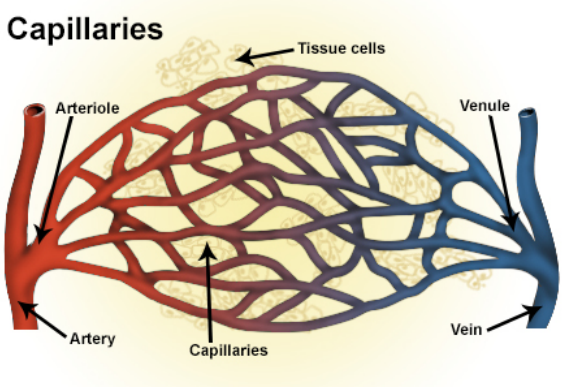


Figure **5.4.5**: Capillaries form beds of tiny blood vessels that exchange substances with the cells of tissues.

STRUCTURE OF BLOOD VESSELS

All blood vessels are basically hollow tubes with an internal space, called a lumen, through which blood flows. The lumen of an artery is shown in cross-section in the photomicrograph below. The width of blood vessels varies, but they all have a lumen. The walls of blood vessels differ depending on the type of vessel. In general, arteries and veins are more similar to one another than capillaries in the structure of their walls.

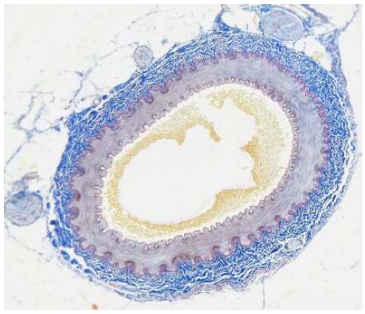


Figure **5.4.6**: The lumen is the white space in the center of this cross-sectional slice of an artery. You can see that the walls of the artery have multiple layers.

WALLS OF ARTERIES AND VEINS

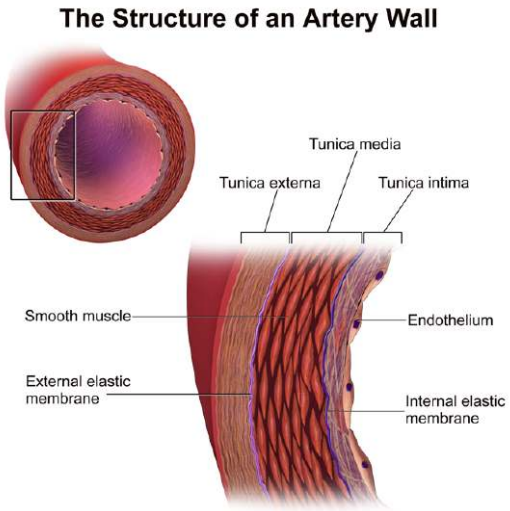


Figure **5.4.7**: The wall of an artery is made of three layers: tunica intima, tunica media, and tunica externa. A vein has the same three layers as the artery shown here, but the middle layer (tunica media) of a vein is thinner and lacks smooth muscle tissue.

The walls of both arteries and veins have three layers: the tunica intima, tunica media, and tunica adventitia. You can see the three layers for an artery in Figure **5.4.7**.

1. The tunica intima is the inner layer of arteries and veins. It is also the thinnest layer, consisting of a single layer of endothelial cells surrounded by a thin layer of connective tissues. It reduces friction between the blood and the inside of the blood vessel walls.
2. The tunica media is the middle layer of arteries and veins. In arteries, this is the thickest layer. It consists mainly of elastic fibers and connective tissues. In arteries, this is the thickest layer because it also contains smooth muscle tissues, which control the diameter of the vessels.
3. The tunica externa (also called tunica adventitia) is the outer layer of arteries and veins. It consists of connective tissue and also contains nerves. In veins, this is the thickest layer. In general, the tunica externa protects and strengthens vessels and attaches them to surrounding structures.

CAPILLARY WALLS

The walls of capillaries consist of little more than a single layer of epithelial cells. Being just one cell thick, the walls are well suited for the exchange of substances between the blood inside them and the cells of surrounding tissues. Substances including water, oxygen, glucose, and other nutrients as well as waste products such as carbon dioxide can pass quickly and easily through the extremely thin walls of capillaries.

BLOOD PRESSURE

The blood in arteries is normally under pressure because of the beating of the heart. The pressure is highest when the heart contracts and pumps out blood, and lowest when the heart relaxes and refills with blood. (You can feel this variation in pressure in your wrist or neck when you count your pulse.) **Blood pressure** is a measure of

the force that blood exerts on the walls of arteries. It is generally measured in millimeters of mercury (mm Hg) and expressed as a double number: a higher number for systolic pressure when the ventricles contract; and a lower number for diastolic pressure when the ventricles relax. Normal blood pressure is generally defined as less than 120 mm Hg (systolic)/80 mm Hg (diastolic) when measured in the arm at the level of the heart. It decreases as blood flows farther away from the heart and into smaller arteries.

As arteries grow smaller, there is increasing resistance to blood flow through them because of the friction of the blood against the arterial walls. This resistance restricts blood flow so less blood reaches smaller, downstream vessels, thus reducing blood pressure before the blood flows into the tiniest vessels, the capillaries. Without this reduction in blood pressure, capillaries would not be able to withstand the pressure of the blood without bursting. By the time blood flows through the veins, it is under very little pressure. The pressure of blood against the walls of veins is always about the same and normally no more than 10 mm Hg.

VASOCONSTRICTION AND VASODILATION

Smooth muscles in the walls of arteries can contract or relax to cause vasoconstriction (narrowing of the lumen of blood vessels) or vasodilation (widening of the lumen of blood vessels). This allows the arteries — especially the arterioles — to contract or relax as needed to help regulate blood pressure. In this regard, the arterioles act like an adjustable nozzle on a garden hose. When they narrow, the increased friction with the arterial walls causes less blood to flow downstream from the narrowing, resulting in a drop in blood pressure. These actions are controlled by the autonomic nervous system in response to pressure-sensitive sensory receptors in the walls of larger arteries.

Arteries can also dilate or constrict to help regulate body temperature by allowing more or less blood to flow from the warm body core to the body's surface. In addition, vasoconstriction and vasodilation play roles in the fight-or-flight response, under the control of the sympathetic nervous system. For example, vasodilation allows more blood to flow to skeletal muscles and vasoconstriction reduces blood flow to digestive organs.

FEATURE: MY HUMAN BODY

The lumpy appearance of this man's leg is caused by *varicose veins*. Do you have varicose veins? If you do, you may wonder whether they are a sign of a significant health problem. You may also wonder whether you should have them treated, and if so, what treatments are available. As is usually the case, when it comes to your health, "knowledge is power."



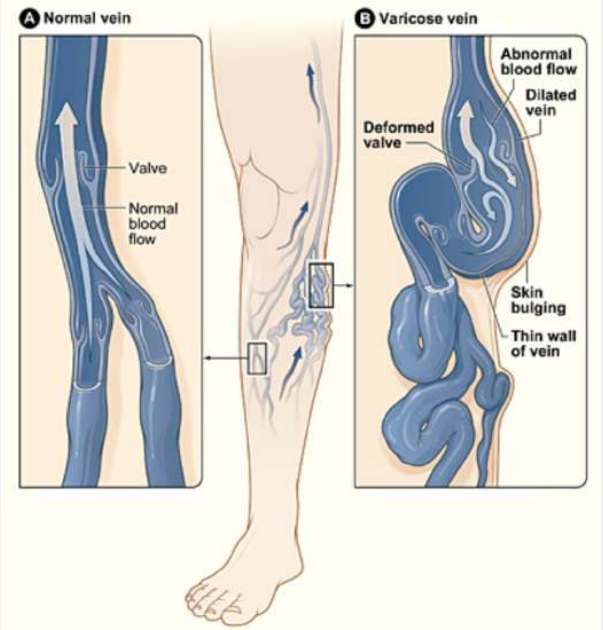


Figure 5.4.8: Varicose veins form when a deformed valve allows blood to pool creating a bulge in the vein.

First, the "back story:" varicose veins are veins that have become enlarged and twisted because their valves have become ineffective (see Figure 5.4.8). As a consequence, blood pools in the veins and stretches them out. Varicose veins occur most frequently in the superficial veins of the legs, but they may also occur in other parts of the body. They are most common in older adults, females, and people who have a family history of the condition. Obesity and pregnancy also increase the risk of developing varicose veins. A job that requires standing for long periods of time, chronic constipation, and long-term alcohol consumption are additional risk factors.

Varicose veins usually are not serious. In many people, they are only a cosmetic issue. However, in severe cases, varicose veins may cause pain and other problems. For example, the affected leg(s) may feel heavy and achy, especially after long periods of standing. Ankles may become swollen by the end of the day. Minor injuries may bleed more than normal. The skin over varicosity may become red, dry, and itchy. In very severe cases, skin ulcers may develop.

If you are concerned about varicose veins, call them to the attention of your doctor, who can determine the best course of action for your case. There are many potential treatments for varicose veins. Some of the treatments have potential adverse side effects; and with many of the treatments, varicose veins

may return. Which treatment is best for a given patient depends in part on the severity of the condition.

- If varicose veins are not serious, then conservative treatment options may be recommended. These include avoiding standing or sitting for long periods, frequently elevating the legs, and wearing graduated compression stockings.
- For more serious cases, less conservative but non-surgical options may be advised. These include sclerotherapy, in which medicine is injected into the veins to make them shrink. Another non-surgical approach is endovenous thermal ablation. In this type of treatment, laser light, radio-frequency energy, or steam is used to heat the walls of the veins, causing them to shrink and collapse.
- For the most serious cases, surgery may be the best option. The most invasive surgery is vein stripping, in which all or part of the main trunk of a vein is tied off and removed from the leg while the patient is under general anesthesia. In a less invasive surgery, called ambulatory phlebectomy, short segments of a vein are removed through tiny incisions under local anesthesia.

REVIEW

1. What are the blood vessels? Name the three major types of blood vessels.
2. Describe arteries. Identify the largest artery in the body.
3. How are veins defined? What are the two largest veins in the body?
4. Compare and contrast how blood moves through arteries and veins.
5. What are capillaries, and what is their function?
6. Compare and contrast the structure of the walls of arteries, veins, and capillaries.
7. What is blood pressure, and how is it expressed? What blood pressure is considered normal?
8. Identify the functions of vasoconstriction and vasodilation of arteries.
9. Does the blood in most veins have any oxygen at all? Explain your answer.
10. *True or False.* Only one red blood cell can pass through the lumen of a capillary at a given time.
11. *True or False.* The pulmonary artery carries oxygenated blood.
12. Which tissue in blood vessels is responsible for vasodilation and vasoconstriction? Where is it located?
13. The blood pressure at the arterioles is generally _____ the blood pressure at the aorta.
    A. lower than
    B. higher than
    C. the same as
    D. not related to
14. Explain why it is important that the walls of capillaries are very thin.
15. Most of the blood in the body is in the:
    A. Capillaries
    B. Arteries
    C. Heart
    D. Veins

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5.5: BLOOD

VAMPIRES

From Bram Stoker's famous novel about Count Dracula to the campy TV series *Buffy the Vampire Slayer*, fantasies featuring vampires, like the one in Figure **5.5.1**, have been popular for decades. In fact, vampires are found in centuries-old myths from many cultures. In such myths, vampires are generally described as creatures that drink blood, preferably of the human variety, for sustenance. Dracula, for example, is based on Eastern European folklore about a human who attains immortality (and eternal damnation) by drinking the blood of others.



Figure **5.5.1**: Dracula

FUNCTIONS OF BLOOD

Blood performs many important functions in the body. Major functions of blood include:

- supplying tissues with oxygen, which is needed by all cells for aerobic cellular respiration.
- supplying cells with nutrients, including glucose, amino acids, and fatty acids.
- removing metabolic wastes from cells, including carbon dioxide, urea, and lactic acid.
- helping to defend the body from pathogens and other foreign substances.
- forming clots to seal broken blood vessels and stop bleeding.
- transporting hormones and other messenger molecules.
- regulating the pH of the body, which must be kept within a narrow range (7.35 to 7.45).
- helping to regulate body temperature (through vasoconstriction and vasodilation).

WHAT IS BLOOD?

Blood is a fluid connective tissue that circulates throughout the body through blood vessels of the cardiovascular system. What makes blood so special that it features in widespread myths? Although blood accounts for less than 10 percent of human body weight, it is quite literally the elixir of life. As blood travels through the vessels of the cardiovascular system, it delivers vital substances such as nutrients and oxygen to all of the cells and carries away their metabolic wastes. It is no exaggeration to say that without blood, cells could not survive. Indeed, without the oxygen carried in the blood, cells of the brain start to die within just a matter of minutes.

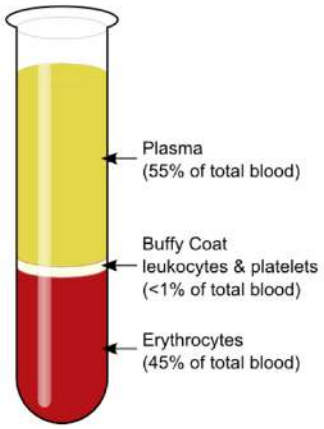


Figure **5.5.2**: If blood is centrifuged (spun at high speed), it separates into its major components based on density, as shown here: plasma, leukocytes (white blood cells) and platelets, and erythrocytes (red blood cells). Plasma makes up about 55% of the blood. Leukocytes and platelets make up less than 1%. Erythrocytes make up about 45%.

The average adult body contains between 4.7 and 5.7 liters (5-6 quarts) of blood. More than half of that amount is fluid. Most of the rest of that amount consists of cells. The relative amounts of the various components in the blood are illustrated in Figure **5.5.2**. The components are also described in the text.

BLOOD PLASMA

Plasma is the liquid component of human blood and makes up about 55 percent of blood by volume. It is about 92 percent water and contains many dissolved substances. Most of these substances are proteins, but plasma also contains trace amounts of glucose, mineral ions, hormones, carbon dioxide, and other substances.

FORMED ELEMENTS

The formed elements in the blood include red blood cells, white blood cells, and platelets. These different types of elements are pictured in Figure **5.5.3** and described in the sections that follow.

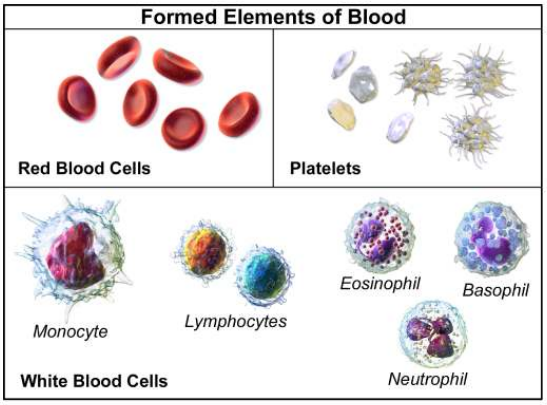


Figure **5.5.3**: Highly magnified blood cells in this image include donut-shaped red blood cells, rough-surfaced white blood cells, and small disc-shaped platelets.

RED BLOOD CELLS

The most numerous cells in the blood are **red blood cells,** also called erythrocytes. One microliter of blood contains between 4.2 and 6.1 million red blood cells, and red blood cells make up about a quarter of all the cells in the human body. The cytoplasm of a mature red blood cell is almost completely filled with hemoglobin, the iron-containing protein that binds with oxygen and gives the cell its red color. Mature red blood cells lack a cell nucleus and most organelles in order to provide maximum space for hemoglobin. They are little more than sacks of hemoglobin.

Red blood cells also carry proteins called antigens that determine blood type. Blood type is a genetic characteristic. The best known human blood type systems are the ABO and Rhesus systems. These are described in the next section.

WHITE BLOOD CELLS (WBC)

White blood cells are cells in the blood that defend the body against invading microorganisms and other threats. There are far fewer white blood cells (also called leukocytes) than red blood cells in the blood. There are normally only about 1,000 to 11,000 white blood cells per microliter of blood. Unlike red blood cells, white blood cells have a nucleus. White blood cells are part of the body's immune system. They destroy and remove old or abnormal cells and cellular debris, as well as attack pathogens and foreign substances. There are two categories of WBCs, granulocytes (contain visible granules in the cytoplasm) and agranulocytes (do not contain granules). The Granulocytes include neutrophils, eosinophils, and basophils. The agranulocytes include lymphocytes and monocytes. The five types differ in their specific immune functions. The relative percent and functions of WBCs are summarized in Table **5.5.1**:

Table **5.5.1**: Major Types of White Blood Cells

Type of Leukocyte	Percent of All Leukocytes	Main Function(s)
Neutrophil	62	Phagocytize (engulf and destroy) bacteria and fungi in the blood
Eosinophil	2	Attack and kill large parasites; carry out allergic responses
Basophil	<1	Release histamines in inflammatory responses
Lymphocyte	30	Attack and destroy virus-infected and tumor cells; create lasting immunity to specific pathogens
Monocyte	5	Phagocytize pathogens and debris in tissues

PLATELETS

Platelets, also called thrombocytes, are actually cell fragments. Like red blood cells, they lack a nucleus and are more numerous than white blood cells. There are about 150,000 to 400,000 platelets per microliter of blood.

The main function of platelets is blood clotting or **coagulation.** This is the process by which blood changes from a liquid to a gel, forming a plug in a damaged blood vessel. If blood clotting is successful, it results in hemostasis, which is the cessation of blood loss from the damaged vessel. A blood clot consists of both platelets and proteins, especially the protein fibrin. You can see a scanning electron microscope micrograph of a blood clot in Figure **5.5.4**.

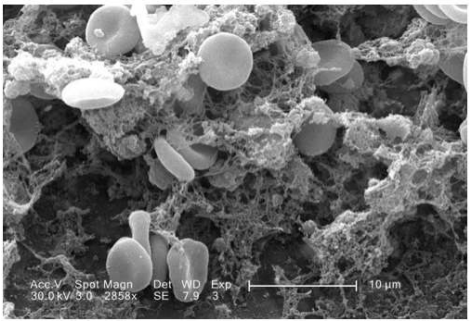


Figure **5.5.4**: Red blood cells become trapped in a coagulating clot so they cannot escape through a break in a blood vessel.

Coagulation begins almost instantly after an injury to the endothelium of a blood vessel occurs. Platelets become activated and change their shape from spherical to star-shaped, as shown in Figure **5.5.5**. This helps them aggregate with one another at the site of injury to start forming a plug in the vessel wall. Activated platelets also release substances into the blood that activate additional platelets and start a sequence of reactions leading to fibrin formation. Strands of fibrin crisscross the platelet plug and strengthen it, much as rebar strengthens concrete.

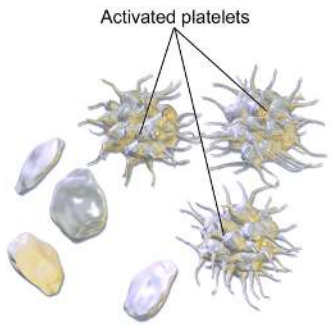


Figure 5.5.5: The shape of platelets after they are activated helps them to stick together and form a plug for a damaged blood vessel.

FORMATION AND DEGRADATION OF BLOOD CELLS

Blood is considered to be a connective tissue because blood cells form inside bones. All three types of blood cells are made in the red marrow of bones in a process called hematopoiesis. The formation of blood cells occurs by the proliferation of stem cells in the marrow. These stem cells are self-renewing: when they divide, some of the daughter cells remain stem cells, so the pool of stem cells is not used up. Other daughter cells follow various pathways to differentiate into a variety of types of blood cells. Once the cells have differentiated, they cannot divide to form copies of themselves.

Eventually, blood cells die and must be replaced through the formation of new blood cells from proliferating stem cells. After blood cells die, the dead cells are phagocytized (engulfed and destroyed) by white blood cells and removed from the circulation. This most often takes place in the spleen and liver.

BLOOD DISORDERS

Many human disorders primarily affect the blood. They include cancers, genetic disorders, poisoning by toxins, infections, and nutritional deficiencies.

- **Leukemia** is a group of cancers of the blood-forming tissues in the bone marrow. It is the most common type of cancer in children, although most cases occur in adults. Leukemia is generally characterized by large numbers of abnormal white blood cells. Symptoms may include excessive bleeding and bruising, fatigue, fever, and an increased risk of infections. Leukemia is thought to be caused by a combination of genetic and environmental factors.
- **Hemophilia** refers to any of several genetic disorders that cause dysfunction in the blood clotting process. People with hemophilia are prone to potentially uncontrollable bleeding even with otherwise inconsequential injuries. They also commonly suffer bleeding into the spaces between joints, which can cause crippling.
- Carbon monoxide poisoning occurs when inhaled carbon monoxide (for example, in fumes from a faulty home furnace) binds irreversibly to the hemoglobin in red blood cells. As a result, oxygen cannot bind to the red cells for transport throughout the body, and this can quickly lead to suffocation. Carbon monoxide is extremely dangerous because it is colorless and odorless so it cannot be detected in the air by human senses.
- HIV is a virus that infects certain types of white blood cells and interferes with the body's ability to defend itself from pathogens and other causes of illness. HIV infection may eventually lead to AIDS or acquired immunodeficiency syndrome. AIDS is characterized by rare infections and cancers that people with a healthy immune system almost never acquire.

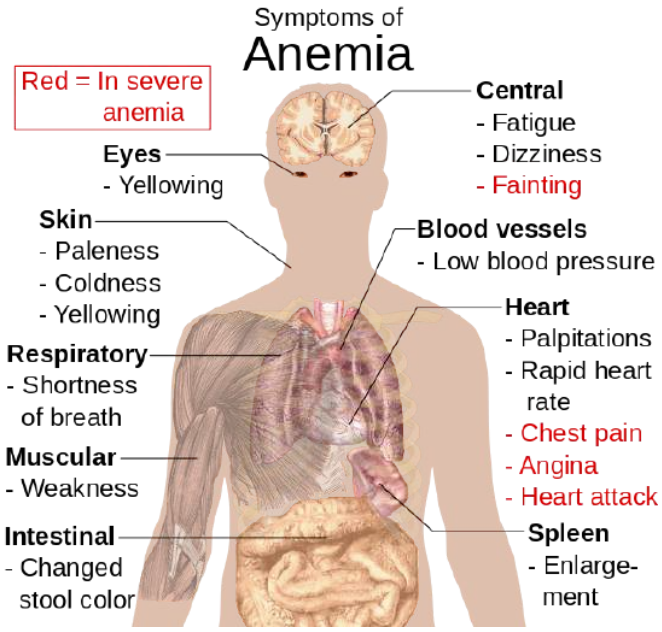


Figure **5.5.6**: Anemia has wide-ranging effects on the human body because oxygen is essential for the normal functioning of cells in every organ system. The most severe symptoms include fainting, chest pain, angina, and heart attack.

- **Anemia** is a disorder in which the blood has an inadequate volume of red blood cells. This reduces the amount of oxygen that the blood can carry and may cause weakness and fatigue. These and other signs and symptoms of anemia are shown in the figure below. Anemia has many possible causes, including excessive bleeding, inherited disorders such as sickle cell hemoglobin, or nutritional deficiencies (iron, folate, or B12). Severe anemia may require transfusions of donated blood.

FEATURE: MYTH VS. REALITY

Donating blood saves lives. In fact, with each blood donation, as many as three lives may be saved. The feeling that comes from knowing you have saved lives is well worth the short amount of time it takes to make a blood donation. Nonetheless, only a minority of potential donors actually donate blood. There are many myths about blood donation that contribute to the small percentage of donors. Knowing the facts may reaffirm your decision to donate if you are already a donor. If you aren't a donor already, getting the facts may help you decide to become one.

Myth: Your blood might become contaminated with an infection during the donation.

Reality: There is no risk of contamination because only single-use, disposable catheters, tubing, and other equipment are used to collect blood for a donation.

Myth: You are too old (or too young) to donate blood.

Reality: There is no upper age limit on donating blood as long as you are healthy. The lower age limit is 16 years.

Myth: You can't donate blood if you have high blood pressure.

Reality: As long as your blood pressure is below 180/100 at the time of donation, you can give blood. Even if you take blood pressure medication to keep your blood pressure below this level, you can donate.

Myth: You can't give blood if you have high cholesterol.

Reality: Having high cholesterol does not affect your ability to donate blood. Taking cholesterol-lowering medication also does not disqualify you.

Myth: You can't donate blood if you have had a flu shot.

Reality: Having a flu shot has no effect on your ability to donate blood. You can even donate on the same day that you receive a flu shot.

Myth: You can't donate blood if you take medication.

Reality: As long as you are healthy, in most cases taking medication does not preclude you from donating blood.

Myth: Your blood isn't needed if it's a common blood type.

Reality: All types of blood are in constant demand.

REVIEW

1. What is blood? Why is blood considered to be a connective tissue?
2. Identify four physiological roles of blood in the body.
3. Describe plasma and its components.
4. Identify red blood cells and their major function.
5. What are white blood cells? Which body system besides the cardiovascular system includes white blood cells?
6. Explain how platelets cause coagulation.
7. Summarize the formation and degradation of blood cells.
8. Identify three disorders of the blood.
9. For each of the descriptions below, choose the blood cell that best fits the description. Blood cells: red blood cells; white blood cells; platelets

    A. Has a nucleus
    B. Responsible for blood clotting
    C. Carbon monoxide binds to a protein in these cells

10. What is another name for erythrocytes? What is another name for leukocytes?
11. *True or False.* Plasma refers to the cytoplasm within blood cells.
12. *True or False.* Platelets are cell fragments.

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5.6: BLOOD TYPES

GIVING THE GIFT OF LIFE

Did you ever donate blood as the individual in Figure **5.6.1** is doing? If you did, then you probably know that your blood type is an important factor in blood transfusions. People vary in the type of blood they inherit, and this determines which type(s) of blood they can safely receive in a transfusion. Do you know your blood type?



Figure **5.6.1**: Donating Blood

WHAT ARE BLOOD TYPES?

Blood type (or blood group) is a genetic characteristic associated with the presence or absence of certain molecules, called antigens, on the surface of red blood cells. These molecules may help maintain the integrity of the cell membrane, act as receptors, or have other biological functions. A **blood group system** refers to all of the gene(s), alleles, and possible genotypes and phenotypes that exist for a particular set of blood type antigens. Human blood group systems include the well-known ABO and Rhesus (Rh) systems, as well as at least 33 others that are less well known.

ANTIGENS AND ANTIBODIES

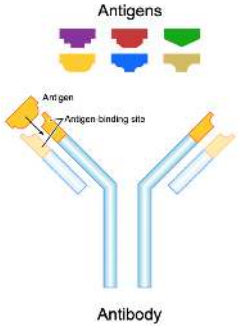


Figure **5.6.2**: Model of antigen and matching antibody

Antigens such as those on the red blood cells are molecules that the immune system identifies as either self (produced by your own body) or non-self (not produced by your own body). Blood group antigens may be proteins, carbohydrates, glycoproteins (proteins attached to chains of sugars), or glycolipids (lipids attached to chains of sugars), depending on the particular blood group system. If antigens are identified as nonself, the immune system responds by forming antibodies that are specific to the non-self antigens. **Antibodies** are large, Y-shaped proteins produced by the immune system that recognize and bind to non-self antigens. The analogy of a lock and key is often used to represent how an antibody and antigen fit together, as shown in Figure **5.6.2**. When antibodies bind to antigens, it marks them for destruction by other immune system cells. Nonself antigens may enter your body on pathogens such as bacteria or viruses, on foods, or on red blood cells in a blood transfusion from someone with a different blood type than your own. The last way is virtually impossible nowadays because of effective blood typing and screening protocols.

GENETICS OF BLOOD TYPE

An individual's blood type depends on which alleles for a blood group system were inherited from their parents. Generally, blood type is controlled by alleles for a single gene or for two or more very closely linked genes. Closely linked genes are almost always inherited together because there is little or no recombination between them. Like other genetic traits, a person's blood type is generally fixed for life, but there are rare instances in which blood type can change. This could happen, for example, if an individual receives a bone marrow transplant to treat a disease such as leukemia. If the bone marrow comes from a donor who has a different blood type, the patient's blood type may eventually convert to the donor's blood type because red blood cells are produced in the bone marrow.

ABO BLOOD GROUP SYSTEM

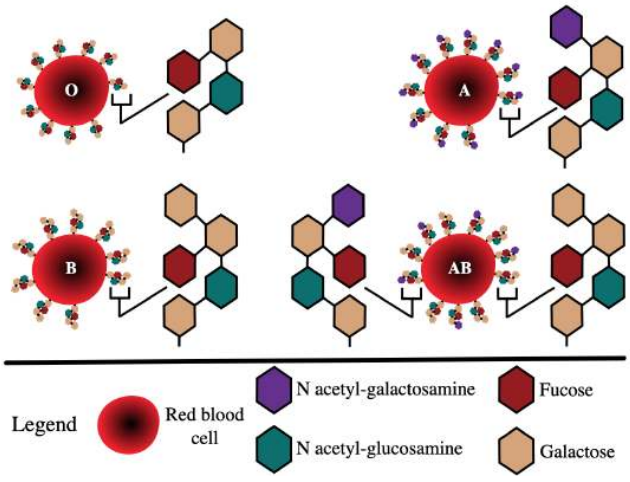


Figure **5.6.3**: ABO antigen molecules

The **ABO blood group system** is the best known human blood group system. Antigens in this system are glycoproteins. These antigen compounds are shown in Figure **5.6.3**. There are four common blood types for the ABO system:

1. Type A, in which only the A antigen is present
2. Type B, in which only the B antigen is present

3. Type AB, in which both the A and B antigens are present
4. Type O, in which neither the A nor the B antigen is present

GENETICS OF THE ABO SYSTEM

The ABO blood group system is controlled by a single gene on chromosome 9. There are three common alleles for the gene, often represented by the letters I^A (or A), I^B (or B), and i (or O). With three alleles, there are six possible genotypes for the ABO blood group. However, alleles I^A and I^B are both dominant to allele i and codominant to each other. This results in just four possible phenotypes (blood types) for the ABO system. These genotypes and phenotypes are shown in Table **5.6.1**.

Table **5.6.1**: **ABO Blood Group System**

Genotype	Phenotype (Blood Type, or Group)
I^Ai	A
I^AI^A	A
I^AI^B	AB
I^Bi	B
I^BI^B	B
ii	O

The diagram in Figure **5.6.4** shows an example of how ABO blood type is inherited. In this particular example, the father has blood type A (genotype AO) and the mother has blood type B (genotype BO). This mating type can produce children with each of the four possible ABO phenotypes, although in any given family not all phenotypes may be present in the children.

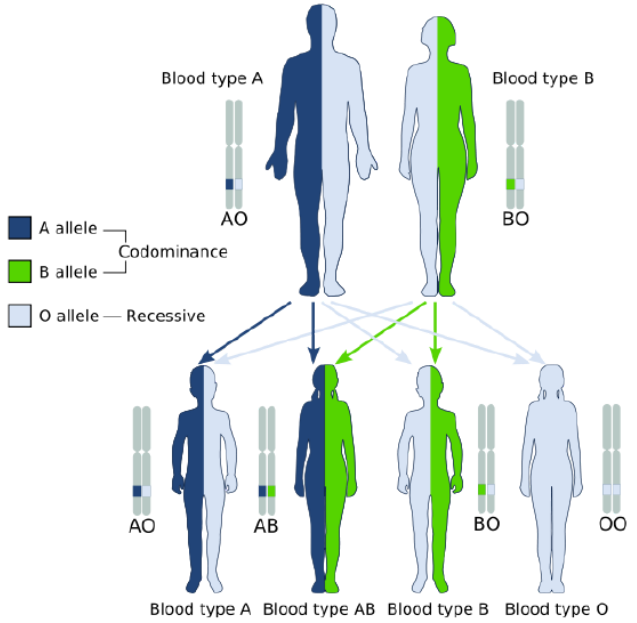


Figure **5.6.4**: Example of ABO blood group inheritance. A male who is type A (genotype of AO) and a female who is type B (genotype BO) can have children with blood types: A, AB, B, and O.

MEDICAL SIGNIFICANCE OF ABO BLOOD TYPE

The ABO system is the most important blood group system in blood transfusions. If red blood cells containing a particular ABO antigen are transfused into a person who lacks that antigen, the person's immune system will recognize the antigen on the red blood cells as non-self. Antibodies specific to that antigen will attack the red blood cells, causing them to agglutinate, or clump and break apart. If a unit of incompatible blood were to be accidentally transfused into a patient, a severe reaction (called acute hemolytic transfusion reaction) is likely to occur in which many red blood cells are destroyed. This may result in kidney failure, shock, and even death. Fortunately, such medical accidents virtually never occur today.

ABO antibodies are likely to already be present in a recipient's blood for antigens that the person lacks. These antibodies are produced in the first years of life by sensitization to similar antigens commonly occurring in the environment. Anti-A antibodies are thought to originate from an immune response to an antigen on the influenza virus, and anti-B antibodies are thought to originate from an immune response to an antigen found on bacteria such as *E. coli*. Once the antibodies have been produced, they circulate in the plasma. The relationship between ABO red blood cell antigens and plasma antibodies is shown in Table **5.6.2**.

Table **5.6.2**: The antibodies that circulate in the plasma are for different antigens than those on red blood cells, which are recognized as self-antigens.

Blood group	A	B	AB	O
Antibodies in plasma	Anti-B	Anti-A	None	Anti-A and Anti-B
Antigens on the red blood cell	A antigen	B antigen	A and B antigen	None

Which blood types are compatible and which are not? Type O blood contains both anti-A and anti-B antibodies, so people with type O blood can only receive type O blood. However, they can donate blood to people of any ABO blood type. That's why individuals with type O blood are called **universal donors.** Type AB blood contains neither anti-A nor anti-B antibodies, so people with type AB blood can receive blood from people of any ABO blood type. That's why individuals with type AB blood are called **universal recipients.** However, they can donate blood only to people who also have type AB blood. These and other relationships between blood types of donors and recipients are summarized in Figure **5.6.5**.

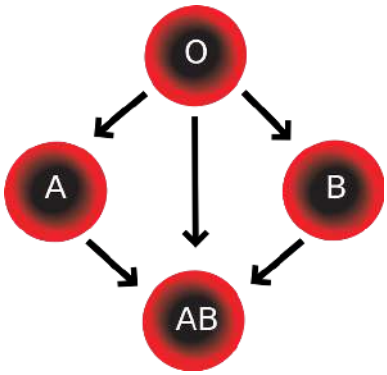


Figure **5.6.5**: You can always donate blood to someone who has the same blood type as yours, but you may or may not be able to donate to people who have other blood types, as indicated in this diagram.

ABO blood type antigens are found not only on red blood cells but also on platelets, in other body fluids such as tears and urine, and on cells of other types of tissues. Blood type compatibility is important to consider for successful organ transplantation. If a transplanted organ has nonself antigens for ABO, it may be attacked by antibodies and rejected by the body.

RHESUS BLOOD GROUP SYSTEM

Another well-known blood group system is the **Rhesus (Rh) blood group system**. The Rhesus system has dozens of different antigens but only five main antigens (named D, C, c, E, and e). The major Rhesus antigen is the D antigen. People with the D antigen are called Rh-positive (Rh+), and people who lack the D antigen are called Rh-negative (Rh-). Rhesus antigens are thought to play a role in transporting ions across cell membranes by acting as channel proteins.

The Rhesus blood group system is controlled by two linked genes on chromosome 1. One gene, called RHD, produces a single antigen, antigen D. The other gene, called RHCE, produces the other four relatively common Rhesus antigens (C, c, E, and e), depending on which alleles for this gene are inherited.

RHESUS BLOOD GROUP AND TRANSFUSIONS

After the ABO system, the Rhesus system is the second most important blood group system in blood transfusions. The D antigen is the one most likely to provoke an immune response in people who lack the antigen. People who have the D antigen (Rh+) can be safely transfused with either Rh+ or Rh- blood, whereas people who lack the D antigen (Rh-) can be safely transfused only with Rh- blood.

Unlike anti-A and anti-B antibodies to ABO antigens, anti-D antibodies for the Rhesus system are not usually produced by sensitization to environmental substances. However, people who lack the D antigen (Rh-) may produce anti-D antibodies if exposed to Rh+ blood. This may happen accidentally in a blood transfusion, although this is extremely unlikely today. It may also happen during pregnancy with an Rh+ fetus if some of the fetal blood cells pass into the mother's blood circulation.

HEMOLYTIC DISEASE OF THE NEWBORN

If a woman who is Rh- is carrying an Rh+ fetus, the fetus may be at risk. This is especially likely if the mother has formed anti-D antibodies during a prior pregnancy because of a mixing of maternal and fetal blood during childbirth. Unlike antibodies against ABO antigens, antibodies against the Rhesus D antigen can cross the placenta and enter the blood of the fetus. This may cause **hemolytic disease of the newborn (HDN)**, also called erythroblastosis fetalis, an illness in which fetal red blood cells are destroyed by maternal antibodies, causing anemia. This illness may range from mild to severe. If it is severe, it may cause brain damage and is sometimes fatal for the fetus or newborn. Fortunately, HDN can be prevented by preventing the formation of anti-D antibodies in the Rh- mother. This is achieved through an injection into the mother of a medication called Rho(D) immune globulin.

FEATURE: MYTH VS. REALITY

Myth: Your nutritional needs can be determined by your ABO blood type. Knowing your blood type allows you to choose the appropriate foods that will help you lose weight, increase your energy, and live a longer, healthier life.

Reality: This idea was proposed in 1996 in a *New York Times* bestseller *Eat Right for Your Type*, by Peter D'Adamo, a naturopath. Naturopathy is a method of treating disorders that involve the use of herbs, sunlight, fresh air, and other natural substances. Some medical doctors consider naturopathy a pseudoscience. A major scientific review of the blood type diet could find no evidence to support it. In one study, adults eating the diet designed for blood type A showed improved health, but this occurred in everyone regardless of their blood type. Because the blood type diet is based solely on blood type, it fails to account for other factors that might require dietary adjustments or restrictions. For example, people with diabetes but different blood types would follow different diets, and one or both of the diets might conflict with standard diabetes dietary recommendations and be dangerous.

Myth: ABO blood type is associated with certain personality traits. For example, people with blood type A are patient and responsible but may also be stubborn and tense, whereas people with blood type B are energetic and creative but may also be irresponsible and unforgiving. In selecting a spouse, both your own and your potential mate's blood type should be taken into account to ensure the compatibility of your personality.

Reality: The belief that blood type is correlated with personality is widely held in Japan and other East Asian countries (the Japanese booth pictured below offers fortunes based on blood type). The idea was originally introduced in the 1920s in a study commissioned by the Japanese government but later shown to have no scientific support. The idea was revived in the 1970s by a Japanese broadcaster who wrote popular books about it. There is no scientific basis for the idea, and it is generally dismissed as pseudoscience by the scientific community. Nonetheless, it remains popular in East Asian countries, like astrology in many other countries.

REVIEW

1. Define blood type and blood group system.
2. Explain the relationship between antigens and antibodies.
3. Identify the alleles, genotypes, and phenotypes in the ABO blood group system.
4. Discuss the medical significance of the ABO blood group system.
5. Give examples of how different ABO blood types vary in their susceptibility to diseases.
6. Describe the Rhesus blood group system.
7. Relate Rhesus blood groups to blood transfusions.
8. What causes hemolytic disease of the newborn?

9. A woman is blood type O and Rh- and her husband is blood type AB and Rh+. Answer the following questions about this couple and their offspring.

   a. What are the possible genotypes of their offspring in terms of ABO blood group?

   b. What are the possible phenotypes of their offspring in terms of ABO blood group?

   c. Can the woman donate blood to her husband? Explain your answer.

   d. Can the man donate blood to his wife? Explain your answer.

10. *True or False.* The D antigen is part of the ABO blood group system.
11. Explain why hemolytic disease of the newborn may be more likely to occur in a second pregnancy than in a first.

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5.7: CARDIOVASCULAR DISEASE

HEART ATTACK ON A PLATE

Eating this greasy cheeseburger smothered in bacon may not literally cause a heart attack. However, regularly eating high-fat, low-fiber foods such as this may increase the risk of a heart attack or other type of cardiovascular disease. In fact, unhealthy lifestyle choices such as this may account for as many as 90 percent of cases of cardiovascular disease.



Figure 5.7.1: Bacon Cheeseburger

WHAT IS CARDIOVASCULAR DISEASE?

Cardiovascular disease is a class of diseases that involve the cardiovascular system. They include diseases of the coronary arteries that supply the heart muscle with oxygen and nutrients; diseases of arteries such as the carotid artery that provide blood flow to the brain; and diseases of the peripheral arteries that carry blood throughout the body. Worldwide, cardiovascular disease is the leading cause of death, causing about a third of all deaths each year.

Most cases of the cardiovascular disease occur in people over the age of 60, with disease onset typically being about a decade earlier in males than females. The LGBT (lesbian, gay, bisexual, and transgender) community belongs to almost every race, ethnicity, religion, age, and socioeconomic group. The LGBT youth are at a higher risk for cardiovascular diseases, obesity, anxiety, and depression as compared to the general population. LGBT youth receive poor quality of care due to stigma, lack of healthcare providers' awareness, and insensitivity to the unique needs of this community. Young LGBT individuals find it difficult to report their sexual identity to their clinicians. Some clinicians are not well trained in addressing the concerns of members of this community.

You can't control your age or sex, but you can control other factors that increase the risk of cardiovascular disease. Not smoking, maintaining a healthy weight, eating a healthy diet, taking medications as needed to control diabetes and cholesterol, and getting regular exercise are all ways to prevent cardiovascular disease or keep it from progressing. It should be noted that high blood lipid levels are definitely risk factors for cardiovascular disease. High levels of cholesterol in the diet do not appear to lead directly to high levels of cholesterol in the blood. Clearly, cardiovascular disease is multifactorial in terms of its causes.

PRECURSORS OF CARDIOVASCULAR DISEASE

There are two very common conditions that are precursors to virtually all cases of cardiovascular disease: hypertension (hypertension) and atherosclerosis (hardening of blood wall). Both conditions affect the arteries and their ability to maintain normal blood flow.

HYPERTENSION

Hypertension is a chronic medical condition in which the blood pressure in the arteries is persistently elevated, as defined in Table 5.7.1. Hypertension usually does not cause symptoms, so more than half of the people with high blood pressure are unaware of their condition. Hypertension is typically diagnosed when blood pressure is routinely measured during a medical visit for some other health problem.

Table 5.7.1: Classification of Blood Pressure (in Adults)

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Normal blood pressure	90-119	60-79
Prehypertension	120-139	80-89
Hypertension	140 or higher	90 or higher

High blood pressure is classified as either primary or secondary high blood pressure. At least 90% of cases are primary high blood pressure, which is caused by some combination of genetic and lifestyle factors. Numerous genes have been identified as having small effects on blood pressure. Lifestyle factors that increase the risk of high blood pressure include excess dietary salt and alcohol consumption in addition to the risk factors for cardiovascular disease stated above. Secondary high blood pressure, which makes up the remaining 10% of cases of hypertension, is attributable to chronic kidney disease or an endocrine disorder such as Cushing's disease.

Treating hypertension is important for reducing the risk of all types of cardiovascular disease, especially stroke. These and other complications of persistent high blood pressure are shown in Figure 5.7.2. Lifestyle changes, such as reducing salt intake and adopting a healthier diet may be all that is needed to lower blood pressure to the normal range. In many cases, however, medications are also required.

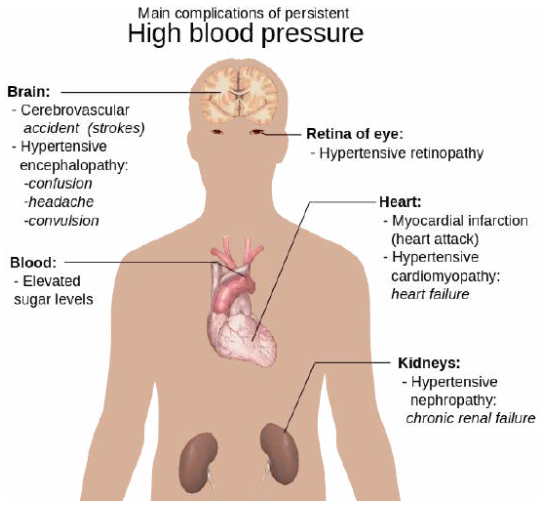


Figure **5.7.2**: If high blood pressure is not brought under control, it can eventually cause hypertensive retinopathy, myocardial infarction, heart failure, nephropathy, stokes, confusion, headache, convulsion, and elevated sugar levels.

ATHEROSCLEROSIS

Atherosclerosis is a condition in which artery walls thicken and stiffen as a result of the buildup of plaques inside the arteries. Plaques consist of white blood cells, cholesterol, and other fats. Typically, there is also a proliferation of smooth muscle cells that make the plaque fibrous as well as fatty. Over time, the plaques may harden with the addition of calcium crystals. This reduces the elasticity of the artery walls. As plaques increase in size, the artery walls dilate to compensate so blood flow is not affected. Eventually, however, the lumen of the arteries is likely to become so narrowed by plaque buildup that blood flow is reduced or even blocked entirely. Figure **5.7.3** illustrates the formation of a plaque in a coronary artery.

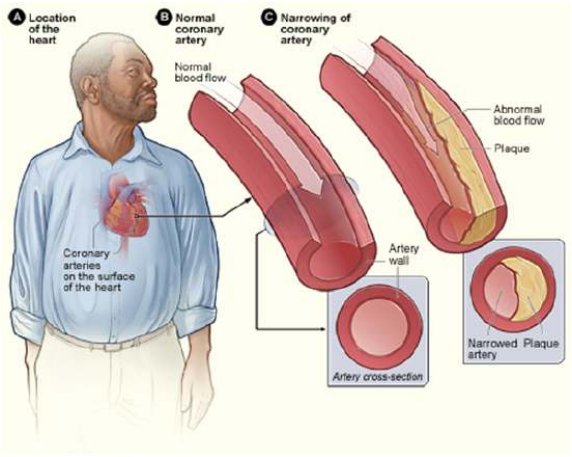


Figure **5.7.3**: Plaque accumulation in a coronary artery may reduce blood flow to cardiac muscle cells.

In most people, plaques start to form in arteries during childhood and progress throughout life. Individuals may develop just a few plaques or dozens of them. Plaques typically remain asymptomatic for decades. Signs and symptoms appear only after there is severe narrowing (stenosis) or complete blockage of arteries. As plaques increase in size and interfere with blood flow, they commonly lead to the formation of blood clots. These may plug arteries at the site of the plaque or travel elsewhere in the circulation. Sometimes plaques rupture or become detached from an arterial wall and become lodged in a smaller, downstream artery. Blockage of arteries by plaques or clots may cause a heart attack, stroke, or other potentially life-threatening cardiovascular events. If blood flow to the kidneys is affected, it may lead to chronic kidney disease.

The process in which plaques form is not yet fully understood, but it is thought that it begins when low-density lipoproteins (LDLs) accumulate inside endothelial cells in artery walls, causing inflammation. The inflammation attracts white blood cells that start to form a plaque. Continued inflammation and a cascade of other immune responses cause the plaque to keep growing. Risk factors for the development of atherosclerosis include hypertension, high cholesterol (especially LDL cholesterol), diabetes, and smoking. The chance of developing atherosclerosis also increases with age, male sex, and a family history of cardiovascular disease.

Treatment of atherosclerosis often includes both lifestyle changes and medications to lower cholesterol, control blood pressure, and reduce the risk of blood clot formation. In extreme cases or when other treatments are inadequate, surgery may be recommended. Surgery may involve the placement of stents in arteries to keep them open and improve blood flow or the use of grafts to divert blood flow around blocked arteries.

CORONARY ARTERY DISEASE

Coronary artery diseases are a group of diseases that result from atherosclerosis of coronary arteries. Treatment of the diseases mainly involves treating underlying atherosclerosis. Two of the most common coronary artery diseases are angina and myocardial infarction.

ANGINA

Angina is chest pain or pressure that occurs when heart muscle cells do not receive adequate blood flow and become starved of oxygen (a condition called ischemia). It is illustrated in Figure **5.7.4**. There may also be a pain in the back, neck, shoulders, or jaw; and in some cases, the pain may be accompanied by shortness of breath, sweating, or nausea. The main goals of the treatment of angina are relieving the symptoms and slowing the progression of underlying atherosclerosis.

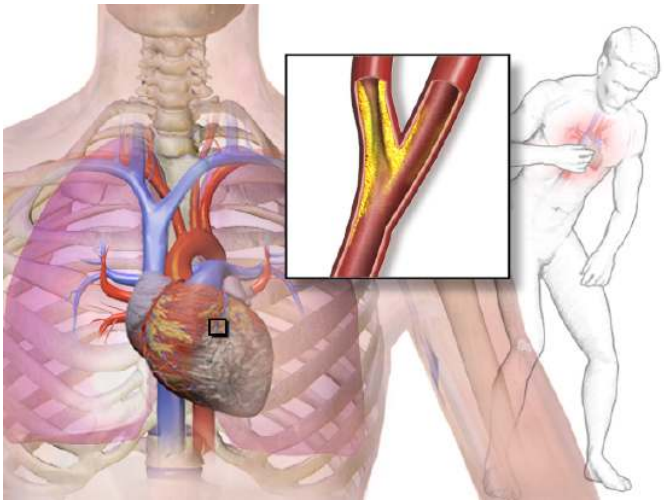


Figure 5.7.4: Angina is a pain in the chest due to reduced blood flow in coronary arteries so the heart muscle does not receive adequate oxygen.

Angina may be classified as either stable angina or unstable angina:

- Stable angina is angina in which pain is precipitated by exertion (say, from brisk walking or running) and improves quickly with rest or the administration of nitroglycerin, which dilates coronary arteries and improves blood flow. Stable angina may develop into unstable angina.
- Unstable angina is angina in which pain occurs during rest, lasts more than 15 minutes, and is of new onset. This type of angina is more dangerous and may be a sign of an imminent heart attack. It requires urgent medical attention.

MYOCARDIAL INFARCTION

A **myocardial infarction (MI)**, commonly known as a heart attack, occurs when blood flow stops to a part of the heart causing damage to the heart muscle and the death of myocardial cells. An MI usually occurs because of complete blockage of a coronary artery, often due to a blood clot or the rupture of a plaque (Figure 5.7.5). An MI typically causes chest pain and pressure, among other possible symptoms, but at least one-quarter of MIs do not cause any symptoms.

In the worst case, an MI may cause sudden death. Even if the patient survives, an MI often causes permanent damage to the heart. This puts the heart at risk of heart arrhythmias, heart failure, and cardiac arrest.

- Heart arrhythmias are abnormal heart rhythms, which are potentially life-threatening. Heart arrhythmias often can be interrupted with a cardiac defibrillator, which delivers an electrical shock to the heart, in effect “rebooting” it.
- Heart failure occurs when the pumping action of the heart is impaired so tissues do not get adequate oxygen. This is a chronic condition that tends to get worse over time, although it can be managed with medications.
- Cardiac arrest occurs when the heart no longer pumps blood or pumps blood so poorly that vital organs can no longer function. This is a medical emergency requiring immediate intervention.

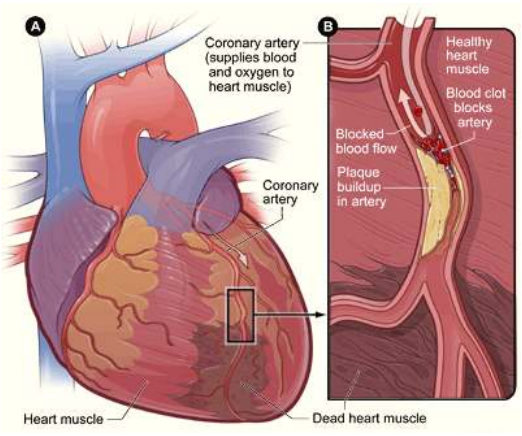


Figure 5.7.5: A myocardial infarction occurs when cardiac muscle cells die due to blockage of a coronary artery.

OTHER CARDIOVASCULAR DISEASES

Hypertension and atherosclerosis often cause other cardiovascular diseases. These commonly include stroke and peripheral artery disease.

STROKE

A **stroke,** also known as a cerebrovascular accident or brain attack, occurs when blocked or broken arteries in the brain result in the death of brain cells. There are two main types of stroke: ischemic stroke and hemorrhagic stroke. Ischemic storke is illustrated in Figure 5.7.6.

1. An ischemic stroke occurs when an embolus (blood clot) breaks off from a plaque or forms in the heart because of arrhythmia and travels to the brain where it becomes lodged in an artery. This blocks blood flow to the part of the brain that is served by arteries downstream from the blockage. Lack of oxygen causes the death of brain cells. Treatment with a clot-busting drug within a few hours of the stroke may prevent permanent damage. Almost 90 percent of strokes are ischemic strokes.
2. A hemorrhagic stroke occurs when an artery in the brain ruptures and causes bleeding in the brain. This deprives downstream tissues of adequate blood flow and also puts pressure on brain tissue. Both factors can lead to the death of brain cells. Surgery to temporarily open the cranium may be required to relieve the pressure. Only about 10 percent of strokes are hemorrhagic strokes, but they are more likely to be fatal than ischemic strokes.

In both types of stroke, the part of the brain that is damaged loses is the ability to function normally. Signs and symptoms of stroke may include an inability to move, feel, or see on one side of the body; problems understanding speech or difficulty speaking; memory problems; confusion; and dizziness. Hemorrhagic strokes may also cause a severe headache. The symptoms of a stroke usually occur within seconds or minutes of the brain injury. Depending on the severity of the stroke and how quickly treatment is provided, the symptoms may be temporary or permanent. If the symptoms of a stroke go away on their own in less than an hour or two, the stroke is

called a transient ischemic attack. Stroke is the leading cause of disability in the United States, but rehabilitation with physical, occupational, speech, or other types of therapy may significantly improve functioning.

The main risk factor for stroke is high blood pressure. Therefore, keeping blood pressure within the normal range, whether with lifestyle changes or medications, is the best way to reduce the risk of stroke. Another possible cause of stroke is the use of illicit drugs such as amphetamines or cocaine. Having had a stroke in the past greatly increases one's risk of future strokes. Men are also more likely than women to have strokes.

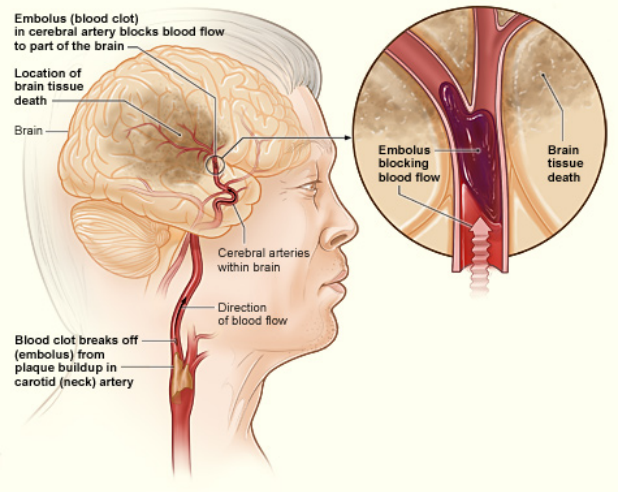


Figure **5.7.6**: In an ischemic stroke, brain cells die due to a blocked artery in the brain. The blockage happens when a blood clot breaks from a buildup in the carotid artery and blocks blood flow to part of the brain. As a result, the brain tissue dies. The traveling clot is called embolus.

PERIPHERAL ARTERY DISEASE

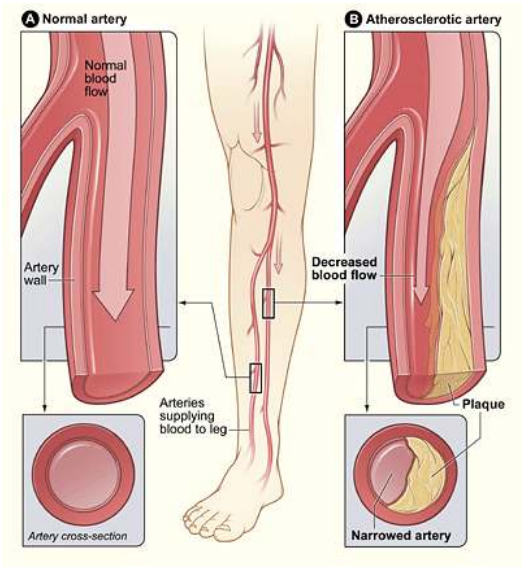


Figure **5.7.7**: Peripheral artery disease (PAD) develops when plaque accumulates in the wall of the leg artery. PAD typically causes pain and other symptoms because of decreased blood flow in the leg or other areas of the body served by peripheral arteries.

Peripheral artery disease (PAD) is the narrowing of the arteries other than those that supply the heart or brain due to atherosclerosis. Figure **5.7.7** shows how the PAD occurs. PAD most commonly affects the legs, but other arteries may also be involved. The classic symptom is leg pain when walking, which usually resolves with rest. This symptom is known as intermittent claudication. Other symptoms may include skin ulcers, bluish skin, cold skin, or poor nail and hair growth in the affected leg(s). However, up to half of all cases of PAD do not have any symptoms.

The main risk factor for PAD is smoking. Other risk factors include diabetes, high blood pressure, and high blood cholesterol. The underlying mechanism is usually atherosclerosis. PAD is typically diagnosed when blood pressure readings taken at the ankle are lower than blood pressure readings taken at the upper arm. It is important to diagnose PAD and treat underlying atherosclerosis because people with this disorder have a four to five times higher risk of myocardial infarction or stroke. Surgery to expand the affected arteries or to graft vessels in order to bypass blockages may be recommended in some cases.

FEATURE: MY HUMAN BODY

You read in this concept about the many dangers of hypertension. Do you know whether you have hypertension? The only way to know for sure is to have your blood pressure measured. Measuring blood pressure is quick and painless, but several measurements are needed to accurately diagnose hypertension. Some people have what is called "white coat disease." Their blood pressure rises just because they are being examined by a physician (in a white coat). Blood pressure also fluctuates from time to time due to factors such as hydration, stress, and time of day. Repeatedly measuring and recording your own blood pressure at home can provide your doctor with valuable diagnostic data. Digital blood pressure monitors for home use, like the one pictured in Figure **5.7.8**, are relatively inexpensive, easy to use, and available at most pharmacies.



Figure **5.7.8**: This personal blood pressure monitor is worn on the wrist.

REVIEW

1. What is cardiovascular disease? How much mortality do cardiovascular diseases cause?
2. List risk factors for cardiovascular disease.
3. What is hypertension?

4. Define atherosclerosis.
5. What is coronary artery disease?
6. Identify two specific coronary artery diseases.
7. Explain how a stroke occurs and how it affects the patient.
8. Describe the cause of peripheral artery disease.
9. What are two cardiovascular diseases that can be caused by atherosclerosis? Explain specifically how atherosclerosis contributes to each of them.
10. *True or False.* A heart attack is the same thing as cardiac arrest.
11. *True or False.* Plaques in arteries can cause blood clots.
12. What are the similarities between angina and ischemic stroke?
13. How can kidney disease be caused by problems in the cardiovascular system?
14. In peripheral artery disease, the blood pressure at the ankle is typically _____ the blood pressure at the upper arm.

    A. erratic compared to B. the same as

    C. higher than D. lower than
15. Name three components of the plaque that can build up in arteries.

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5.8: CASE STUDY CONCLUSION- FLIGHT AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: FLIGHT RISK

At the beginning of this chapter, you learned about Antônio and Ahaya, who met while sitting next to each other on a plane. During the flight, Ahaya got up to take frequent walks and was doing leg exercises to try to avoid the medical condition depicted in Figure 5.8.1—**deep vein thrombosis** (DVT). DVT occurs when a blood clot forms in a deep vein, usually in the leg. It can be very dangerous—even deadly.

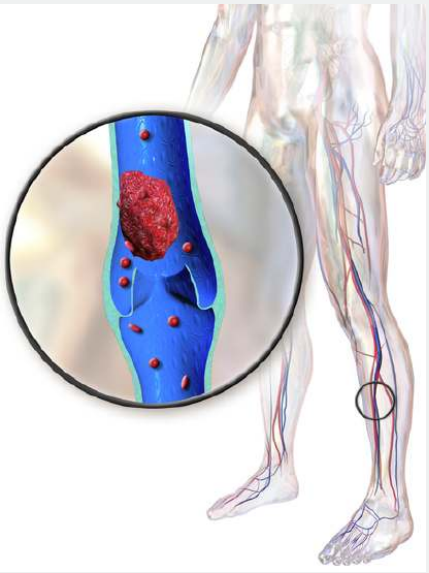


Figure **5.8.1**: Illustration of a blood clot in a deep vein in the leg, which is called deep vein thrombosis (DVT).

As you learned in this chapter, a blood clot is an aggregation of platelets and proteins. Blood clots are helpful to prevent blood loss when a blood vessel is damaged. But in some situations, they can be extremely dangerous. For example, blood clots can cause heart attacks or strokes by blocking the flow of blood to the heart or brain, respectively.

When DVT occurs, one of the major risks is pulmonary embolism (PE). PE is when the blood clot breaks off, travels through the blood vessels, and lodges in a pulmonary artery, like the blood clot shown in Figure **5.8.2**. Recall what the pulmonary arteries do: they carry deoxygenated blood from the heart to the lungs, where the blood picks up oxygen and releases carbon dioxide due to gas exchange between the capillaries and the alveoli of the lungs. Imagine what would happen if this flow of blood to the lungs was partially or completely blocked by a blood clot. Depending on the size of the blood clot and where it is lodged, a PE can cause a variety of serious consequences ranging from lung damage to instant death, because of the disruption of the pulmonary circulation.

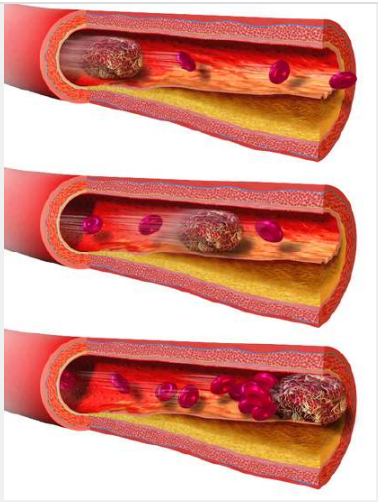


Figure **5.8.2**: Illustration of how a moving blood clot can get stuck in a blood vessel. When this occurs in a pulmonary artery, it is called a pulmonary embolism (PE).

Ahaya has a higher risk of DVT and its consequences because he has heart failure. As you have learned, heart failure is a chronic condition in which the pumping action of the heart is impaired. One reason that heart failure is thought to increase the risk of DVT is that the blood is not being pushed strongly enough through the cardiovascular system, allowing blood clots to form more easily.

Ahaya needs to be particularly concerned about DVT while on a long plane flight. Why do you think this is? Think about how blood flows through arteries and veins. Blood is pushed through arteries mainly due to the pumping action of the heart. Veins, on the other hand, rely on the movement of the surrounding skeletal muscles to help push blood through them. Sitting still for long periods of time in cramped quarters, such as on a plane, can cause blood to pool in the deep veins of the legs. This can lead to the formation of a blood clot.

CHAPTER SUMMARY

In this chapter, you learned about the structure, functions, and disorders of the cardiovascular system. Specifically, you learned that:

- The cardiovascular system is the organ system that transports materials to and from all the cells of the body. The main components of the cardiovascular system are the heart, blood vessels, and blood.
- The cardiovascular system has two interconnected circulations. The pulmonary circulation carries blood between the heart and lungs, where blood is oxygenated. The systemic circulation carries blood between the heart and the rest of the body, where it delivers oxygen.
- The heart is a muscular organ in the chest that consists mainly of cardiac muscle and pumps blood through blood vessels by repeated, rhythmic contractions.

- The wall of the heart consists of three layers. The middle layer, the myocardium, is the thickest layer and consists mainly of cardiac muscle.
- The interior of the heart consists of four chambers, with an upper atrium and lower ventricle on each side of the heart. Blood enters the heart through the atria, which pump it to the ventricles. Then the ventricles pump blood out of the heart. Four valves in the heart keep blood flowing in the correct direction and prevent backflow.
- Deoxygenated blood flows into the right atrium through veins from the upper and lower body (superior and inferior vena cava, respectively), and oxygenated blood flows into the left atrium through four pulmonary veins from the lungs. Each atrium pumps the blood to the ventricle below it. From the right ventricle, deoxygenated blood is pumped to the lungs through the two pulmonary arteries. From the left ventricle, oxygenated blood is pumped to the rest of the body through the aorta.
- The coronary circulation consists of blood vessels that carry blood to and from the heart muscle cells. There are two coronary arteries that supply the two sides of the heart with oxygenated blood. Cardiac veins drain deoxygenated blood back into the heart.
- The cardiac cycle refers to a single complete heartbeat. It includes diastole when the atria contract; and systole when the ventricles contract.
- The normal, rhythmic beating of the heart is called sinus rhythm. It is established by the heart's pacemaker cells in the sinoatrial node. Electrical signals from the pacemaker cells travel to the atria and cause them to contract. Then the signals travel to the atrioventricular node and from there to the ventricles, causing them to contract. Electrical stimulation from the autonomic nervous system and hormones from the endocrine system can also influence heartbeat.

- Blood vessels carry blood throughout the body. Major types of blood vessels are arteries, veins, and capillaries.
  - Arteries are blood vessels that usually carry blood away from the heart (except for coronary arteries that supply the heart muscle with blood). Most arteries carry oxygenated blood. The largest artery is the aorta, which is connected to the heart and extends into the abdomen. Blood moves through arteries due to pressure from the beating of the heart.
  - Veins are blood vessels that usually carry blood toward the heart. Most veins carry deoxygenated blood. The largest veins are the superior and inferior venae cavae. Blood moves through veins by the squeezing action of surrounding skeletal muscles. Valves in veins prevent the backflow of blood.
  - Capillaries are the smallest blood vessels. They connect arterioles and venules. They form capillary beds where substances are exchanged between the blood and surrounding tissues.
  - The walls of arteries and veins have three layers. The middle layer is thickest in arteries, in which it contains smooth muscle tissue that controls the diameter of the vessels. The outer layer is thickest in veins and consists mainly of connective tissue. The walls of capillaries consist of little more than a single layer of epithelial cells.
  - Blood pressure is a measure of the force that blood exerts on the walls of arteries. It is expressed as a double number, with the higher number representing systolic pressure when the ventricles contract and the lower number representing diastolic pressure when the ventricles relax. Normal blood pressure is generally defined as a pressure of 120/80 mm Hg or less.
  - Vasoconstriction (narrowing) and vasodilation (widening) of arteries can occur to help regulate blood pressure or body temperature or to change blood flow as part of the fight-or-flight response.
- Blood is a fluid connective tissue that circulates throughout the body in blood vessels. Blood supplies tissues with oxygen and nutrients and removes their metabolic wastes. Blood helps defend the body from pathogens and other threats, transports hormones and other substances, and helps to keep the body's pH and temperature in homeostasis. Blood consists of a liquid part, called plasma, and cells, including red blood cells, white blood cells, and platelets.
  - Plasma makes up more than half of blood by volume. It consists of water and many dissolved substances. Blood also contains blood cells and platelets.
  - Red blood cells are the most numerous cells in the blood and consist mostly of hemoglobin, which carries oxygen. Red blood cells also carry antigens that determine blood types. White blood cells are less numerous than red blood cells and are part of the body's immune system. They protect the body from abnormal cells, microorganisms, and other harmful substances. There are several different types of white blood cells that differ in their specific immune functions.
  - Platelets are cell fragments that play important roles in blood clotting or coagulation. They stick together at breaks in blood vessels to form a clot and stimulate the production of fibrin, which strengthens the clot.
  - All blood cells form by the proliferation of stem cells in red bone marrow in a process called hematopoiesis. When blood cells die, they are phagocytized by white blood cells and removed from circulation.
  - Disorders of the blood include leukemia, which is a cancer of the bone-forming cells; hemophilia, which is any of several genetic blood-clotting disorders; carbon monoxide poisoning, which prevents red blood cells from binding with oxygen and causes suffocation; HIV infection, which destroys certain white blood cells and can cause AIDS; and anemia, in which there are not enough red blood cells to carry adequate oxygen to body tissues.
- Blood type (or blood group) is a genetic characteristic associated with the presence or absence of antigens on the surface of red blood cells. A blood group system refers to all of the gene(s),

alleles, and possible genotypes and phenotypes that exist for a particular set of blood type antigens.

- Cardiovascular disease is a class of diseases that involve the cardiovascular system. Worldwide, it is the leading cause of death. Most cases occur in people over age 60, and onset is typically about a decade earlier in males than females. Other risk factors include smoking, obesity, diabetes, high blood cholesterol, and lack of exercise.
- Antigens are molecules that the immune system identifies as either self or nonself. If antigens are identified as nonself, the immune system responds by forming antibodies that are specific to the nonself antigens, leading to the destruction of cells bearing the antigens.
- The ABO blood group system is a system of red blood cell antigens controlled by a single gene with three common alleles on chromosome 9. There are four possible ABO blood types: A, B, AB, and O. The ABO system is the most important blood group system in blood transfusions. People with type O blood are universal donors, and people with type AB blood are universal recipients.
- The Rhesus blood group system is a system of red blood cell antigens controlled by two genes with many alleles on chromosome 1. There are five common Rhesus antigens, of which antigen D is most significant. Individuals who have antigen D are called Rh+, and individuals who lack antigen D are called Rh-. Rh- mothers of Rh+ fetuses may produce antibodies against the D antigen in the fetal blood, causing hemolytic disease of the newborn (HDN).

- Two common conditions that lead to most cases of cardiovascular disease are hypertension and atherosclerosis. Hypertension is blood pressure that is persistently at or above 140/90 mm Hg. Atherosclerosis is a buildup of fatty, fibrous plaques in arteries that may reduce or block blood flow. Treating these conditions is important for preventing cardiovascular disease.
  - Coronary artery disease is a group of diseases that result from atherosclerosis of coronary arteries. Two of the most common are angina and myocardial infarction (heart attack). In angina, cardiac cells receive inadequate oxygen, which causes chest pain. In a heart attack, cardiac cells die because blood flow to part of the heart is blocked. A heart attack may cause death or lead to heart arrhythmias, heart failure, or cardiac arrest.
  - A stroke occurs when blocked or broken arteries in the brain result in the death of brain cells. This may occur when an artery is blocked by a clot or plaque or when an artery ruptures and bleeds in the brain. In both cases, part of the brain is damaged and functions such as speech and controlled movements may be impaired, either temporarily or permanently.
  - Peripheral artery disease occurs when atherosclerosis narrows peripheral arteries, usually in the legs, often causing pain when walking. It is important to diagnose this disease so underlying atherosclerosis can be treated before it causes a heart attack or stroke.

In this chapter, you learned that the cardiovascular system carries nutrients to the cells of the body. Read the next chapter about the Digestive System to learn about how your body transforms your meals into the nutrients that cells need to function.

CHAPTER SUMMARY REVIEW QUESTIONS

1. Alex goes to the doctor and learns that his blood pressure is 135/90 mm Hg. Answer the following questions about his blood pressure.
   A. Is this normal blood pressure? Why or why not?
   B. Which number refers to the systolic pressure and which number refers to the diastolic pressure?
   C. Describe what the atria and ventricles of Alex's heart are doing when the pressure is at 135 mm Hg.
   D. Alex's doctor would like him to lower his blood pressure. Why do you think he would like Alex to do this and what are some ways in which he may be able to lower his blood pressure?
2. What are the three functions of the cardiovascular system?
3. What is the watery part of the blood called?
4. Which are the chambers of the heart that receive blood? Which are the chambers of the heart that pump blood out of the heart?
5. Which chambers of the heart contain deoxygenated blood?
   A. Right and left atria
   B. Right and left ventricles
   C. Right atrium and right ventricle
   D. Left atrium and left ventricle
6. What are two different places in the cardiovascular system where valves are located?
7. Valves prevent blood from flowing backward in the cardiovascular system. Why do you think this is important?
8. Explain how pacemaker cells in the heart work together with the nervous system to regulate the beating of the heart.
9. *True or False.* Red marrow is the source of white blood cells.
10. *True or False.* Plaques that build up in arteries are made completely of fats.
11. The aorta is:
    A. An artery
    B. A chamber of the heart
    C. A vein
    D. A valve
12. Compare the coronary arteries, pulmonary arteries, and arteries elsewhere in the body in terms of their target tissues (i.e. where they bring blood to) and whether they are carrying oxygenated or deoxygenated blood.
13. The superior vena cava empties into which structure of the heart? The inferior vena cava empties into which structure of the heart?
    A. right atrium; left atrium
    B. right atrium; right atrium

C. right atrium; right ventricle
D. right ventricle; left ventricle

14. Venules receive blood from what?
15. Define blood type and blood group system. Explain the relationship between antigens and antibodies.
16. Identify the alleles, genotypes, and phenotypes in the ABO blood group system.
17. Discuss the medical significance of the ABO blood group system.
18. Give examples of how different ABO blood types vary in their susceptibility to diseases.
19. Describe the Rhesus blood group system.
20. Relate Rhesus blood groups to blood transfusions.
21. What causes hemolytic disease of the newborn?
22. A woman is blood type O and Rh- and her husband is blood type AB and Rh+. Answer the following questions about this couple and their offspring.
    A. What are the possible genotypes of their offspring in terms of ABO blood group?
    B. What are the possible phenotypes of their offspring in terms of ABO blood group?
    C. Can the woman donate blood to her husband? Explain your answer.
    D. Can the man donate blood to his wife? Explain your answer.
23. *True or False.* The D antigen is part of the ABO blood group system.
24. Explain why hemolytic disease of the newborn may be more likely to occur in a second pregnancy than in a first.
25. Anemia causes weakness and fatigue due to a reduction in the amount of oxygen that gets to the cells of the body. Explain how oxygen is transported to the cells of the body and which blood cells are affected in anemia.
26. What are the two conditions that are precursors to virtually all cases of cardiovascular disease?
27. What is another name for a heart attack?
    A. Heart arrhythmia
    B. Myocardial infarction
    C. Angina
    D. Heart failure
28. *True or False.* Strokes can be due to a blood clot or to a broken artery.
29. *True or False.* After an injury to a blood vessel, platelets respond by losing their nuclei.
30. What are the main differences between coronary circulation, pulmonary circulation, and systemic circulation?
31. Define the term *sinus rhythm.*
32. Which is generally a more serious and immediately life-threatening condition: heart failure or cardiac arrest? Explain your answer.
33. Match each of the following descriptions to the disease or disorder from the list below that *best* matches it. Use each disease or disorder only once. Diseases and disorders: hypertension; atherosclerosis; coronary artery disease; peripheral artery disease
    A. Blood flow to the muscle cells of the heart is impaired.
    B. Blood pressure is too high.
    C. Arteries in the legs specifically become more narrow.
    D. Plaque builds up in arteries (in general).

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CHAPTER OVERVIEW

6: RESPIRATORY SYSTEM

This chapter describes the structure and function of the respiratory system, including how breathing occurs and what controls it, as well as how the process of gas exchange takes place in the lungs. The chapter also describes several disorders of the respiratory system and details the adverse health effects of smoking.

6.1: Case Study- Respiratory System and Gas Exchange

6.2: Structure and Function of the Respiratory System

6.3: Breathing

6.4: Disorders of the Respiratory System

6.5: Smoking and Health

6.6: Case Study Conclusion- Bronchitis and Chapter Summary

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6.1: CASE STUDY- RESPIRATORY SYSTEM AND GAS EXCHANGE

CASE STUDY: COUGH THAT WON'T QUIT

Three weeks ago, 20-year-old Sacheen came down with symptoms typical of the common cold. She had a runny nose, fatigue, and a mild cough. Her symptoms had been starting to improve, but recently her cough has been getting worse. She coughs up a lot of thick mucus, her throat is sore from frequent coughing, and her chest feels very congested. According to her wife, Sacheen has a "chest cold." Sacheen is a smoker and wonders if her habit is making her cough worse. She decides that it is time to see a doctor.



Figure **6.1.1**: Coughing

Dr. Tsosie examines Sacheen and asks about her symptoms and health history. She checks the level of oxygen in Sacheen's blood by attaching a device called a pulse oximeter to Sacheen's finger (Figure **6.1.2**). Dr. Tsosie concludes that Sacheen has bronchitis, an infection that commonly occurs after a person has a cold or flu. Bronchitis is sometimes referred to as a "chest cold," so Sacheen's wife was right! Bronchitis causes inflammation and a build-up of mucus in the bronchial tubes in the chest.



Figure **6.1.2**: A pulse oximeter, used to measure blood oxygen levels.

Because viruses, and not bacteria, usually cause bronchitis, Dr. Tsosie tells Sacheen that antibiotics are not likely to help. Instead, she recommends that Sacheen try to thin and remove the mucus by drinking plenty of fluids and using a humidifier, or spending time in a steamy shower. She also recommends that Sacheen get plenty of rest.

Dr. Tsosie also tells Sacheen some things *not* to do—most importantly, not to smoke while she is sick and to try to quit smoking in the long term. She explains that smoking can make people more susceptible to bronchitis and can hinder recovery. She also advises Sacheen not to take over-the-counter cough suppressant medication.

As you read this chapter on the respiratory system, you will better understand what bronchitis is and why Dr. Tsosie made the treatment recommendations that she did. At the end of the chapter, you will learn more about acute bronchitis, which is the type that Sacheen has. This information may come in handy to you personally because the chances are high that you will get this common infection at some point in your life—there are millions of bronchitis cases every year!

CHAPTER OVERVIEW: RESPIRATORY SYSTEM

In this chapter, you will learn about the respiratory system, the system that exchanges gases such as oxygen and carbon dioxide between the body and the outside air. Specifically, you will learn about:

- The process of respiration, in which oxygen moves from the outside air into the body and carbon dioxide and other waste gases move from inside the body into the outside air.
- The organs of the respiratory system, including the lungs, bronchial tubes, and the rest of the respiratory tract.
- How the respiratory tract protects itself from pathogens and other potentially harmful substances in the air.
- How the rate of breathing is regulated to maintain homeostasis of blood gases and pH.
- How ventilation, or breathing, allows us to inhale air into the body and exhale air out of the body.
- The conscious and unconscious control of breathing.
- Nasal breathing compared to mouth breathing.
- What happens when a person is drowning.
- How gas exchange occurs between the air and blood in the alveoli of the lungs, and between the blood and cells throughout the body.
- Disorders of the respiratory system, including asthma, pneumonia, chronic obstructive pulmonary disease (COPD), and lung cancer.
- The negative health effects of smoking.

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

1. Where are the bronchial tubes, and what is their function?
2. What is the function of mucus, and why can too much mucus be a bad thing?
3. Why did Dr. Tsosie check Sacheen's blood oxygen level?
4. Why do you think Dr. Tsosie warned Sacheen not to take cough suppressant medications?
5. How does acute bronchitis compare to chronic bronchitis, and how do they both relate to smoking?

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6.2: STRUCTURE AND FUNCTION OF THE RESPIRATORY SYSTEM

SEEING YOUR BREATH

Why can you "see your breath" on a cold day? The air you exhale through your nose and mouth is warm, like the inside of your body. Exhaled air also contains a lot of water vapor because it passes over moist surfaces from the lungs to the nose or mouth. The water vapor in your breath cools suddenly when it reaches the much colder outside air. This causes the water vapor to condense into a fog of tiny droplets of liquid water. You release water vapor and other gases from your body through the process of respiration.



Figure **6.2.1**: Breath on a cold day

WHAT IS RESPIRATION?

Respiration is the life-sustaining process in which gases are exchanged between the body and the outside atmosphere. Specifically, oxygen moves from the outside air into the body; and water vapor, carbon dioxide, and other waste gases move from inside the body into the outside air. Respiration is carried out mainly by the **respiratory system.** It is important to note that respiration by the respiratory system is not the same process as cellular respiration that occurs inside cells, although the two processes are closely connected. Cellular respiration is the metabolic process in which cells obtain energy, usually by "burning" glucose in the presence of oxygen. When cellular respiration is aerobic, it uses oxygen and releases carbon dioxide as a waste product. Respiration by the respiratory system supplies the oxygen needed by cells for aerobic cellular respiration and removes the carbon dioxide produced by cells during cellular respiration.

Respiration by the respiratory system actually involves two subsidiary processes. One process is ventilation or breathing. This is the physical process of conducting air to and from the lungs. The other process is gas exchange. This is the biochemical process in which oxygen diffuses out of the air and into the blood while carbon dioxide and other waste gases diffuse out of the blood and into the air. All of the organs of the respiratory system are involved in breathing, but only the lungs are involved in gas exchange.

RESPIRATORY ORGANS

The organs of the respiratory system form a continuous system of passages called the **respiratory tract,** through which air flows into and out of the body. The respiratory tract has two major divisions: the upper respiratory tract and the lower respiratory tract. The organs in each division are shown in Figure **6.2.2**. In addition to these organs, certain muscles of the thorax (the body cavity that fills the chest) are also involved in respiration by enabling breathing. Most important is a large muscle called the diaphragm, which lies below the lungs and separates the thorax from the abdomen. Smaller muscles between the ribs also play a role in breathing. You can learn more about breathing muscles in the concept of *Breathing*.

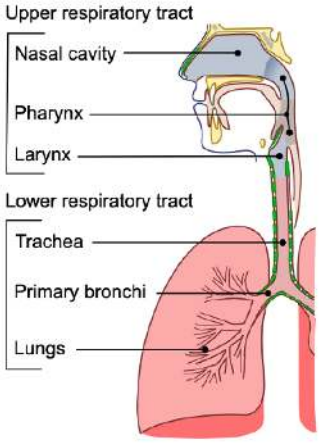


Figure **6.2.2**: During breathing, inhaled air enters the body through the nose and passes through the pharynx, larynx, trachea, bronchi, and then enters the lungs. Exhaled air travels from the lungs in the opposite direction.

UPPER RESPIRATORY TRACT

All of the organs and other structures of the upper respiratory tract are involved in the conduction or the movement of air into and out of the body. Upper respiratory tract organs provide a route for air to move between the outside atmosphere and the lungs. They also clean, humidity, and warm the incoming air. However, no gas exchange occurs in these organs.

NASAL CAVITY

The **nasal cavity** is a large, air-filled space in the skull above and behind the nose in the middle of the face. It is a continuation of the two nostrils. As inhaled air flows through the nasal cavity, it is warmed and humidified. Hairs in the nose help trap larger foreign particles in the air before they go deeper into the respiratory tract. In addition to its respiratory functions, the nasal cavity also contains chemoreceptors that are needed for the sense of smell and that contribute importantly to the sense of taste.

PHARYNX

The **pharynx** is a tube-like structure that connects the nasal cavity and the back of the mouth to other structures lower in the throat, including the larynx. The pharynx has dual functions: both air and

food (or other swallowed substances) pass through it, so it is part of both the respiratory and digestive systems. Air passes from the nasal cavity through the pharynx to the larynx (as well as in the opposite direction). Food passes from the mouth through the pharynx to the esophagus.

LARYNX

The **larynx** connects the pharynx and trachea and helps to conduct air through the respiratory tract. The larynx is also called the voice box because it contains the vocal cords, which vibrate when air flows over them, thereby producing sound. You can see the vocal cords in the larynx in Figure **6.2.3**. Certain muscles in the larynx move the vocal cords apart to allow breathing. Other muscles in the larynx move the vocal cords together to allow the production of vocal sounds. The latter muscles also control the pitch of sounds and help control their volume.

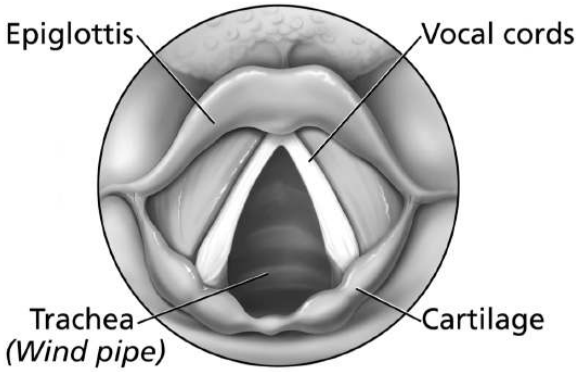


Figure **6.2.3**: The larynx is viewed from the top. opening to the trachea is closed by epiglottis during swallowing. Cartilage and vocal cords are also visible.

A very important function of the larynx is protecting the trachea from aspirated food. When swallowing occurs, the backward motion of the tongue forces a flap called the epiglottis to close over the entrance to the larynx. You can see the epiglottis in Figure **6.2.3**. This prevents swallowed material from entering the larynx and moving deeper into the respiratory tract. If swallowed material does start to enter the larynx, it irritates the larynx and stimulates a strong cough reflex. This generally expels the material out of the larynx and into the throat.

LOWER RESPIRATORY TRACT

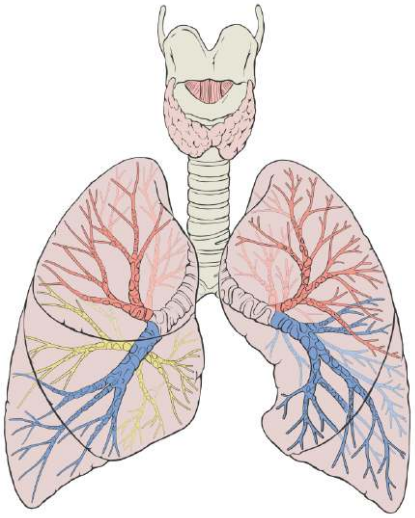


Figure **6.2.4**: This diagram illustrates the tree-like branching of the passages of the lower respiratory tract within the lungs.

The trachea and other passages of the lower respiratory tract conduct air between the upper respiratory tract and the lungs. These passages form an inverted tree-like shape (Figure **6.2.4**), with repeated branching as they move deeper into the lungs. All told, there are an astonishing 1,500 miles of airways conducting air through the human respiratory tract! It is only in the lungs, however, that gas exchange occurs between the air and the bloodstream.

TRACHEA

The **trachea,** or windpipe, is the widest passageway in the respiratory tract. It is about 2.5 cm (1 in.) wide and 10-15 cm (4-6 in.) long. It is formed by rings of cartilage, which make it relatively strong and resilient. The trachea connects the larynx to the lungs for the passage of air through the respiratory tract. The trachea branches at the bottom to form two bronchial tubes.

BRONCHI AND BRONCHIOLES

There are two main bronchial tubes, or **bronchi (singular, bronchus)**, called the right and left bronchi. The bronchi carry air between the trachea and lungs. Each bronchus branches into smaller, secondary bronchi; and secondary bronchi branch into still smaller tertiary bronchi. The smallest bronchi branch into very small tubules called bronchioles. The tiniest bronchioles end in alveolar ducts, which terminate in clusters of minuscule air sacs, called alveoli (singular, alveolus), in the lungs.

LUNGS

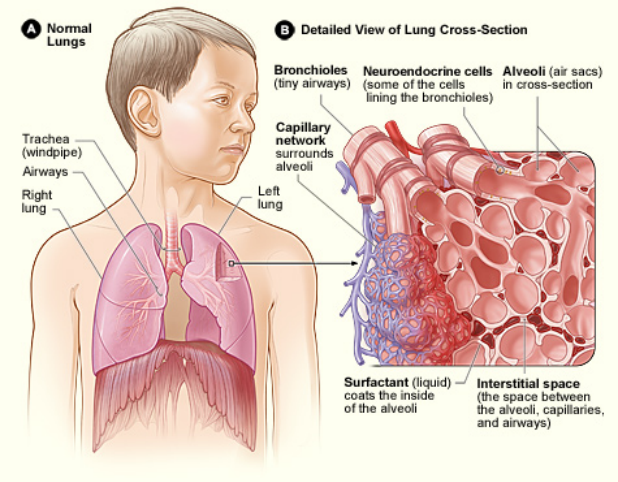


Figure **6.2.5**: The cross-section of lung tissue on the right shows the alveoli in which gas exchange takes place with the capillary network that surrounds them. Neuroendocrine cells lining the bronchioles control their diameter and the flow of air through them. A surfactant is a liquid that covers the inside of the alveoli and prevents them from collapsing and sticking together when air empties out of them during exhalation.

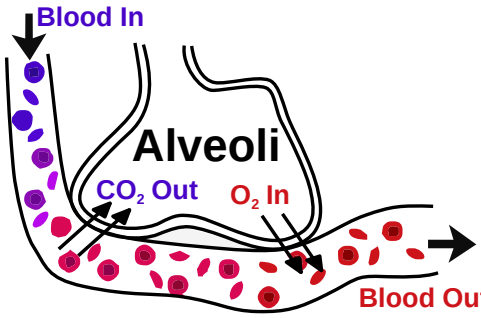


Figure **6.2.6**: The gaseous exchange between blood and outside air inside the lung alveoli.

The **lungs** are the largest organs of the respiratory tract. They are suspended within the pleural cavity of the thorax. In Figure **6.2.5**, you can see that each of the two lungs is divided into sections. These are called lobes, and they are separated from each other by connective tissues. The right lung is larger and contains three lobes. The left lung is smaller and contains only two lobes. The smaller left lung allows room for the heart, which is just left of the center of the chest.

Lung tissue consists mainly of alveoli (Figure **6.2.6**). These tiny air sacs are the functional units of the lungs where gas exchange takes place. The two lungs may contain as many as 700 million alveoli, providing a huge total surface area for gas exchange to take place. In fact, alveoli in the two lungs provide as much surface area as half a tennis court! Each time you breathe in, the alveoli fill with air, making the lungs expand. Oxygen in the air inside the alveoli is absorbed by the blood in the mesh-like network of tiny capillaries that surrounds each alveolus. The blood in these capillaries also releases carbon dioxide into the air inside the alveoli. Each time you breathe out, air leaves the alveoli and rushes into the outside atmosphere, carrying waste gases with it.

The lungs receive blood from two major sources. They receive deoxygenated blood from the heart. This blood absorbs oxygen in the lungs and carries it back to the heart to be pumped to cells throughout the body. The lungs also receive oxygenated blood from the heart that provides oxygen to the cells of the lungs for cellular respiration.

PROTECTING THE RESPIRATORY SYSTEM

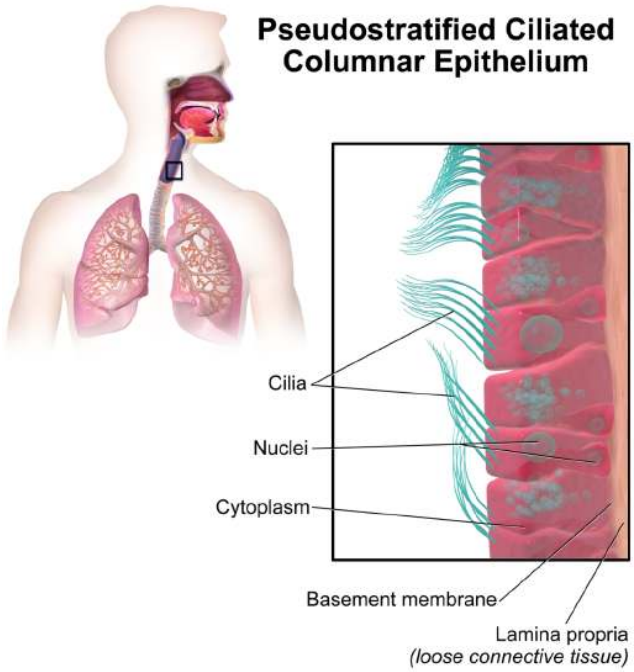


Figure **6.2.7**: The upward sweeping motion of cilia lining the respiratory tract helps keep it free from dust, pathogens, and other harmful substances.

You may be able to survive for weeks without food and for days without water, but you can survive without oxygen for only a matter of minutes except under exceptional circumstances. Therefore, protecting the respiratory system is vital. That's why making sure a patient has an open airway is the first step in treating many medical emergencies. Fortunately, the respiratory system is well protected by the ribcage of the skeletal system. However, the extensive surface area of the respiratory system is directly exposed to the outside world and all its potential dangers in inhaled air. Therefore, it should come as no surprise that the respiratory system has a variety of ways to protect itself from harmful substances such as dust and pathogens in the air.

The main way the respiratory system protects itself is called the mucociliary escalator. From the nose through the bronchi, the respiratory tract is covered in the epithelium that contains mucus-secreting goblet cells. The mucus traps particles and pathogens in the incoming air. The epithelium of the respiratory tract is also covered with tiny cell projections called cilia (singular, cilium), as shown in Figure **6.2.7**. The cilia constantly move in a sweeping motion upward toward the throat, moving the mucus and trapped particles and pathogens away from the lungs and toward the outside of the body.

What happens to the material that moves up the mucociliary escalator to the throat? It is generally removed from the respiratory tract by clearing the throat or coughing. Coughing is a largely involuntary response of the respiratory system that occurs when nerves lining the airways are irritated. The response causes air to be expelled forcefully from the trachea, helping to remove mucus and any debris it contains (called phlegm) from the upper respiratory tract to the mouth. The phlegm may spit out (expectorated), or it may be swallowed and destroyed by stomach acids.

Sneezing is a similar involuntary response that occurs when nerves lining the nasal passage are irritated. It results in forceful expulsion of air from the mouth, which sprays millions of tiny droplets of mucus and other debris out of the mouth and into the air, as shown in Figure **6.2.8**. This explains why it is so important to sneeze into a sleeve rather than the air to help prevent the transmission of respiratory pathogens.



Figure **6.2.8**: Sneezing results in tiny particles from the mouth being forcefully ejected into the air.

HOW THE RESPIRATORY SYSTEM WORKS WITH OTHER ORGAN SYSTEMS

The amount of oxygen and carbon dioxide in the blood must be maintained within a limited range for the survival of the organism. Cells cannot survive for long without oxygen, and if there is too much carbon dioxide in the blood, the blood becomes dangerously acidic (pH is too low). Conversely, if there is too little carbon dioxide in the blood, the blood becomes too basic (pH is too high). The respiratory system works hand-in-hand with the nervous and cardiovascular systems to maintain homeostasis in blood gases and pH.

It is the level of carbon dioxide rather than the level of oxygen that is most closely monitored to maintain blood gas and pH homeostasis. The level of carbon dioxide in the blood is detected by cells in the brain, which speed up or slow down the rate of breathing through the autonomic nervous system as needed to bring the carbon dioxide level within the normal range. Faster breathing lowers the carbon dioxide level (and raises the oxygen level and pH); slower breathing has the opposite effects. In this way, the levels of carbon dioxide and oxygen, as well as pH, are maintained within normal limits.

The respiratory system also works closely with the cardiovascular system to maintain homeostasis. The respiratory system exchanges gases between the blood and the outside air, but it needs the cardiovascular system to carry them to and from body cells. Oxygen is absorbed by the blood in the lungs and then transported through a vast network of blood vessels to cells throughout the body where it is needed for aerobic cellular respiration. The same system absorbs carbon dioxide from cells and carries it to the respiratory system for removal from the body.

FEATURE: MY HUMAN BODY

Choking is the mechanical obstruction of the flow of air from the atmosphere into the lungs. It prevents breathing and may be partial or complete. Partial choking allows some though inadequate airflow into the lung—prolonged or complete choking results in asphyxia, or suffocation, which is potentially fatal.

Obstruction of the airway typically occurs in the pharynx or trachea. Young children are more prone to choking than are older people, in part because they often put small objects in their mouths and do not appreciate the risk of choking that they pose. Young children may choke on small toys or parts of toys or on household objects in addition to food. Foods that can adapt their shape to that of the pharynx, such as bananas and marshmallows, are especially dangerous and may cause choking in adults as well as children.

How can you tell if a loved one is choking? The person cannot speak or cry out or has great difficulty doing so. Breathing, if possible, is labored, producing gasping or wheezing. The person may desperately clutch at his or her throat or mouth. If breathing is not soon restored, the person's face will start to turn blue from lack of oxygen. This will be followed by unconsciousness if oxygen deprivation continues beyond a few minutes.

If an infant is choking, turning the baby upside down and slapping on the back may dislodge the obstructing object. To help an older person who is choking, first, encourage the person to cough. Give them a few hardback slaps to help force the lodged object out of the airway. If these steps fail, perform the Heimlich maneuver on the person. You can easily find instructional videos online to learn how to do it. If the Heimlich maneuver also fails, call for emergency medical care immediately.



Figure **6.2.9**: The Heimlich maneuver may be needed to help force an aspirated object out of the respiratory tract.

REVIEW

1. What is respiration, as carried out by the respiratory system? Name the two subsidiary processes it involves.
2. Describe the respiratory tract.
3. Identify the organs of the upper respiratory tract, and state their functions.
4. List the organs of the lower respiratory tract. Which organs are involved only in conduction?
5. Where does gas exchange take place?
6. How does the respiratory system protect itself from potentially harmful substances in the air?
7. Explain how the rate of breathing is controlled.
8. Why does the respiratory system need the cardiovascular system to help it perform its main function of gas exchange?
9. Place the following organs or structures of the respiratory system in order of when they are encountered by air entering the body — from earliest to latest.

   trachea; nasal cavity; alveoli; bronchioles; larynx; bronchi; pharynx
10. Which organ is part of both the digestive and respiratory systems?

    A. Larynx

    B. Trachea

    C. Pharynx

    D. Bronchus
11. Describe two ways in which the body prevents food from entering the lungs.
12. *True or False.* The lungs receive some oxygenated blood.
13. *True or False.* Gas exchange occurs in both the upper and lower respiratory tracts.
14. Coughing can expel _____ from the body.

    A. mucus

    B. food particles

    C. phlegm

    D. All of the above
15. What is the relationship between respiration and cellular respiration?

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6.3: BREATHING

DOING THE 'FLY

The swimmer in this photo is doing the butterfly stroke. This swimming style requires the swimmer to carefully control his breathing so it is coordinated with his swimming movements. Breathing is the process of moving air into and out of the lungs, which are the organs in which gas exchange takes place between the atmosphere and the body. Breathing is also called **ventilation,** and it is one of two parts of the life-sustaining process of respiration, the other part being gas exchange. Before you can understand how breathing is controlled, you need to know how breathing occurs.



Figure **6.3.1**: Butterfly stroke

HOW BREATHING OCCURS

Breathing is a two-step process that includes drawing air into the lungs, or inhaling, and letting the air out of the lungs, or exhaling. Both processes are illustrated in Figure **6.3.2**.

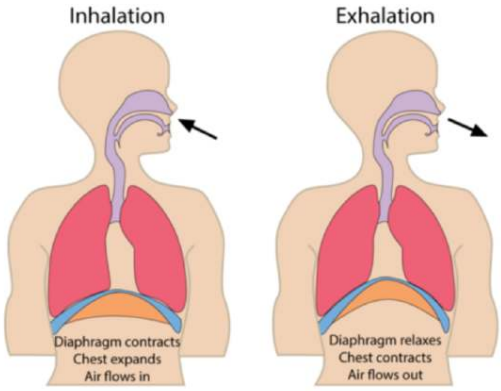


Figure **6.3.2**: Inhalation and exhalation during breathing depend mainly on repeated contractions of the diaphragm.

INHALING

Inhaling is an active process that results mainly from the contraction of a muscle called the diaphragm, shown in Figure **6.3.2**. The **diaphragm** is a large, dome-shaped muscle below the lungs that separates the thoracic (chest) and abdominal cavities. When the diaphragm contracts, the thoracic cavity expands and the contents of the abdomen are pushed downward. Other muscles, such as external intercostal muscles between the ribs, also contribute to the process of inhalation, especially when inhalation is forced, as when taking a deep breath. These muscles help increase thoracic volume by expanding the ribs outward. With the chest expanded, there is lower air pressure inside the lungs than outside the body, so outside air flows into the lungs via the respiratory tract.

EXHALING

Exhaling involves the opposite series of events. The diaphragm relaxes, so it moves upward and decreases the volume of the thorax (Figure **6.3.2**. Air pressure inside the lungs increases so it is higher than the air pressure outside the lungs. Exhaling, unlike inhaling, is typically a passive process that occurs mainly due to the elasticity of the lungs. With the change in air pressure, the lungs contract to their pre-inflated size, forcing out the air they contain in the process. Air flows out of the lungs, similar to the way air rushes out of a balloon when it is released. If exhalation is forced, internal intercostal and abdominal muscles may help move the air out of the lungs.

CONTROL OF BREATHING

Breathing is one of the few vital bodily functions that can be controlled consciously as well as unconsciously. Think about using your breath to blow up a balloon. You take a long, deep breath, and then you exhale the air as forcibly as you can into the balloon. Both the inhalation and exhalation are consciously controlled.

CONSCIOUS CONTROL OF BREATHING

You can control your breathing by holding your breath, slowing your breathing, or **hyperventilating,** which is breathing more quickly and shallowly than necessary. You can also exhale or inhale more forcefully or deeply than usual. Conscious control of breathing is common in many activities besides blowing up balloons, including swimming, speech training, singing, playing many different musical instruments (Figure **6.3.3**), and doing yoga, to name just a few.



Figure **6.3.3**: Playing the oboe is hard work. Exhaled air must be forced through a tiny opening between two very small wooden reeds.

There are limits on the conscious control of breathing. For example, it is not possible for a healthy person to voluntarily stop breathing indefinitely. Before long, there is an irrepressible urge to breathe. If you were able to stop breathing for a long enough time, you would lose consciousness. The same thing would happen if you were to

hyperventilate for too long. Once you lose consciousness so you can no longer exert conscious control over your breathing, involuntary control of breathing takes over.

UNCONSCIOUS CONTROL OF BREATHING

Unconscious breathing is controlled by **respiratory centers** in the medulla and pons of the brainstem (Figure **6.3.4**). The respiratory centers automatically and continuously regulate the rate of breathing depending on the body's needs. These are determined mainly by blood acidity or pH. When you exercise, for example, carbon dioxide levels increase in the blood because of increased cellular respiration by muscle cells. The carbon dioxide reacts with water in the blood to produce carbonic acid, making the blood more acidic, so pH falls. The drop in pH is detected by chemoreceptors in the medulla. Blood levels of oxygen and carbon dioxide, in addition to pH, are also detected by chemoreceptors in major arteries, which send the "data" to the respiratory centers. The respiratory center responds by sending nerve impulses to the diaphragm, "telling" it to contract more quickly so the rate of breathing speeds up. With faster breathing, more carbon dioxide is released into the air from the blood, and blood pH returns to the normal range.

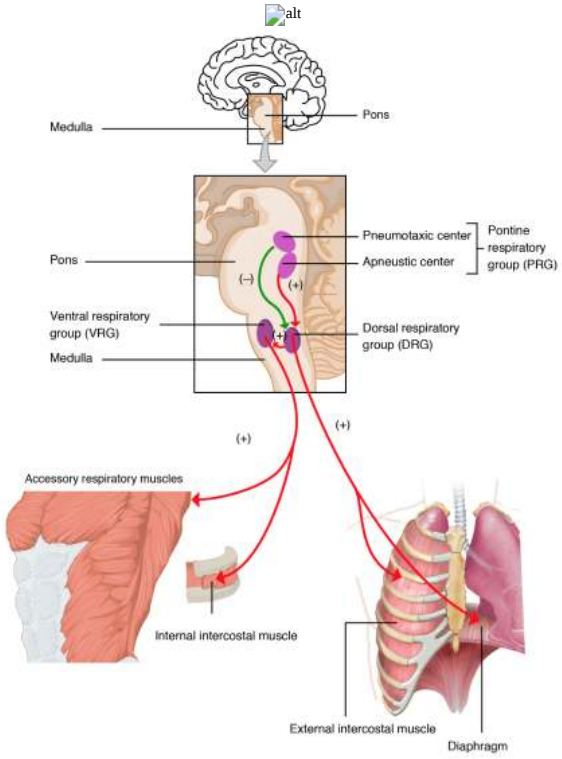


Figure **6.3.4**: Clusters of cells in the pons and medulla of the brain stem are the respiratory centers of the brain that have involuntary control over breathing muscles, such as the diaphragm and external and internal intercostal.

The opposite events occur when the level of carbon dioxide in the blood becomes too low and blood pH rises. This may occur with involuntary hyperventilation, which can happen in panic attacks, episodes of severe pain, asthma attacks, and many other situations. When you hyperventilate, you blow off a lot of carbon dioxide, leading to a drop in blood levels of carbon dioxide. The blood becomes more basic (alkaline), causing its pH to rise.

NASAL VS. MOUTH BREATHING

Nasal breathing is breathing through the nose rather than the mouth, and it is generally considered to be superior to mouth breathing. The hair-lined nasal passages do a better job of filtering particles out of the air before it moves deeper into the respiratory tract. The nasal passages are also better at warning and moistening the air, so nasal breathing is especially advantageous in the winter when the air is cold and dry. In addition, the smaller diameter of the nasal passages creates greater pressure in the lungs during exhalation. This slows the emptying of the lungs, giving them more time to extract oxygen from the air.

FEATURE: MYTH VS. REALITY

Drowning is defined as respiratory impairment from being in or under a liquid. It is further classified according to its outcome into death, ongoing health problems, or no ongoing health problems (full recovery). In the United States, accidental drowning is the second leading cause of death (after motor vehicle crashes) in children aged 12 years and younger. There are some potentially dangerous myths about drowning. Knowing what they are might save your life or the life of a loved one, especially a child.

Myth: People drown when they aspirate water into their lungs.

Reality: Generally, in the early stages of drowning, very little water enters the lungs. A small amount of water entering the trachea causes a muscular spasm in the larynx that seals the airway and prevents the passage of water into the lungs. This spasm is likely to last until unconsciousness occurs.

Myth: You can tell when someone is drowning because they will shout for help and wave their arms to attract attention.

Reality: The muscular spasm that seals the airway prevents the passage of air as well as water, so a person who is drowning is unable to shout or call for help. In addition, instinctive reactions that occur in the final minute or so before a drowning person sinks under the water may look similar to calm, safe behavior. The head is likely to be low in the water, tilted back with the mouth open. The person may have uncontrolled movements of the arms and legs, but they are unlikely to be visible above the water.

Myth: It is too late to save a person who is unconscious in the water.

Reality: An unconscious person rescued with an airway still sealed from the muscular spasm of the larynx stands a good chance of full recovery if they start receiving CPR within minutes. Without water in the lungs, CPR is much more effective. Even if the cardiac arrest has occurred so the heart is no longer beating, there is still a chance of recovery. However, the longer the brain goes without oxygen, the more likely brain

cells will die. Brain death is likely after about six minutes without oxygen, except in exceptional circumstances, such as young people drowning in very cold water. There are examples of children surviving, apparently without lasting ill effects, for as long as an hour in cold water (see Explore More below for an example). Therefore, rescuers retrieving a child from cold water should attempt resuscitation even after a protracted period of immersion.

Myth: If someone is drowning, you should start administering CPR immediately, even before you try to get the person out of the water.

Reality: Removing a drowning person from the water is the first priority because CPR is ineffective in the water. The goal should be to bring the person to stable ground as quickly as possible and then to start CPR.

Myth: You are unlikely to drown unless you are in water over your head.

Reality: Depending on circumstances, people have drowned in as little as 30 mm (about 1 ½ in.) of water. For example, inebriated people or those under the influence of drugs have been known to have drowned in puddles. Hundreds of children have drowned in the water in toilets, bathtubs, basins, showers, pails, and buckets (see figure below).



Figure **6.3.5**: Young children should never be left unattended around sources of water that pose a risk of drowning, including water in toilets, bathtubs, and buckets.

REVIEW

1. Define breathing.
2. What is another term for the process of breathing?
3. What is the main difference between the processes of inhaling and exhaling?
4. Give examples of activities in which breathing is consciously controlled.
5. Young children sometimes threaten to hold their breath until they get something they want. Why is this an idle threat?
6. Explain how unconscious breathing is controlled.
7. Why is nasal breathing generally considered to be superior to mouth breathing?
8. For each of the following, indicate whether it occurs during the process of inhalation (I) or exhalation (E).
   A. The diaphragm moves downward.
   B. The diaphragm relaxes.
   C. The thoracic cavity becomes smaller.
   D. The air pressure in the lungs is lower than outside the body.
9. Give one example of a situation that would cause blood pH to rise excessively and explain why this occurs.
10. Blood levels of oxygen and carbon dioxide and pH are detected by which of these:
    A. Mechanoreceptors
    B. Chemoreceptors
    C. Lung receptors
    D. Carbon receptors
11. True or False. The diaphragm can contract due to conscious control.
12. True or False. Hypoventilating is breathing that is fast and shallow.

EXPLORE MORE

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6.4: DISORDERS OF THE RESPIRATORY SYSTEM

A "MITEY" MONSTER

The scary beast in Figure **6.4.1** is likely to be lurking in your own home, where it feeds on organic debris, including human skin. What is it? It's the common dust mite, a close relative of spiders. The dust mite is so small that it is barely visible with the unaided eye, so it's obviously shown above greatly enlarged. If you think you can get rid of dust mites in your home by frequent and thorough cleaning, think again. There may be thousands of dust mites in just one gram of dust! Regardless of how clean you keep your house, you can't eliminate dust mites entirely. So why even bother trying? The feces of dust mites contain proteins that are a common trigger of asthma attacks.



Figure **6.4.1**: Dust mite

ASTHMA

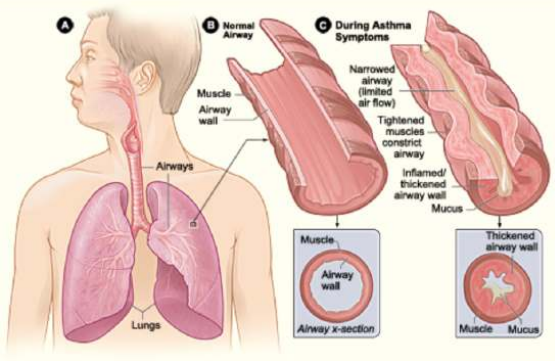


Figure **6.4.2**: During an asthma attack, airways narrow and may become clogged with mucus, making breathing difficult.

Asthma is a chronic inflammatory disease of the airways in the lungs, in which the airways periodically become inflamed. As you can see in Figure **6.4.2**, this causes swelling and narrowing of the airways, often accompanied by excessive mucus production. Symptoms of asthma include difficulty breathing, coughing, wheezing, shortness of breath, and chest tightness. Some people with asthma rarely experience symptoms, and then usually only in response to certain triggers in the environment. Other people may have symptoms almost all of the time.

Asthma is thought to be caused by a combination of genetic and environmental factors. A person with a family history of asthma is more likely to develop the disease. Dozens of genes have been found to be associated with asthma, many of which are related to the immune system. Additional risk factors include obesity and sleep apnea (see the feature My Human Body below). Environmental factors trigger asthma attacks in people who have a genetic predisposition to the disease. Besides dust mite feces, triggers may include other allergens (such as pet dander, cockroaches, and mold), certain medications including aspirin, air pollution, and stress, among other possible factors. Symptoms tend to be worse at night and early in the morning. They may also worsen during upper respiratory tract infections, strenuous exercise, or when the airways are exposed to cold air.

There is no cure for asthma at present, but the symptoms of asthma attacks usually can be reversed with the use of inhaled medications called bronchodilators. These medications soothe the constricted air passages and help to re-expand them, making breathing easier. The medications usually start to take effect almost immediately. Other medications can be taken for long-term control of the disease. These medications help prevent asthma attacks from occurring. Corticosteroids are generally considered the most effective treatment for long-term control. Another way to prevent asthma attacks is by avoiding triggers whenever possible.

PNEUMONIA

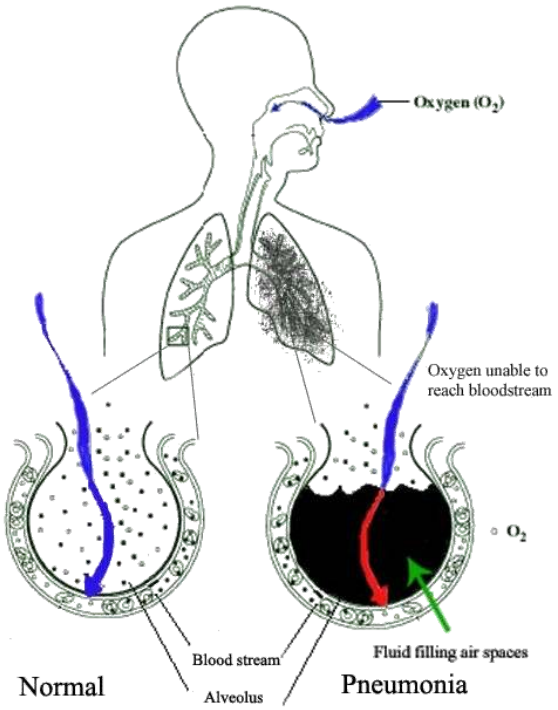


Figure **6.4.3**: Fluid-filled alveoli characteristic of pneumonia inhibit normal gas exchange with the blood.

Another common inflammatory disease of the respiratory tract is **pneumonia.** In pneumonia, the inflammation affects primarily the alveoli, which are the tiny air sacs of the lungs. Inflammation causes some of the alveoli to become filled with fluid so that gas exchange cannot occur. This is illustrated in Figure **6.4.3**. Symptoms of pneumonia typically include coughing, chest pain, difficulty breathing, and fever.

Pneumonia often develops as a consequence of an upper respiratory tract infection such as the common cold or flu, especially in the very young and the elderly. It is usually caused by bacteria or viruses, although some cases may be caused by other microorganisms such as fungi. The majority of cases are caused by just a few pathogens, the most common being the bacterium *Streptococcus pneumoniae.* Pneumonia is more likely to develop in people who have other lung diseases such as asthma, a history of smoking, heart failure, or a weakened immune system.

Vaccines are available to prevent certain types of bacterial and viral pneumonia, including pneumonia caused by *Streptococcus pneumoniae.* Treatment of pneumonia depends on the cause. For example, if it is caused by bacteria, antibiotics are generally prescribed. In cases of severe pneumonia, hospitalization and supplemental oxygen may be required.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic poor airflow. The main symptoms include shortness of breath and a cough that produces phlegm. These symptoms are usually present for a long period of time and typically become worse over time. Eventually, walking upstairs and similar activities become difficult because of shortness of breath.

COPD formerly was referred to as chronic bronchitis or emphysema. Now, the term *chronic bronchitis* is used to refer to the symptoms of COPD, and the term *emphysema* is used to refer to the lung changes that occur with COPD. Some of these lung changes are shown in Figure **6.4.4**. They include a breakdown of connective tissues that reduces the number and elasticity of alveoli. As a result, the patient can no longer fully exhale air from the lungs, so the air becomes trapped in the lungs. Gas exchange is hampered and may lead to low oxygen levels and too much carbon dioxide in the blood.

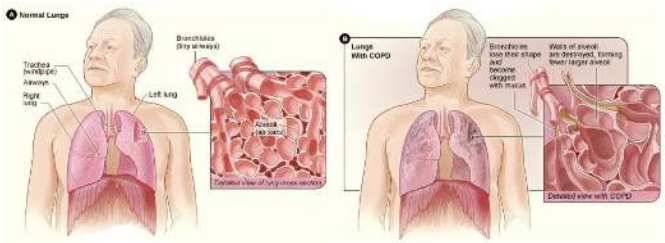


Figure **6.4.4**: The physiological changes that occur with COPD include a breakdown of alveolar walls, reducing the surface area for gas exchange.

Tobacco smoking is the major cause of COPD, with a number of other factors such as air pollution and genetics playing smaller roles. Of people who are life-long smokers, about half will eventually develop COPD. Exposure to secondhand smoke in nonsmokers also increases the risk of COPD and accounts for about 20 percent of cases. Most cases of COPD could have been prevented by never smoking. In people who have already been diagnosed with COPD, cessation of smoking can slow down the rate at which COPD worsens. People with COPD may be treated with supplemental oxygen and inhaled bronchodilators. These treatments may reduce the symptoms but there is no cure for COPD except, in very severe cases, lung transplantation (see the Explore More video below).

LUNG CANCER

Lung cancer is a malignant tumor characterized by uncontrolled cell growth in tissues of the lung. The tumor may arise directly from lung tissue (primary lung cancer) or as a result of metastasis from cancer in another part of the body (secondary lung cancer). Primary lung cancer may also metastasize and spread to other parts of the body. Lung cancer develops following genetic damage to DNA that affects the normal functions of the cell. As more damage accumulates, the risk of cancer increases. The most common symptoms of lung cancer include coughing (especially coughing up blood), wheezing, shortness of breath, chest pain, and weight loss.

The major cause of primary lung cancer is tobacco smoking, which accounts for about 85 percent of cases. Cigarette smoke contains numerous cancer-causing chemicals. Besides smoking, other potential causes of lung cancer include exposure to radon gas, asbestos, secondhand smoke, or other air pollutants. When tobacco smoking is combined with other risk factors such as exposure to radon or asbestos, the risk of lung cancer is heightened. People who have close biological relatives with lung cancer are also at increased risk of developing the disease.

Most cases of lung cancer cannot be cured. In many people, cancer has already spread beyond the original site by the time they have symptoms and seek medical attention. About 10 percent of people with lung cancer do not have symptoms when they are diagnosed, and the cancers are found when they have a chest X-ray for another problem. In part because of its typically late diagnosis, lung cancer is the most common cause of cancer-related death in men and the second most common cause in women (after breast cancer). Common treatments for lung cancer include surgical removal of the tumor, radiation therapy, chemotherapy, or some combination of these three types of treatment.

FEATURE: MY HUMAN BODY

Do you — or someone you love — snore? Snoring may be more than just an annoyance. It may also be a sign of a potentially dangerous and common disorder known as sleep apnea. **Sleep apnea** is characterized by pauses in breathing that occur most often because of physical blockage to airflow during sleep. When breathing is paused, carbon dioxide builds up in the bloodstream. The higher-than-normal level of carbon dioxide in the blood causes the respiratory centers in the brain to wake the person enough to start breathing normally. This reduces the carbon dioxide level, and the person falls back asleep. This occurs repeatedly throughout the night, causing serious disruption in sleep. Most people with sleep apnea are unaware that they have the disorder because they don't awake fully enough to remember the repeated awakenings throughout the night. Instead, sleep apnea is more commonly recognized by other people who witness the episodes.

Figure 6.4.5 shows how sleep apnea typically occurs. The muscle tone of the body normally relaxes during sleep, allowing the soft tissues in the throat to collapse and block the airway. The relaxation of muscles may be exacerbated by the use of alcohol, tranquilizers, or muscle relaxants. The risk of sleep apnea is greater in people who are overweight, smoke tobacco, or have diabetes. The disorder is also more likely to occur in older people and males. Common symptoms of sleep apnea include loud snoring, restless sleep, and daytime sleepiness and fatigue. Daytime sleepiness, in turn, increases the risk of driving and work-related accidents. Continued sleep deprivation may cause moodiness and belligerence. Lack of adequate oxygen to the body because of sleep apnea may also lead to other health problems including fatty liver diseases and high blood pressure. Symptoms of sleep apnea may be present for years or even decades until (and if) a diagnosis is finally made.

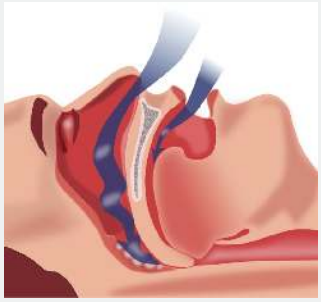


Figure 6.4.5: Sleeping on one's back may increase the risk of the airway becoming temporarily blocked during sleep, resulting in sleep apnea.

Treatment of sleep apnea may include avoiding alcohol, quitting smoking, or losing weight. Elevating the upper body during sleep or sleeping on one's side may help prevent airway collapse in many people with sleep apnea. Another type of treatment is the use of an oral device during sleep that shifts the lower jaw forward to help keep the airway open. The most common treatment for moderate to severe sleep apnea is the use during sleep of CPAP (continuous positive airway pressure), which keeps the airway open by means of pressurized air. In this treatment, the person typically wears a plastic facial mask that is connected by a flexible tube to a small bedside CPAP machine. Although CPAP is effective, long-term compliance is often poor because patients find the mask uncomfortable or they experience unpleasant side effects such as dry mouth and nose. A more extreme form of treatment is surgery to remove some of the tissues — such as the tonsils or part of the soft palate — that tend to collapse and block the airway in people with sleep apnea.

REVIEW

1. What is asthma, and what are its symptoms and causes?
2. Identify common risk factors and triggers of asthma attacks.
3. How can asthma attacks be prevented or controlled?
4. What are the causes and symptoms of pneumonia?
5. How can pneumonia be prevented? How is it treated?
6. Define COPD. How is it related to chronic bronchitis and emphysema?
7. Relate COPD to tobacco smoking.
8. What is the difference between primary and secondary lung cancer?
9. What is the major cause of primary lung cancer?
10. Discuss lung cancer as a cause of death.
11. How is lung cancer treated?
12. Define sleep apnea.
13. What is the difference between how COPD and pneumonia affect the alveoli?

EXPLORE MORE

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6.5: SMOKING AND HEALTH

SURE DEATH

The anti-smoking cartoon in Figure **6.5.1** clearly makes the point that smoking causes death. The cartoon is not using hyperbole, because smoking actually is deadly. It causes about six million deaths each year and is the single greatest cause of preventable death worldwide. As many as half of all people who smoke tobacco die from it. As a result of smoking's deadly effects, the life expectancy of long-term smokers is significantly less than that of non-smokers. In fact, long-term smokers can expect their lifespan to be reduced by as much as 18 years, and they are three times as likely to die before the age of 70 as non-smokers.



Figure **6.5.1**: Have another! Sure death

WHY IS SMOKING DEADLY?

As shown in Figure **6.5.2**, tobacco smoking has adverse effects on just about every bodily system and organ. The detrimental health effects of smoking depend on the number of years that a person smokes and how much the person smokes. Contrary to popular belief, all forms of tobacco smoke — including smoke from cigars and tobacco pipes — have similar health risks as those of cigarette smoke. Smokeless tobacco may be less of a danger to the lungs and heart, but it too has serious health effects. It significantly increases the risk of cancers of the mouth and throat, among other health problems.

Even non-smokers may not be spared the deadly risks of tobacco smoke. If you spend time around smokers either at home or on the job, then you are at risk of the dangers of secondhand smoke. **Secondhand smoke** enters the air directly from burning cigarettes (and cigars and pipes) and indirectly from the lungs of smokers. This smoke may linger in indoor air for hours and increase the risk of a wide range of adverse health effects. For example, non-smokers who are exposed to secondhand smoke may have as much as a 30 percent increase in their risk of lung cancer and heart disease. The 2014 U.S. Surgeon General's Report concluded that there is no established risk-free level of exposure to secondhand smoke.

Tobacco contains **nicotine,** which is a psychoactive drug. Although nicotine in tobacco smoke does not directly cause cancer or most of the other health risks of smoking, it is a highly addictive drug. In fact, nicotine is even more addictive than cocaine or heroin. The addictive nature of nicotine explains why it is so difficult for smokers to quit the habit even when they know the health risks and really want to stop smoking. The good news is that if someone does stop smoking, his or her risks of smoking-related diseases and death soon start to fall. For example, by one year after quitting, the risk of heart disease drops to only half of that of a continuing smoker.



Figure **6.5.2**: Smoking is known to cause many different cancers and chronic diseases such as stroke, blindness, gum infection, aortic rupture, heart disease, pneumonia, hardening of the arteries, chronic lung diseases, reduced fertility, and hip fracture.

SMOKING AND CANCER

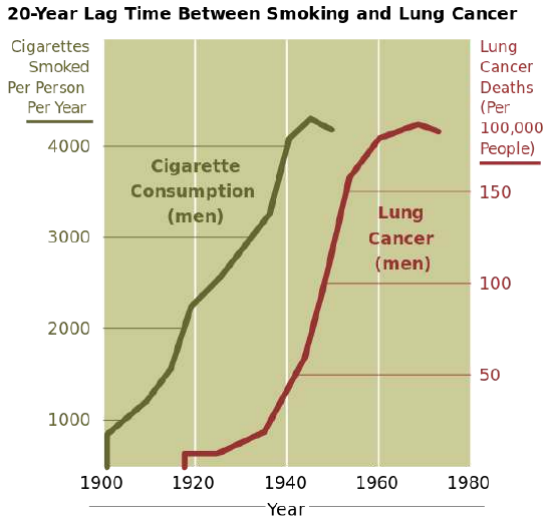


Figure **6.5.3**: Cigarette smoking by men in the U.S. began to decline in the 1950s, but it wasn't until the 1970s — roughly 20 years later — that this was reflected by a concomitant decline in lung cancer deaths in men.

One of the main health risks of smoking is cancer, particularly cancer of the lung. Because of the increased risk of lung cancer with

smoking, the risk of dying from lung cancer before age 85 is more than 20 times higher for a male smoker than for a male non-smoker. As the rate of smoking increases, so does the rate of lung cancer deaths, although the effects of smoking on lung cancer deaths can take up to 20 years to manifest themselves, as shown in Figure **6.5.3**.

Besides lung cancer, several other forms of cancer are also significantly more likely in smokers than non-smokers, including cancers of the kidney, larynx, mouth, lip, tongue, throat, bladder, esophagus, pancreas, and stomach. Unfortunately, many of these cancers have extremely low cure rates.

When you consider the composition of tobacco smoke, it's not surprising that it increases the risk of cancer. Tobacco smoke contains dozens of chemicals that have been proven to be carcinogens or causes of cancer. Many of these chemicals bind to DNA in a smoker's cells and may either kill the cells or cause mutations. If the mutations inhibit programmed cell death, the cells can survive to become cancer cells. Some of the most potent carcinogens in tobacco smoke include benzopyrene, acrolein, and nitrosamines. Other carcinogens in tobacco smoke are radioactive isotopes, including lead-210 and polonium-210.

RESPIRATORY EFFECTS OF SMOKING

Long-term exposure to the compounds found in cigarette smoke, such as carbon monoxide and cyanide, is thought to be responsible for much of the lung damage caused by smoking. These chemicals reduce the elasticity of alveoli, leading to chronic obstructive pulmonary disease (COPD). COPD is a permanent, incurable, and often fatal reduction in the capacity of the lungs, reducing the ability of the lungs to fully exhale air. The chronic inflammation that is also present in COPD is exacerbated by the tobacco smoke carcinogen acrolein and its derivatives. COPD is almost completely preventable simply by not smoking and by also avoiding secondhand smoke.

CARDIOVASCULAR EFFECTS OF SMOKING

Inhalation of tobacco smoke causes several immediate responses in the heart and blood vessels. Within one minute of inhalation of smoke, the heart rate begins to rise, increasing by as much as 30 percent during the first 10 minutes of smoking. Carbon monoxide in tobacco smoke binds with hemoglobin in red blood cells, thereby reducing the blood's ability to carry oxygen. Hemoglobin bound to carbon monoxide forms such a stable complex that it may result in a permanent loss of red blood cell function. Several other chemicals in tobacco smoke lead to the narrowing and weakening of blood vessels and an increase in substances that contribute to blood clotting. These changes increase blood pressure and the chances of a blood clot forming and blocking a vessel, thereby elevating the risk of heart attack and stroke. A recent study found that smokers are five times more likely than non-smokers to have a heart attack before the age of 40.

Smoking has also been shown to have a negative impact on the levels of blood lipids. Total cholesterol levels tend to be higher in smokers than non-smokers. Ratios of "good" cholesterol to "bad" cholesterol tend to be lower in smokers than in non-smokers.

ADDITIONAL ADVERSE HEALTH EFFECTS OF SMOKING

A wide diversity of additional adverse health effects are attributable to smoking. Here are just a few of them:

- Smokers are at a significantly increased risk of developing chronic kidney disease (in addition to kidney cancer). For example, smoking hastens the progression of kidney damage in people with diabetes.
- People who smoke, especially the elderly, have a greater risk of influenza and other infectious diseases than non-smokers. Smoking more than 20 cigarettes a day has been found to increase the risk of infectious diseases by as much as four times the risk in non-smokers. These effects occur because of damage to both the respiratory system and the immune system.
- In addition to oral cancer, smoking causes other oral problems including periodontitis (gum disease). Roughly half of the cases of gum inflammation are attributable to current or former smoking. Such inflammation increases the risk of tooth loss, which is also higher in smokers than non-smokers. In addition, smoking stains the teeth and causes halitosis (bad breath).
- Smoking is a key cause of erectile dysfunction (ED), probably because it leads to narrowing of arteries in the penis as it does elsewhere in the body. The incidence of ED is about 85 percent higher in males who smoke than it is in non-smokers.
- Smoking also has adverse effects on the female reproductive system, potentially causing infertility, in part because it interferes with the body's ability to produce estrogen. Female smokers are about 60 percent more likely to be infertile than non-smokers. Pregnant women who smoke or are exposed to secondhand smoke have a higher risk of miscarriages and low-birth-weight infants.
- Certain therapeutic drugs, including some antidepressants and anticonvulsants, are less effective in smokers than in non-smokers. This occurs because smoking increases levels of liver enzymes that break down the drugs.
- Smoking causes an estimated 10 percent of all deaths due to fires worldwide. Smokers are also at greater risk of dying in motor vehicle crashes and other accidents.
- Smoking leads to an increased risk of bone fractures, especially of the hip. It also leads to slower wound healing after surgery and an increased rate of postoperative complications.

FEATURE: HUMAN BIOLOGY IN THE NEWS

The item in Figure **6.5.4** looks like a regular cigarette, but it's actually an electronic cigarette or e-cigarette. E-cigarettes are battery-powered devices that change flavored liquids and nicotine into a vapor that is inhaled by the user. E-cigarettes are often promoted as being safer than traditional tobacco products and their use is touted as a good way to quit smoking. They are often not banned in smoke-free areas where it is illegal to smoke tobacco cigarettes.



Figure **6.5.4**: e-cigarette

A study completed in 2015 by researchers at the Harvard School of Public Health and widely reported in the mass media found that e-cigarettes may in fact be very harmful to the user's health. E-cigarettes contain nicotine and cancer-causing chemicals such as formaldehyde. According to the study, about three-quarters of flavored e-cigarettes also contain a chemical named diacetyl that causes an incurable and potentially fatal disorder of the lungs, commonly called "popcorn lung" (bronchiolitis obliterans). In this disorder, the bronchioles compress and narrow due to the formation of scar tissue. This greatly diminishes the breathing capacity of people with the disorder. Popcorn lung gained its common name in 2004 when it was diagnosed in workers at popcorn factories. The buttery flavoring used in the factories contained diacetyl.

Some manufacturers of e-cigarettes and flavorings advertise that their products are now free of diacetyl. However, because e-cigarettes are not currently regulated by the FDA, there is no way of knowing for sure whether the products are actually safe. Equally disturbing is the appeal of flavored e-cigarettes to teens and the attempts of producers to specifically market their products to this age group. Flavors such as "cotton candy," "Katy Perry's cherry," and "alien blood" are obviously marketed to youth. Not surprisingly, the use of e-cigarettes is on the rise in middle and high school students, who are more likely to use them than regular cigarettes. Public health officials fear that e-cigarettes will be a gateway for teens to move on to smoking tobacco cigarettes. Some states have recently passed laws prohibiting minors from buying e-cigarettes. As more questions are raised about their potential negative health effects, it is likely that more laws will be passed to regulate them. Watch the news for updates on this issue.

REVIEW

1. What percentage of people who smoke are likely to die from it?
2. Contrast the life expectancy of long-term smokers and non-smokers.
3. What factors related to smoking determine how smoking affects a smoker's health?
4. What are the two sources of secondhand cigarette smoke? How does exposure to secondhand smoke affect non-smokers?
5. Why is it so difficult for smokers to quit the habit? How is their health likely to be affected by quitting?
6. List five types of cancer that are significantly more likely in smokers than non-smokers.
7. Why does smoking cause cancer?
8. Explain how smoking causes COPD.
9. Identify some of the adverse effects of smoking on the cardiovascular system.
10. Give three examples of additional adverse health effects that are more likely with smoking.
11. Do you think e-cigarettes can be addictive? Explain your reasoning.
12. People who smoke are more likely to get which of these than people who do not smoke.

    A. lung cancer
    B. influenza
    C. kidney disease
    D. All of the above

13. Name three toxic chemicals present in tobacco smoke.
14. *True or False.* Nicotine is more addictive than heroin.
15. *True or False.* Smoking has many negative effects on the respiratory and cardiovascular systems, but not on other systems of the body.

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6.6: CASE STUDY CONCLUSION- BRONCHITIS AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: COUGH THAT WON'T QUIT

The little child shown in Figure **6.6.1** seems to be enjoying the air coming out of a humidifier. Inhaling the moist air from a humidifier or steamy shower can feel particularly good if you have a respiratory system infection, such as bronchitis. The moist air helps to loosen and thin mucus in the respiratory system, allowing you to breathe easier.



Figure **6.6.1**: Enjoying the Humidifier

At the beginning of this chapter, you learned about Sacheen, who developed acute bronchitis after getting a cold. She had a worsening cough, sore throat due to coughing, and chest congestion. She was also coughing up thick mucus.

Acute bronchitis usually occurs after a cold or flu, usually due to the same viruses that cause cold or flu. Because bronchitis is not usually caused by bacteria (although it can be), antibiotics are not an effective treatment in most cases.

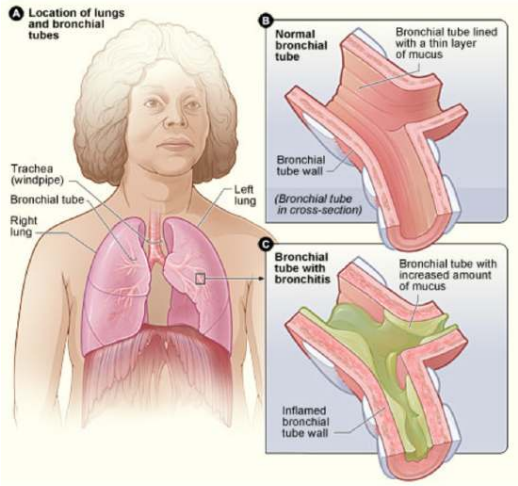


Figure **6.6.2**: Acute Bronchitis

Bronchitis affects the bronchial tubes, which, as you have learned, are air passages in the lower respiratory tract. The main bronchi branch off of the trachea and then branch into smaller bronchi and then bronchioles. In bronchitis, the walls of the bronchi become inflamed, which makes them narrower. Also, there is excessive production of mucus in the bronchi, which further narrows the pathway through which can flow. Figure **6.6.2** shows how bronchitis affects the bronchial tubes.

The function of mucus is to trap pathogens and other potentially dangerous particles that enter the respiratory system from the air. However, when too much mucus is produced in response to an infection (as in the case of bronchitis), it can interfere with normal airflow. The body responds by coughing as it tries to rid itself of the pathogen-laden mucus.

The treatment for most cases of bronchitis involves thinning and loosening the mucus so that it can be effectively coughed out of the airways. This can be done by drinking plenty of fluids, using humidifiers or steam, and in some cases, using over-the-counter medications such as expectorants that are found in some cough medicines. This is why Dr. Tsosie recommended some of these treatments to Sacheen and also warned against using cough suppressants. Cough suppressants work on the nervous system to suppress the cough reflex. When a patient has a “productive” cough —i.e. they are coughing up mucus—doctors generally advise them to not take cough suppressants so that they can cough the mucus out of their bodies.

When Dr. Tsosie was examining Sacheen, she used a pulse oximeter to measure the oxygen level in her blood. Why did she do this? As you have learned, the bronchial tubes branch into bronchioles, which ultimately branch into the alveoli of the lungs. The alveoli are where gas exchange occurs between the air and the blood to take in oxygen and remove carbon dioxide and other wastes. By checking Sacheen’s blood oxygen level, Dr. Tsosie was making sure that her clogged airways were not impacting her level of much-needed oxygen.

Sacheen has acute bronchitis, but you may recall that *chronic* bronchitis was discussed earlier in this chapter as a term that describes the symptoms of chronic obstructive pulmonary disease (COPD). COPD is often due to tobacco smoking and causes damage to the walls of the alveoli, whereas acute bronchitis typically occurs after a cold or flu and involves inflammation and mucus build-up in the bronchial tubes. As implied by the difference in their names, chronic bronchitis is an ongoing, long-term condition, while acute bronchitis is likely to resolve relatively quickly with proper rest and treatment.

However, Sacheen smokes cigarettes, so she is more likely to develop chronic respiratory conditions such as COPD. As you have learned, smoking damages the respiratory system as well as many other systems of the body. Smoking increases the risk of respiratory infections, including bronchitis and flu, due to its damaging effects on the respiratory and immune systems. Dr. Tsosie strongly encouraged Sacheen to quit smoking, not only so that her acute bronchitis resolves, but so that she can avoid future infections and other negative health outcomes associated with smoking, including COPD and lung cancer.

As you have learned in this chapter, the respiratory system is critical to carry out the gas exchange necessary for life’s functions and to

protect the body from pathogens and other potentially harmful substances in the air. But this ability to interface with the outside air has a cost. The respiratory system is prone to infections, as well as damage and other negative effects from allergens, mold, air pollution, and cigarette smoke. Although exposure to most of these things cannot be avoided, not smoking is an important step you can take to protect this organ system—as well as many other systems of your body.

CHAPTER SUMMARY

In this chapter, you learned about the respiratory system. Specifically, you learned that:

- Respiration is the process in which oxygen moves from the outside air into the body and carbon dioxide and other waste gases move from inside the body into the outside air. It involves two subsidiary processes: ventilation and gas exchange.
- The organs of the respiratory system form a continuous system of passages called the respiratory tract. It has two major divisions: the upper respiratory tract and the lower respiratory tract.
    - The upper respiratory tract includes the nasal cavity, pharynx, and larynx. All of these organs are involved in conduction or the movement of air into and out of the body. Incoming air is also cleaned, humidified, and warmed as it passes through the upper respiratory tract. The larynx is also called the voice box because it contains the vocal cords, which are needed to produce vocal sounds.
    - The lower respiratory tract includes the trachea, bronchi and bronchioles, and the lungs. The trachea, bronchi, and bronchioles are involved in conduction. Gas exchange takes place only in the lungs, which are the largest organs of the respiratory tract. Lung tissue consists mainly of tiny air sacs called alveoli, which is where gas exchange takes place between the air in the alveoli and the blood in capillaries surrounding them.
- The respiratory system protects itself from potentially harmful substances in the air by the mucociliary escalator. This includes mucus-producing cells, which trap particles and pathogens in the incoming air. It also includes tiny hair-like cilia that continually move to sweep the mucus and trapped debris away from the lungs and toward the outside of the body.
- The level of carbon dioxide in the blood is monitored by cells in the brain. If the level becomes too high, it triggers a faster rate of breathing, which lowers the level to the normal range. The opposite occurs if the level becomes too low. The respiratory system exchanges gases with the outside air, but it needs the cardiovascular system to carry the gases to and from cells throughout the body.
- Breathing, or ventilation, is the two-step process of drawing air into the lungs (inhaling) and letting the air out of the lungs (exhaling). Inhaling is an active process that results mainly from the contraction of a muscle called the diaphragm. Exhaling is typically a passive process that occurs mainly due to the elasticity of the lungs when the diaphragm relaxes.
    - Breathing is one of the few vital bodily functions that can be controlled consciously as well as unconsciously. Conscious control of breathing is common in many activities, including swimming and singing. However, there are limits on the conscious control of breathing. If you try to hold your breath, for example, you will soon have an irrepressible urge to breathe.
    - Unconscious breathing is controlled by respiratory centers in the medulla and pons of the brainstem. They respond to variations in blood pH by either increasing or decreasing the rate of breathing as needed to return the pH level to the normal range.
    - Nasal breathing is generally considered to be superior to mouth breathing because it does a better job of filtering, warming, and moistening incoming air. It also results in slower emptying of the lungs, which allows more oxygen to be extracted from the air.
- Gas exchange is the biological process through which gases are transferred across cell membranes to either enter or leave the blood. Gas exchange takes place continuously between the blood and cells throughout the body and also between the blood and the air inside the lungs.
    - Gas exchange in the lungs takes place in alveoli. The pulmonary artery carries deoxygenated blood from the heart to the lungs, where it travels through pulmonary capillaries, picking up oxygen, and releasing carbon dioxide. The oxygenated blood then leaves the lungs through pulmonary veins.
    - Gas exchange occurs by diffusion across cell membranes. Gas molecules naturally move down a concentration gradient from an area of higher concentration to an area of lower concentration. This is a passive process that requires no energy.
    - Gas exchange by diffusion depends on the large surface area provided by the hundreds of millions of alveoli in the lungs. It also depends on a steep concentration gradient for oxygen and carbon dioxide. This gradient is maintained by continuous blood flow and constant breathing.
- Asthma is a chronic inflammatory disease of the airways in the lungs, in which the airways periodically become inflamed. This causes swelling and narrowing of the airways, often with excessive mucus production, leading to difficulty breathing and other symptoms. Asthma is thought to be caused by a combination of genetic and environmental factors. Asthma attacks are triggered by allergens, air pollution, or other factors.
- Pneumonia is a common inflammatory disease of the respiratory tract in which inflammation affects primarily the alveoli, which become filled with fluid that inhibits gas exchange. Most cases of pneumonia are caused by viral or bacterial infections.

Vaccines are available to prevent pneumonia; treatment often includes prescription antibiotics.

- Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic poor airflow, which causes shortness of breath and a productive cough. It is caused most often by tobacco smoking, which leads to the breakdown of connective tissues in the lungs. Alveoli are reduced in number and elasticity, making it impossible to fully exhale air from the lungs. There is no cure for COPD, but stopping smoking may reduce the rate at which COPD worsens.
- Lung cancer is a malignant tumor characterized by uncontrolled cell growth in tissues of the lung. It results from accumulated DNA damage, most often caused by tobacco smoking. Lung cancer is typically diagnosed late, so most cases cannot be cured. It may be treated with surgery, chemotherapy, and/or radiation therapy.
- Smoking is the single greatest cause of preventable death worldwide. It has adverse effects on just about every body system and organ. Tobacco smoke affects not only smokers but also non-smokers who are exposed to secondhand smoke. The nicotine in tobacco is highly addictive, making it very difficult to quit smoking.
    - The major health risk of smoking is cancer of the lungs. Smoking also increases the risk of many other types of cancer. Tobacco smoke contains dozens of chemicals that are known carcinogens.
    - Smoking is the primary cause of COPD. Chemicals such as carbon monoxide and cyanide in tobacco smoke reduce the elasticity of alveoli so the lungs can no longer fully exhale air.
    - Smoking damages the cardiovascular system and increases the risk of high blood pressure, blood clots, heart attack, and stroke. Smoking also has a negative impact on levels of blood lipids.
    - A wide diversity of additional adverse health effects are attributable to smoking, such as erectile dysfunction, female infertility, and slow wound healing.

CHAPTER SUMMARY REVIEW

1. Describe the relationship between the bronchi, secondary bronchi, tertiary bronchi, and bronchioles.
2. What is the uppermost structure in the lower respiratory tract?
    A. Bronchus
    B. Lung
    C. Alveolus
    D. Trachea
3. Deoxygenated and oxygenated blood both travel to the lungs. Describe what happens to each there.
4. *True or False.* There are radioactive isotopes in cigarette smoke.
5. *True or False.* The right and left lungs are identical in structure.
6. Explain the difference between ventilation and gas exchange.
7. Which way do oxygen and carbon dioxide flow during a gas exchange in the lungs?
    A. Why does this happen?
    B. Which way do oxygen and carbon dioxide flow during the gas exchange between the blood and the body's cells?
    C. Why does this happen?
8. Why does the body require oxygen and give off carbon dioxide as a waste product?
9. *True or False.* Conduction refers to the movement of gases across cell membranes.
10. *True or False.* Gas exchange does not require energy.
11. What do coughing and sneezing have in common?
12. What is the name of the escalator that protects the respiratory system?
    A. phlegmociliary
    B. mucociliary
    C. mucoflagellar
    D. surfactociliary
13. COPD can lead to too much carbon dioxide in the blood. Answer the following questions about this.
    A. Why can COPD cause there to be too much carbon dioxide in the blood?
    B. What does this do to the blood pH?
    C. How does the body respond to this change in blood pH?
14. From the following list of diseases, choose which one best fits each description. Each disease is used only once. Diseases: asthma, pneumonia, COPD, lung cancer
    A. Alveoli become inflamed and fill with fluid
    B. Can be caused by exposure to inhaled carcinogens
    C. There is a reduction in the number of alveoli
    D. Airways periodically narrow and fill with mucus
15. *True or False.* Pneumonia can be caused by fungi.
16. *True or False.* The diaphragm contracts during exhalation.
17. What are three different types of things that can enter the respiratory system and cause illness or injury? Describe the negative health effects of each in your answer.
18. Where are the respiratory centers of the brain located? What is the main function of the respiratory centers of the brain?
19. Smoking increases the risk of getting influenza, commonly known as the flu. Explain why this could lead to a greater risk of getting pneumonia.
20. If people had a gene that caused them to get asthma, could changes to their environment (such as more frequent cleaning) help their asthma? Why or why not?
21. What does the term *bronchodilator* refer to?
    A. The largest bronchial tube
    B. An area of the brain that increases breathing rate
    C. A medication that opens constricted airways
    D. A medication that clears the nasal cavity
22. Explain why nasal breathing generally stops particles from entering the body at an earlier stage than mouth breathing.

ATTRIBUTIONS

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CHAPTER OVERVIEW

7: SKELETAL SYSTEM

This chapter describes the structure and functions of the skeletal system and its two major divisions, the axial skeleton and the appendicular skeleton. It details the structure of bone, how bones grow, and how they are remodeled and repaired. The chapter also explains how joints work and how they are classified as well as the causes and effects of major skeletal system disorders.

7.1: Case Study- Your Support System

7.2: Introduction to the Skeletal System

7.3: Divisions of the Skeletal System

7.4: Structure of Bone

7.5: Bone Growth, Remodeling, and Repair

7.6: Joints

7.7: Disorders of the Skeletal System

7.8: Case Study Conclusion- Heels and Chapter Summary

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7.1: CASE STUDY- YOUR SUPPORT SYSTEM

CASE STUDY: A PAIN IN THE FOOT

Amari loves wearing high heels when they go out at night, like the stiletto heels shown in Figure **7.1.1**. Amari uses gender-neutral pronouns, such as they, them, and their. They know high heels are not the most practical shoes, but they like how they look. Lately, Amari has been experiencing pain in the balls of their feet—the area just behind the toes. Even when they trade heels for comfortable sneakers, it still hurts when they stand or walk.



Figure **7.1.1**: high heels

What could be going on? Amari searches online to try to find some answers. They find a reputable source for foot pain information—a website from a professional organization of physicians that peer reviews the content by experts in the field. There, Amari reads about a condition called metatarsalgia, which produces pain in the ball of the foot that sounds very similar to what they are experiencing.

Amari learns that a common cause of metatarsalgia is the wearing of high heels because they push the foot into an abnormal position. This results in excessive pressure being placed onto the ball of the foot. Looking at the photograph above, you can imagine how much of the body weight is focused on the ball of the foot because of the shape of the high heels. If they were not wearing high heels, the weight would be more evenly distributed across the foot.

As they read more about the hazards of high heels, Amari learns that heels can also cause foot deformities such as hammertoes and bunions, small cracks in the bone called stress fractures, and may even contribute to the development of osteoarthritis of the knees at an early age.

These conditions caused by high heels are all problems of the skeletal system, which includes bones and connective tissues that hold bones together and cushion them at joints such as the knee. The skeletal system supports the body's weight and protects internal organs, but as you will learn as you read this chapter, it also carries out a variety of other important physiological functions.

At the end of the chapter, you will find out why high heels can cause these skeletal system problems and the steps Amari takes to recover from their foot pain and prevent long-term injury.

CHAPTER OVERVIEW: SKELETAL SYSTEM

In this chapter, you will learn about the structure, functions, growth, repair, and disorders of the skeletal system. Specifically, you will learn about:

- The components of the skeletal system, which include bones, ligaments, and cartilage.
- The functions of the skeletal system, which include supporting and giving shape to the body, protecting internal organs, facilitating movement, producing blood cells, helping maintain homeostasis, and producing endocrine hormones.
- The organization and functions of the two main divisions of the skeletal system: the axial skeletal system, which includes the skull, spine, and rib cage; and the appendicular skeletal system, which includes the limbs and girdles that attach the limbs to the axial skeleton.
- The tissues and cells that make up bones and their specific functions, including making new bone, breaking down bone, producing blood cells, and regulating mineral homeostasis.
- The different types of bones in the skeletal system, based on shape and location.
- How bones grow, remodel, and repair themselves.
- The different types of joints between bones, where they are located, and the ways in which they allow different types of movement depending on their structure.
- The causes, risk factors, and treatments for the two most common disorders of the skeletal system: osteoporosis and osteoarthritis.

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

1. Amari suspects they have a condition called metatarsalgia. This term is related to the term "metatarsals." What are metatarsals, where are they located, and how do you think they are related to metatarsalgia?
2. High heels can cause stress fractures, which are small cracks in the bone that usually appear after repeated mechanical stress, instead of after a significant acute injury. What other condition described in this chapter involves a similar process?
3. What are bunions and osteoarthritis of the knee? Why do you think they can be caused by wearing high heels?

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7.2: INTRODUCTION TO THE SKELETAL SYSTEM

SKULL AND CROSS-BONES

The skull and cross-bones symbol has been used for a very long time to represent death, perhaps because after death and decomposition, bones are all that remain. Many people think of bones as being dead, dry, and brittle. These adjectives may correctly describe the bones of a preserved skeleton, but the bones of a living human being are very much alive. Living bones are also strong and flexible. Bones are the major organs of the skeletal system.



Figure **7.2.1**: skull and cross-bones flag

The **skeletal system** is the organ system that provides an internal framework for the human body. Why do you need a skeletal system? Try to imagine what you would look like without it. You would be a soft, wobbly pile of skin containing muscles and internal organs but no bones. You might look something like a very large slug. Not that you would be able to see yourself — folds of skin would droop down over your eyes and block your vision because of your lack of skull bones. You could push the skin out of the way if you could only move your arms, but you need bones for that as well!

COMPONENTS OF THE SKELETAL SYSTEM

In adults, the skeletal system includes 206 bones, many of which are shown in Figure **7.2.2**. Bones are organs made of dense connective tissues, mainly the tough protein collagen. Bones contain blood vessels, nerves, and other tissues. Bones are hard and rigid due to deposits of calcium and other mineral salts within their living tissues. Locations, where two or more bones meet, are called joints. Many joints allow bones to move like levers. For example, your elbow is a joint that allows you to bend and straighten your arm.

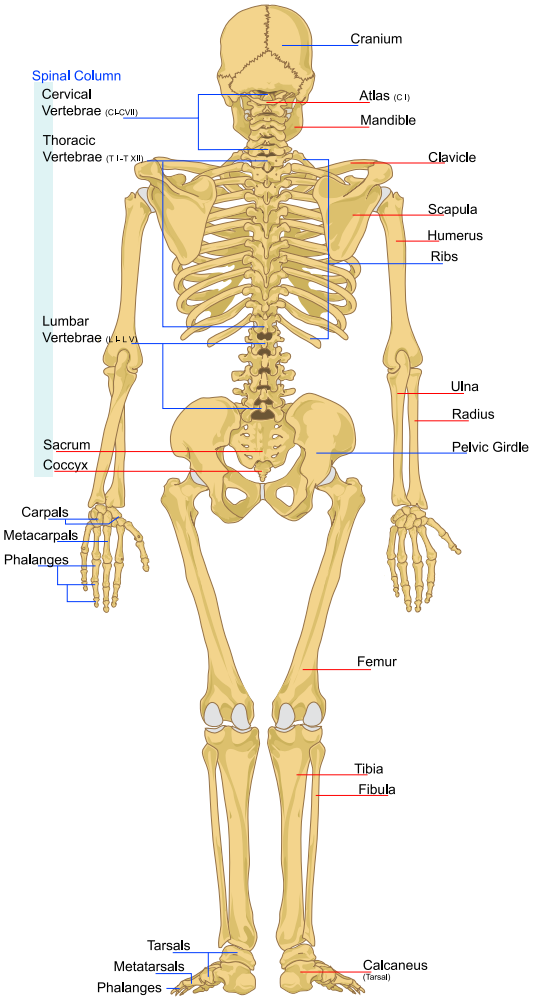


Figure **7.2.2**: Some of the 206 bones are labeled on the adult human skeleton.

Besides bones, the skeletal system includes cartilage and ligaments.

- **Cartilage** is a type of dense connective tissue, made of tough protein fibers. It is strong but flexible and very smooth. It covers the ends of bones at joints, providing a smooth surface for bones to move over.
- **Ligaments** are bands of fibrous connective tissue that hold bones together. They keep the bones of the skeleton in place.

AXIAL AND APPENDICULAR SKELETONS

The skeleton is traditionally divided into two major parts: the axial skeleton and the appendicular skeleton, both of which are pictured in Figure **7.2.3**.

- The axial skeleton forms the axis of the body. It includes the skull, vertebral column (spine), and rib cage. The bones of the axial skeleton, along with ligaments and muscles, allow the human body to maintain its upright posture. The axial skeleton also transmits weight from the head, trunk, and upper extremities

down the back to the lower extremities. In addition, the bones protect the brain and organs in the chest.

- The appendicular skeleton forms the appendages and their attachments to the axial skeleton. It includes the bones of the arms and legs, hands and feet, and shoulder and pelvic girdles. The bones of the appendicular skeleton make possible locomotion and other movements of the appendages. They also protect the major organs of digestion, excretion, and reproduction.

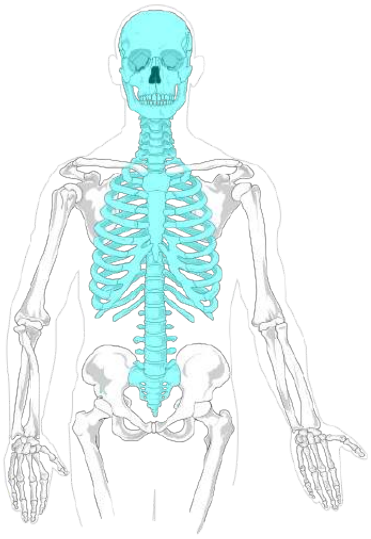


Figure **7.2.3**: Axial skeleton represented in blue

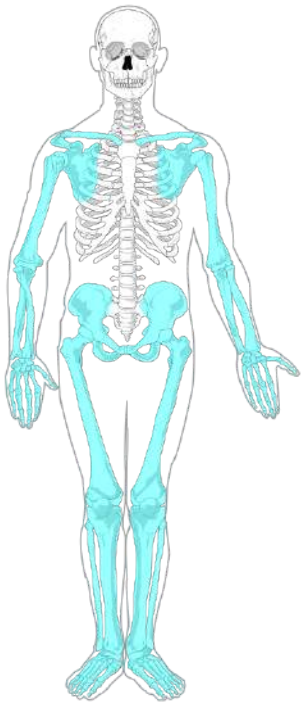


Figure **7.2.3**: Appendicular skeleton represented in blue

FUNCTIONS OF THE SKELETAL SYSTEM

The skeletal system has many different functions that are necessary for human survival. Some of the functions, such as supporting the body, are relatively obvious. Other functions are less obvious but no less important. For example, three tiny bones (hammer, anvil, and stirrup) inside the middle ear transfer sound waves into the inner ear.

SUPPORT, SHAPE, AND PROTECTION

The skeleton supports the body and gives it shape. Without the rigid bones of the skeletal system, the human body would be just a bag of soft tissues, as described above. The bones of the skeleton are very hard and provide protection to the delicate tissues of internal organs. For example, the skull encloses and protects the soft tissues of the brain, and the vertebral column protects the nervous tissues of the spinal cord. The vertebral column, ribs, and sternum (breast bone) protect the heart, lungs, and major blood vessels. Providing protection to these latter internal organs requires the bones to be able to expand and contract. The ribs and the cartilage that connects them to the sternum and vertebrae are capable of small shifts that allow breathing and other internal organ movements.

MOVEMENT

The bones of the skeleton provide attachment surfaces for skeletal muscles. When the muscles contract, they pull on and move the bones. The figure below, for example, shows the muscles attached to the bones at the knee. They help stabilize the joint and allow the leg to bend at the knee. The bones at joints act like levers moving at a fulcrum point, and the muscles attached to the bones apply the force needed for movement.

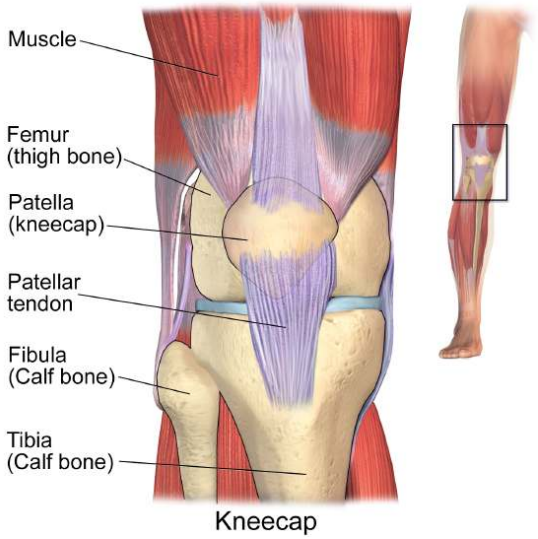


Figure **7.2.4**: Bones that meet at the knee joint include the tibia and fibula in the lower leg, the femur in the upper leg, and the kneecap at the front of the knee. These bones provide attachment surfaces for muscles that move the bones at the joint. Muscles are attached to the bones via tendons.

HEMATOPOIESIS

Hematopoiesis is the process in which blood cells are produced. This process occurs in a tissue called red marrow, which is found

inside some bones, including the pelvis, ribs, and vertebrae. Red marrow synthesizes red blood cells, white blood cells, and platelets. Billions of these blood cells are produced inside the bones every day.

MINERAL STORAGE AND HOMEOSTASIS

Another function of the skeletal system is storing minerals, especially calcium and phosphorus. This storage function is related to the role of bones in maintaining mineral homeostasis. Just the right levels of calcium and other minerals are needed in the blood for the normal functioning of the body. When mineral levels in the blood are too high, bones absorb some of the minerals and store them as mineral salts, which is why bones are so hard. When blood levels of minerals are too low, bones release some of the minerals back into the blood. Bone minerals are alkaline (basic), so their release into the blood buffers the blood against excessive acidity (low pH), whereas their absorption back into bones buffers the blood against excessive alkalinity (high pH). In this way, bones help maintain acid-base homeostasis in the blood.

Another way bones help to maintain homeostasis is by acting as an endocrine organ. One endocrine hormone secreted by bone cells is **osteocalcin,** which helps regulate blood glucose and fat deposition. It increases insulin secretion and also the sensitivity of cells to insulin. In addition, it boosts the number of insulin-producing cells and reduces fat stores.

REVIEW

1. What is the skeletal system? How many bones are there in the adult skeleton?
2. Describe the composition of bones.
3. Besides bones, what other organs are included in the skeletal system?
4. Identify the two major divisions of the skeleton.
5. List several functions of the skeletal system.
6. Discuss sexual dimorphism in the human skeleton.
7. Bones, cartilage, and ligaments are all made of types of _____ tissue.
8. *True or False.* Bones contain living tissue and can affect processes in other parts of the body.
9. *True or False.* Bone cells contract to pull on muscles in order to initiate a movement.
10. If a person has a problem with blood cell production, what type of bone tissue is most likely involved? Explain your answer.
11. Are the pelvic girdles part of the axial or appendicular skeleton?
12. What are three forms of homeostasis that the skeletal system regulates? Briefly explain how each one is regulated by the skeletal system.
13. What do you think would happen to us if we did not have ligaments? Explain your answer.
14. a. Define a joint in the skeletal system.

    b. How is cartilage related to joints?

    c. Identify one joint in the human body and describe its function.

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7.3: DIVISIONS OF THE SKELETAL SYSTEM

SKULLS ON DISPLAY

This somewhat macabre display can be viewed at the Slovak National Museum in Bratislava, Slovakia. The skulls are meant to represent normal human skeletal anatomy. The skull is part of the axial skeleton, which is one of the two major divisions of the human skeleton. The other division is the appendicular skeleton.



Figure **7.3.1**: Skulls on Display

AXIAL SKELETON

The **axial skeleton,** shown in blue in Figure **7.3.2**, consists of a total of 80 bones. Besides the skull, it includes the rib cage and vertebral column. It also includes the three tiny ossicles (hammer, anvil, and stirrup) in the middle ear and the hyoid bone in the throat, to which the tongue and some other soft tissues are attached.

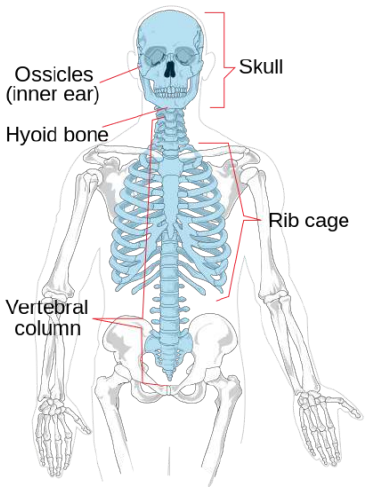


Figure **7.3.2**: The bones of the axial skeleton are shown here in blue.

SKULL

The **skull** is the part of the human skeleton that provides a bony framework for the head. It consists of 22 different bones. There are 8 bones in the cranium, which encloses the brain, and 14 bones in the face.

CRANIUM

The **cranium,** sometimes called the braincase, forms the entire upper portion of the skull. As shown in Figure **7.3.3**, it consists of eight bones: one frontal bone, two parietal bones, two temporal bones, one occipital bone, one sphenoid bone, and one ethmoid bone. The ethmoid bone separates the nasal cavity from the brain. The sphenoid bone is one of several bones, including the frontal bone, that helps form the eye sockets. The other bones of the cranium are large and plate-like. They cover and protect the brain. The bottom of the skull has openings for major blood vessels and nerves. A large opening, called the foramen magnum, allows the spinal cord and brain to connect.

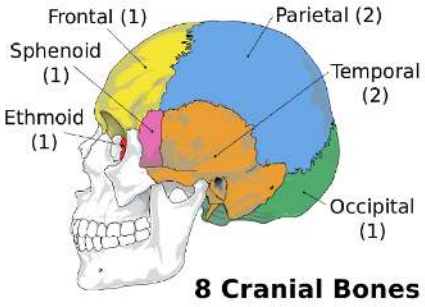


Figure **7.3.3**: The cranium consists of eight bones that are fused together at their joints.

FACIAL BONES

The 14 facial bones of the skull are located below the frontal bone of the cranium. They are depicted in Figure **7.3.4**. Large bones in the face include the upper jawbones, or **maxillae (singular, maxilla),** which form the middle part of the face and the bottom of the two eye sockets. The maxillae are fused together except for an opening between them for the nose. The lower edge of the maxillae contains sockets for the upper teeth. The lower jaw bone, or **mandible,** is also large. The top edge of the mandible contains sockets for the lower teeth. The mandible opens and closes to chew food and is controlled by strong muscles. There are two zygomatic or cheekbones and two nasal bones. The nasal region also contains seven smaller bones, as indicated in the figure.

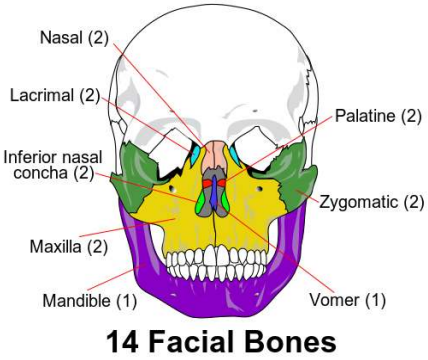


Figure **7.3.4**: The 14 bones that make up the face are labeled in this drawing of the skull.

VERTEBRAL COLUMN

The **vertebral column,** also called the spine or backbone, is the flexible column of **vertebrae (singular, vertebra)** that connects the trunk with the skull and encloses the spinal cord. It consists of 33 vertebrae that are divided into five regions, as shown in Figure **7.3.5**: the cervical, thoracic, lumbar, sacral, and coccygeal regions. From

the neck down, the first 24 vertebrae (cervical, thoracic, and lumbar) are individual bones. The five sacral vertebrae are fused together, as are the four coccygeal vertebrae.

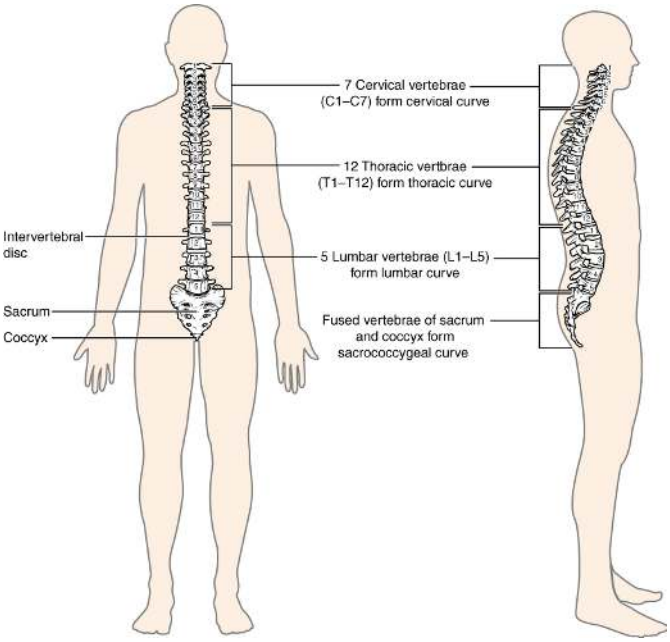


Figure **7.3.5**: The vertebral column consists of 24 individual vertebrae that are separated by intervertebral discs of cartilage. An additional 9 vertebrae are fused together at the base of the spine. Note the S-shaped curve of the vertebral column in the profile view on the right.

The human vertebral column reflects adaptations for upright bipedal locomotion. For example, the vertebral column is less like a rigid column than an S-shaped spring (see a profile view in the figure above). Although newborn infants have a relatively straight spine, the curves develop as the backbone starts taking on its support functions, such as keeping the trunk erect, holding up the head, and helping to anchor the limbs. The S shape of the vertebral column allows it to act as a shock absorber, absorbing much of the jarring of walking and running so the forces are not transmitted directly from the pelvis to the skull. The S shape also helps protect the spine from breaking, which would be more likely with a straight, more rigid vertebral column. In addition, the S shape helps to distribute the weight of the body, and particularly of the internal organs, so the weight load is not all at the bottom, as would occur with a straight spine.

RIB CAGE

The **rib cage** (also called thoracic cage) is aptly named because it forms a sort of cage that holds within it the organs of the upper part of the trunk, including the heart and lungs (Figure **7.3.6**). The rib cage includes the 12 thoracic vertebrae and the breastbone (or sternum) as well as 12 pairs of ribs, which are attached at joints to the vertebrae. The ribs are divided into three groups, called true ribs, false ribs, and floating ribs. The top seven pairs of ribs are true ribs. They are attached by cartilage directly to the sternum. The next three pairs of ribs are false ribs. They are attached by cartilage to the ribs above them, rather than directly to the sternum. The lowest two pairs of ribs are floating ribs. They are attached by cartilage to muscles in the abdominal wall. The attachments of false and floating ribs let the lower part of the rib cage expand to accommodate the internal movements of breathing.

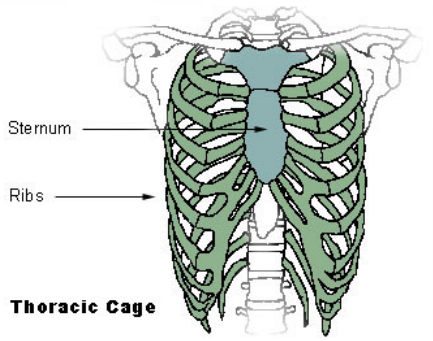


Figure **7.3.6**: The rib cage encloses and protects the thoracic cavity

APPENDICULAR SKELETON

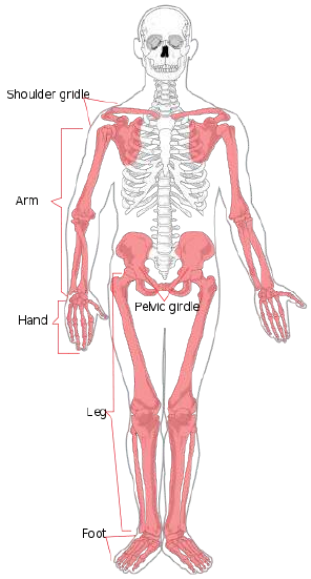


Figure **7.3.7**. The appendicular skeleton (in red) includes the upper and lower appendages and girdles.

The appendicular skeleton, shown in red in Figure **7.3.7**, consists of a total of 126 bones. It includes all the bones of the limbs (arms, legs, hands, and feet) as well as the bones of the shoulder (shoulder girdle) and pelvis (pelvic girdle).

UPPER LIMBS

Each upper limb consists of 30 bones. As shown in Figure **7.3.8**, there is one bone, called the humerus, in each of the upper arms, and there are two bones, called the ulna and radius, in each of the lower arms.

The remaining bones of the upper limb are shown in Figure **7.3.9**. Each wrist contains eight carpal bones, which are arranged in two rows of four bones each; and each hand contains five metacarpal bones. The bones in the fingers of each hand include 14 phalanges (three in each finger except the thumb, which has two phalanges). The thumb has the unique ability to move into opposition with the palm of the hand and with each of the fingers when they are slightly

bent. This allows the hand to handle and manipulate objects such as tools.

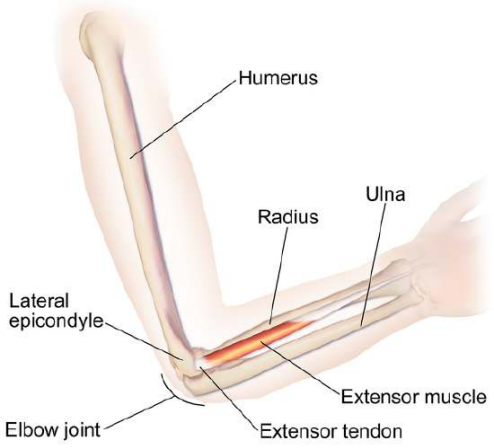


Figure **7.3.8**: In the upper limb, the upper arm contains one bone, Humerus, and the lower arm contains two bone, Ulna and Radius.

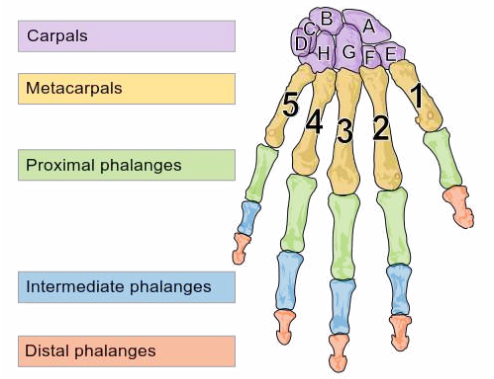


Figure **7.3.9**: Bones of the wrist (carpals A-E) and hand (metacarpals 1-5 and phalanges).

LOWER LIMBS

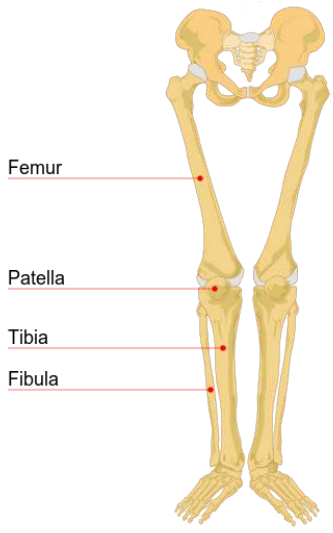


Figure **7.3.10**: Bones of the legs.

Each lower limb consists of 30 bones. As shown in Figure **7.3.10**, there is one bone, called the femur, in each of the upper legs, and there are two bones, called the tibia and fibula, in each of the lower legs. The knee cap, or patella, is an additional leg bone at the front of each knee, which is the largest joint in the human body.

The remaining bones of the lower limbs are shown in Figure **7.3.11**. Each ankle contains seven tarsal bones (including the talus and calcaneus), and each foot contains five metatarsal bones. The tarsals and metatarsals form the ankle, heel, and arch of the foot. They give the foot strength while allowing flexibility. The bones in the toes of each foot consist of 14 phalanges (three in each toe except the big toe, which has two phalanges)

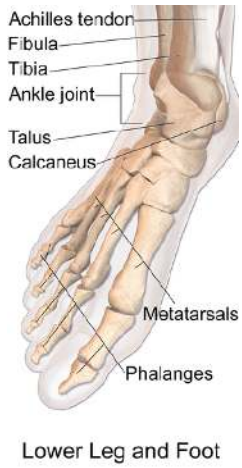


Figure **7.3.11**: Bones of the lower leg (fibula and tibia), ankle (talus), heel (calcaneus), foot (metatarsals), and toes (phalanges).

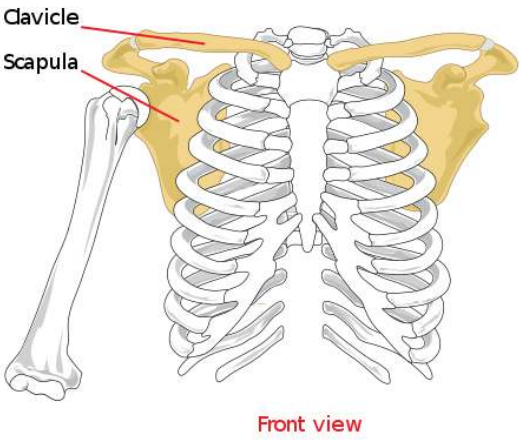


Figure **7.3.12**: Bones of the shoulder girdle are clavicle and scapula.

The pectoral girdle (also called shoulder girdle) attaches the upper limbs to the trunk of the body. Its connection with the axial skeleton is by muscles alone. This allows a considerable range of motion in the upper limbs. The shoulder girdle consists of just two pairs of bones, with one of each pair on opposite sides of the body (Figure **7.3.12**). There is a right and left clavicles (collarbone) and right and left scapulae (shoulder blade). The scapula is a pear-shaped flat bone that helps to form the shoulder joint. The clavicle is a long bone that serves as a strut between the shoulder blade and the sternum.

PELVIC GIRDLE

The **pelvic girdle** attaches the legs to the trunk of the body and also provides a basin to contain and support the organs of the abdomen. It is connected to the vertebral column of the axial skeleton by ligaments. The pelvic girdle consists of two halves, one half for each leg, but the halves are fused with each other in adults at a joint called the pubic symphysis. Each half of the pelvic girdle includes three bones, as shown in the figure below: the ilium (flaring upper part of the pelvic girdle), pubis (lower front), and ischium (lower back). Each of these bones helps form the acetabulum, which is a depression into which the top of the femur (thigh bone) fits. When the body is in a seated position, it rests on protrusions (called tuberosities) of the two ischial bones.

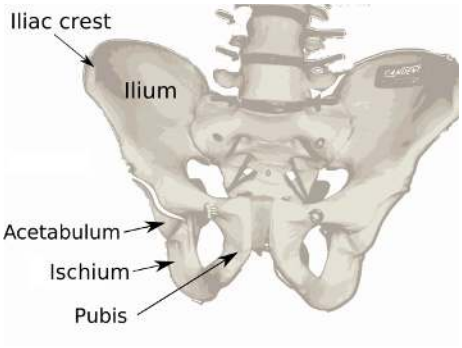


Figure **7.3.13**: Bones of the pelvic girdle.

REVIEW

1. What bones are included in the axial skeleton?
2. Identify the two main parts of the skull. How many bones does each part contain?
3. Describe the vertebral column.
4. What are the advantages of an S-shaped vertebral column?
5. What is the rib cage, and what is its function?
6. What bones are included in the appendicular skeleton?
7. How many bones are found in each upper limb? What are they?
8. Identify the bones in each of the lower limbs.
9. What is the shoulder girdle, and why does it allow considerable upper limb mobility?
10. Describe the pelvic girdle and the bones it contains.
11. *True or False.* False ribs are made of cartilage and are not true rib bones.
12. *True or False.* The jaw contains two maxillae and one mandible.
13. Describe some of the similarities between the upper limbs and the lower limbs.
14. Explain the advantage of having some ribs that are not attached directly to the sternum.
15. Put the following vertebral regions in order, from the closest to the head to the farthest from the head:

    sacral; lumbar; cervical; coccygeal; thoracic

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7.4: STRUCTURE OF BONE

ROASTED BONE MARROW

Do you recognize the food item in the top left of this photo in Figure **7.4.1**? It's roasted bone marrow, still inside the bones. It's considered a delicacy in some cuisines. Marrow is a type of tissue found inside many animal bones, including our own. It's a soft tissue that in adults may be mostly fat. You'll learn more about bone marrow and other tissues that make up bones when you read this concept.



Figure **7.4.1**:Roasted Bone Marrow

Bones are organs that consist primarily of bone tissue, also called osseous tissue. **Bone tissue** is a type of connective tissue consisting mainly of a collagen matrix that is mineralized with calcium and phosphorus crystals. The combination of flexible collagen and hard mineral crystals makes bone tissue hard without making it brittle.

BONE ANATOMY

There are several different types of tissues in bones, including two types of osseous tissues.

TYPES OF OSSEOUS TISSUE

The two different types of osseous tissue are compact bone tissue (also called hard or cortical bone) tissue and spongy bone tissue (also called cancellous or trabecular bone).

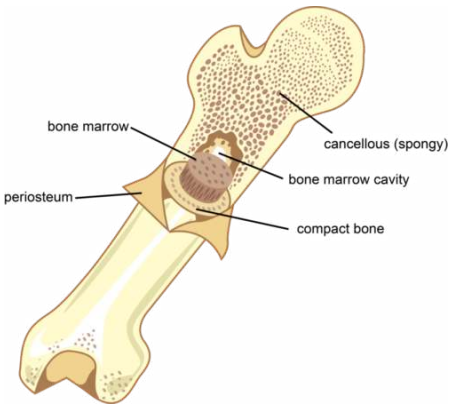


Figure **7.4.2**: Bones are more complex on the inside than you would expect from their outer appearance. There is bone marrow in the hollow part of the long bone. The outer boundary of bone is composed of compact bone tissue, and from the ends, and the rest of the bone interior is composed of cancellous or spongy bone tissue. The bone is covered in connecting tissue called the periosteum.

Compact bone tissue forms the extremely hard outside layer of bones. Cortical bone tissue gives bone its smooth, dense, solid appearance. It accounts for about 80 percent of the total bone mass of the adult skeleton. **Spongy bone tissue** fills part or all of the interior of many bones. As its name suggests, spongy bone is porous like a sponge, containing an irregular network of spaces. This makes spongy bone much less dense than compact bone. Spongy bone has a greater surface area than cortical bone but makes up only 20 percent of bone mass.

Both compact and spongy bone tissues have the same types of cells, but they differ in how the cells are arranged. The cells in the compact bone are arranged in multiple microscopic columns, whereas the cells in the spongy bone are arranged in a looser, more open network. These cellular differences explain why cortical and spongy bone tissues have such different structures.

OTHER TISSUES IN BONES

Besides cortical and spongy bone tissues, bones contain several other tissues, including blood vessels and nerves. In addition, bones contain bone marrow and periosteum. You can see these tissues in Figure **7.4.2**.

- **Bone marrow** is a soft connective tissue that is found inside a cavity, called the marrow cavity. There are two types of marrow in adults, yellow bone marrow, which consists mostly of fat, and red bone marrow. All marrow is red in newborns, but by adulthood, much of the red marrow has changed to yellow marrow. In adults, red marrow is found mainly in the femur, ribs, vertebrae, and pelvic bones. Red bone marrow contains hematopoietic stem cells that give rise to red blood cells, white blood cells, and platelets in the process of hematopoiesis.
- **Periosteum** is a tough, fibrous membrane that covers the outer surface of bones. It provides a protective covering for cortical bone tissue. It is also the source of new bone cells.

BONE CELLS

As shown in Figure **7.4.3**, bone tissues are composed of four different types of bone cells: osteoblasts, osteocytes, osteoclasts, and osteogenic cells.

- **Osteoblasts** are bone cells with a single nucleus that make and mineralize bone matrix. They make a protein mixture that is composed primarily of collagen and creates the organic part of the matrix. They also release calcium and phosphate ions that form mineral crystals within the matrix. In addition, they produce hormones that also play a role in the mineralization of the matrix.
- **Osteocytes** are mainly inactive bone cells that form from osteoblasts that have become entrapped within their own bone matrix. Osteocytes help regulate the formation and breakdown of bone tissue. They have multiple cell projections that are thought to be involved in communication with other bone cells.
- **Osteoclasts** are bone cells with multiple nuclei that resorb bone tissue and break down bone. They dissolve the minerals in bone and release them into the blood.

- **Osteogenic cells** are undifferentiated stem cells. They are the only bone cells that can divide. When they do, they differentiate and develop into osteoblasts.

Bone is a very active tissue. It is constantly remodeled by the work of osteoblasts and osteoclasts. Osteoblasts continuously make new bone, and osteoclasts keep breaking down bone. This allows for minor repair of bones as well as homeostasis of mineral ions in the blood.

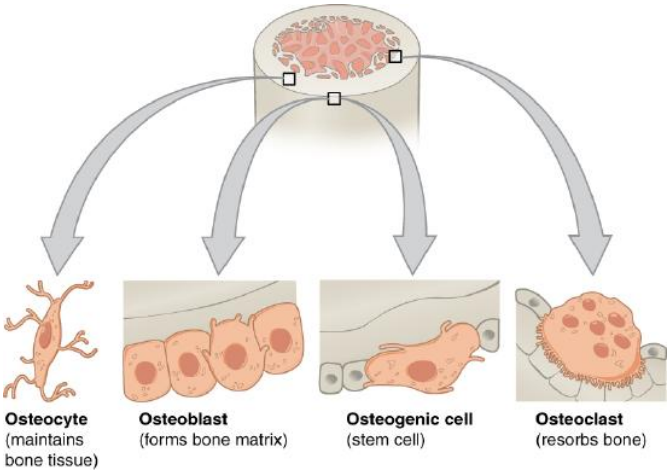


Figure **7.4.3**: Different types of bones cells have different functions.

MICROSCOPIC ANATOMY OF THE COMPACT BONE

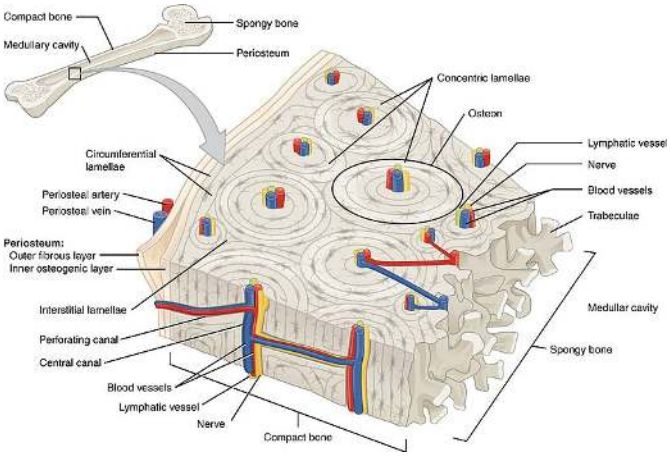


Figure **7.4.4**: Macroscopic and microscopic structures of the compact bone tissue.

The basic microscopic unit of bone is an osteon (or Haversian system). Osteons are roughly cylindrical structures that can measure several millimeters long and around 0.2 mm in diameter. Each osteon consists of lamellae of compact bone tissue that surround a central canal (Haversian canal). The Haversian canal contains the bone's blood supplies. The boundary of an osteon is called the cement line. Osteons can be arranged into woven bone or lamellar bone. Osteoblasts make the matrix of bone which calcifies hardens. This entraps the mature bone cells, osteocytes, in a little chamber called lacunae. The osteocytes receive their nutrition from the central (Haversian) canal via little canals called canaliculi. All of these structures plus more are visible in Figure **7.4.4**.

TYPES OF BONES

There are six types of bones in the human body based on their shape or location: long, short, flat, sesamoid, sutural, and irregular bones. You can see an example of each type of bone in Figure **7.4.5**.

- Long bones are characterized by a shaft that is much longer than it is wide and by a rounded head at each end of the shaft. Long bones are made mostly of compact bone, with lesser amounts of spongy bone and marrow. Most bones of the limbs, including those of the fingers and toes, are long bones.
- Short bones are roughly cube-shaped and have only a thin layer of cortical bone surrounding a spongy bone interior. The bones of the wrists and ankles are short bones.
- Flat bones are thin and generally curved, with two parallel layers of compact bone sandwiching a layer of spongy bone. Most of the bones of the skull are flat bones, as is the sternum (breast bone).
- Sesamoid bones are embedded in tendons, the connective tissues that bind muscles to bones. Sesamoid bones hold tendons farther away from joints so the angle of the tendons is increased, thus increasing the leverage of muscles. The patella (knee cap) is an example of a sesamoid bone.
- Sutural bones are very small bones that are located between the major bones of the skull, within the joints (sutures) between the larger bones. They are not always present.
- Irregular bones are those that do not fit into any of the above categories. They generally consist of thin layers of cortical bone surrounding a spongy bone interior. Their shapes are irregular and complicated. Examples of irregular bones include the vertebrae and the bones of the pelvis.

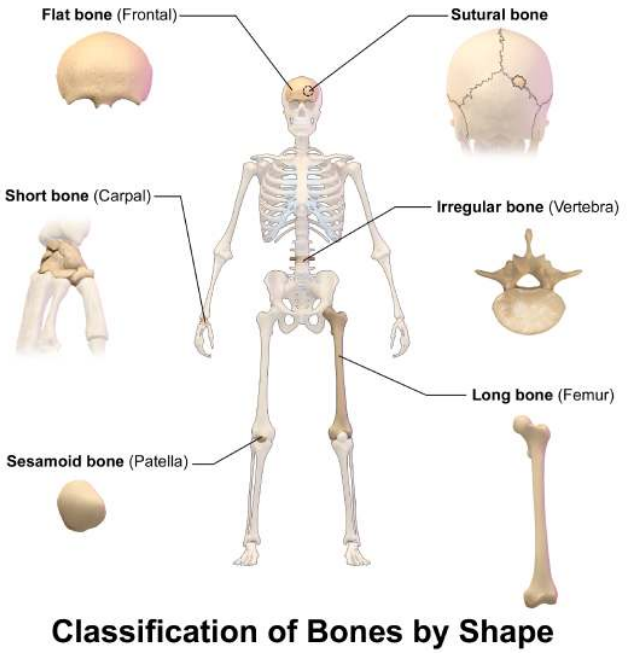


Figure **7.4.5**: six types of bones classified by shape or location.

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FEATURE: RELIABLE SOURCES

Diseased or damaged bone marrow can be replaced by donated bone marrow cells, which help treat and often cure many life-threatening conditions, including leukemia, lymphoma, sickle cell anemia, and thalassemia. If a bone marrow transplant is successful, the new bone marrow will start making healthy blood cells and improve the patient's condition.

Learn more about bone marrow donation, and consider whether you might want to do it yourself. Find reliable sources to answer the following questions:

1. How does one become a potential bone marrow donor?
2. Who can and who cannot donate bone marrow?
3. How is a bone marrow donation made?
4. What risks are there in donating bone marrow?

REVIEW

1. Describe osseous tissue.
2. Why are bones hard but not brittle?
3. Compare and contrast the two main types of osseous tissue.
4. What non-osseous tissues are found in bones?
5. List four types of bone cells and their functions.
6. Identify six types of bones, and give an example of each type.
7. *True or False.* Spongy bone tissue is another name for bone marrow.
8. *True or False.* Periosteum covers osseous tissue.
9. Compare and contrast yellow bone marrow and red bone marrow.
10. Which bone is mostly made of cortical bone tissue?

    A. Pelvis

    B. Vertebrae

    C. Femur

    D. Carpal
11. a. Which type of bone cell divides to produce new bone cells?

    b. Where is this cell type located?
12. Where do osteoblasts and osteocytes come from, and how are they related to each other?
13. Which type of bone is embedded in tendons?
14. *True or False.* Calcium is the only mineral in bones.

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7.5: BONE GROWTH, REMODELING, AND REPAIR

BREAK A LEG

Did you ever break a leg or other bone, like the man looking longingly at the water in this swimming pool? Having a broken bone can really restrict your activity. Bones are very hard, but they will break, or fracture if enough force is applied to them. Fortunately, bones are highly active organs that can repair themselves if they break. Bones can also remodel themselves and grow. You'll learn how bones can do all of these things in this concept.



Figure **7.5.1**: Broken leg

BONE GROWTH

Early in the development of a human fetus, the skeleton is made almost entirely of cartilage. The relatively soft cartilage gradually turns into hard bone through ossification. **Ossification** is a process in which bone tissue is created from cartilage. The steps in which bones of the skeleton form from cartilage are illustrated in Figure **7.5.2**. The steps include the following:

1. Cartilage "model" of bone forms; this model continues to grow as ossification takes place.
2. Ossification begins at a primary ossification center in the middle of the bone.
3. Ossification then starts to occur at secondary ossification centers at the ends of the bone.
4. The medullary cavity forms and will contain red bone marrow.
5. Areas of ossification meet at epiphyseal plates, and articular cartilage forms. Bone growth ends.

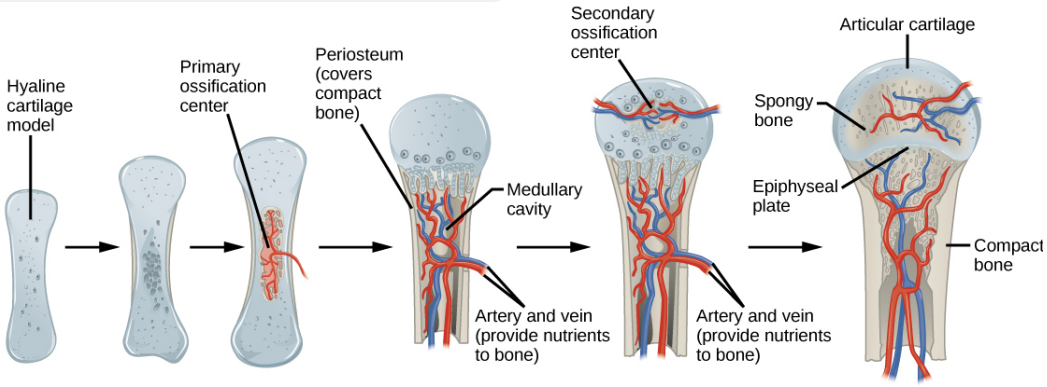


Figure **7.5.2**: The ossification of cartilage in the human skeleton is a process that lasts throughout childhood in some bones.

PRIMARY AND SECONDARY OSSIFICATION CENTERS

When bone forms from cartilage, ossification begins with a point in the cartilage called the primary ossification center. This generally appears during fetal development, although a few short bones begin their primary ossification after birth. Ossification occurs toward both ends of the bone from the primary ossification center, and it eventually forms the shaft of the bone in the case of long bones.

Secondary ossification centers form after birth. Ossification from secondary centers eventually forms the ends of the bones. The shaft and ends of the bone are separated by a growing zone of cartilage until the individual reaches skeletal maturity.

SKELETAL MATURITY

Throughout childhood, the cartilage remaining in the skeleton keeps growing and allows for bones to grow in size. However, once all of the cartilage has been replaced by bone and fusion has taken place at epiphyseal plates, bones can no longer keep growing in length. This is the point at which skeletal maturity has been reached. It generally takes place by age 18 to 25.

The use of anabolic steroids by teens can speed up the process of skeletal maturity, resulting in a shorter period of cartilage growth before fusion takes place. This means that teens who use steroids are likely to end up shorter as adults than they would otherwise have been.

BONE REMODELING

Even after skeletal maturity has been attained, bone is constantly being resorbed and replaced with new bone in a process known as **bone remodeling**. In this lifelong process, mature bone tissue is continually turned over, with about 10 percent of the skeletal mass of an adult being remodeled each year. Bone remodeling is carried

out through the work of osteoclasts, which are bone cells that resorb bone and dissolve its minerals; and osteoblasts, which are bone cells that make the new bone matrix.

Bones remodeling serves several functions. It shapes the bones of the skeleton as a child grows, and it repairs tiny flaws in the bone that result from everyday movements. Remodeling also makes bones thicker at points where muscles place the most stress on them. In addition, remodeling helps regulate mineral homeostasis because it either releases minerals from bones into the blood or absorbs minerals from the blood into bones. The figure below shows how osteoclasts in bones are involved in calcium regulation.

The action of osteoblasts and osteoclasts in bone remodeling and calcium homeostasis is controlled by a number of enzymes, hormones, and other substances that either promote or inhibit the activity of the cells. In this way, these substances control the rate at which bone is made, destroyed, and changed in shape. For example, the rate at which osteoclasts resorb bone and release calcium into the blood is promoted by parathyroid hormone (PTH) and inhibited by calcitonin, which is produced by the thyroid gland (Figure **7.5.3**). The rate at which osteoblasts create new bone is stimulated by growth hormone, which is produced by the anterior lobe of the pituitary gland. Thyroid hormone and sex hormones (estrogens and androgens) also stimulate osteoblasts to create new bone.

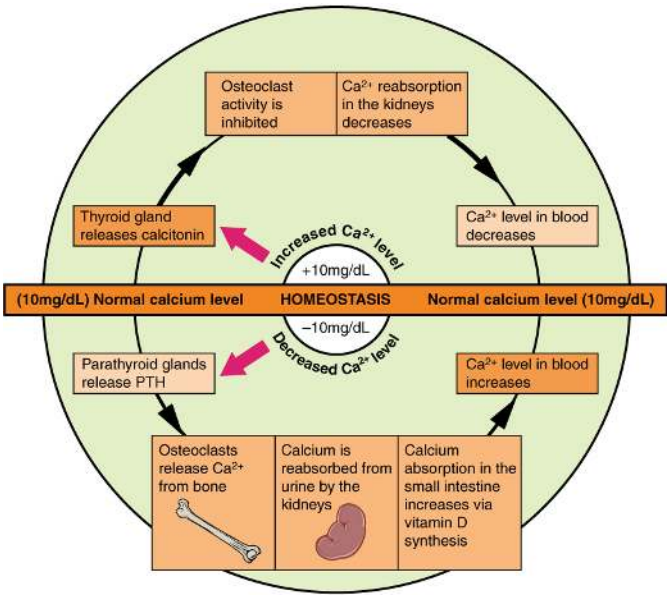


Figure **7.5.3**: Keeping the calcium level in homeostasis includes the work of osteoclasts, the bone cells that resorb bone and release calcium into the blood. If calcium levels increase, the thyroid releases calcitonin which inhibits osteoclast activity. This results in less calcium be reabsorbed in the kidneys which results in the lowering of calcium in the blood. If calcium levels decrease below homeostasis, the parathyroid gland releases PTH. This causes osteoclasts to release calcium from bones and increases calcium absorption in the kidney and small intestines. This brings calcium back to homeostasis.

BONE REPAIR

Bone repair, or healing, is the process in which a bone repairs itself following a bone fracture. You can see an X-ray of bone fracture in Figure **7.5.4**. In this fracture, the humerus in the upper arm has been completely broken through its shaft. Before this fracture heals, a physician must push the displaced bone parts back into their correct positions. Then the bone must be stabilized — for example, with a cast and/or pins surgically inserted into the bone — until the bone's natural healing process is completed. This process may take several weeks.

The process of bone repair is mainly determined by the periosteum, which is the connective tissue membrane covering the bone. The periosteum is the primary source of precursor cells that develop into osteoblasts, which are essential to the healing process. Bones heal as osteoblasts form new bone tissue.

Although bone repair is a natural physiological process, it may be promoted or inhibited by several factors. For example, fracture repair is likely to be more successful with adequate nutrient intake. Age, bone type, drug therapy, and pre-existing bone disease are additional factors that may affect healing. Bones that are weakened by diseases, such as osteoporosis or bone cancer, are not only likely to heal more slowly but are also more likely to fracture in the first place.



Figure **7.5.4**: A bone fracture does not always involve a complete break in the bone, as in this X-ray. Sometimes a fracture is just a crack in the bone. In other cases, the bone not only breaks all the way through, as here but also breaks through the soft tissues around it so it protrudes from the skin. This is called an open fracture.

FEATURE: MYTH VS. REALITY

Bone fractures are fairly common, and there are many myths about them. Knowing the facts is important because fractures generally require emergency medical treatment.

Myth: A bone fracture is a milder injury than a broken bone.

Reality: A bone fracture is the same thing as a broken bone.

Myth: If you still have a full range of motion in a limb, then it must not be fractured.

Reality: Even if a bone is fractured, the muscles and tendons attached to it may still be able to move the bone normally. This

is especially likely if the bone is cracked but not broken into two pieces. Even if a bone is broken all the way through, the range of motion may not be much affected if the bones on either side of the fracture remain properly aligned.

Myth: A fracture always produces a bruise.

Reality: Many but not all fractures produce a bruise. If a fracture does produce a bruise, it may take several hours or even a day or more for the bruise to appear.

Myth: Fractures are so painful that you will immediately know if you break a bone.

Reality: Ligament sprains and muscle strains are also very painful, sometimes more painful than fractures. Additionally, every person has a different pain tolerance. People with high pain tolerance may continue using a broken bone in spite of the pain.

Myth: You can tell when a bone is fractured because there will be very localized pain over the break.

Reality: A broken bone is often accompanied by injuries to surrounding muscles or ligaments. As a result, the pain may extend far beyond the location of the fracture. The pain may be greater directly over the fracture, but the intensity of the pain may make it difficult to pinpoint exactly where the pain originates.

REVIEW

1. Outline how bone develops from early in the fetal stage through the age of skeletal maturity.
2. Describe the process of bone remodeling. When does it occur?
3. What purposes does bone remodeling serve?
4. Define bone repair. How long does this process take?
5. Explain how bone repair occurs.
6. Identify factors that may affect bone repair.
7. Parts of bone that have not yet become ossified are made of _____.
8. If there is a large region between the primary and secondary ossification centers in a bone, is the person young or old? Explain your answer.
9. The region where the primary and secondary ossification centers meet is called the _____.
10. *True or False.* Most bones are made entirely of cartilage at birth.
11. *True or False.* A broken bone is the same as a bone fracture.
12. If bones can repair themselves, why are casts and pins sometimes needed?
13. Which bone cell type causes the release of calcium to the bloodstream when calcium levels are low?
14. Which tissue and bone cell type are mainly involved in bone repair after a fracture?
15. Describe one way in which hormones are involved in bone remodeling.

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7.6: JOINTS

DOUBLE JOINTED?

Is this person double jointed? No; there is no such thing, at least as far as humans are concerned. However, some people, like the individual pictured here, are much more flexible than others, generally because they have looser ligaments. Physicians call the condition joint hypermobility. Regardless of what it's called, the feats of people with highly mobile joints can be quite impressive.



Figure **7.6.1**: Yoga

WHAT ARE JOINTS?

Joints are locations at which bones of the skeleton connect with one another. A joint is also called an articulation. The majority of joints are structured in such a way that they allow movement. However, not all joints allow movement. Of joints that do allow movement, the extent, and direction of the movements they allow also vary.

CLASSIFICATION OF JOINTS

Joints can be classified as structurally or functionally. The structural classification of joints depends on the manner in which the bones connect to each other. The functional classification of joints depends on the nature of the movement the joints allow. There is significant overlap between the two types of classifications because function depends largely on the structure.

STRUCTURAL CLASSIFICATION OF JOINTS

The structural classification of joints is based on the type of tissue that binds the bones to each other at the joint. There are three types of joints in the structural classification: fibrous, cartilaginous, and synovial joints.

1. **Fibrous joints** are joints in which bones are joined by dense connective tissue that is rich in collagen fibers. These joints are also called sutures. The joints between bones of the cranium are fibrous joints.
2. **Cartilaginous joints** are joints in which bones are joined by cartilage. The joints between most of the vertebrae in the spine are cartilaginous joints.
3. **Synovial joints** are characterized by a fluid-filled space, called a synovial cavity, between the bones of the joints. You can see a drawing of a typical synovial joint in Figure **7.6.2**. The cavity is enclosed by a membrane and filled with a fluid, called the synovial fluid, which provides extra cushioning to the ends of the bones. Cartilage covers the articulating surfaces of the two bones, but the bones are actually held together by ligaments. The knee is a synovial joint.

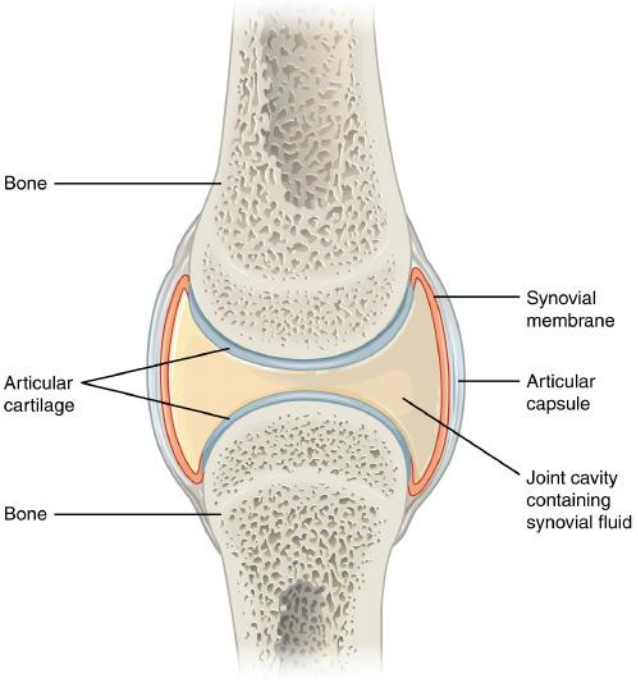


Figure **7.6.2**: The synovial membrane, articular capsule, joint cavity with synovial fluid, articular cartilage, and bone ends are the main components of a typical synovial joint.

FUNCTIONAL CLASSIFICATION OF JOINTS

The functional classification of joints is based on the type and degree of movement that they allow. There are three types of joints in the functional classification: immovable, partly movable, and movable joints.

1. Immovable joints allow little or no movement at the joint. Most immovable joints are fibrous joints. Besides the bones of the cranium, immovable joints include joints between the tibia and fibula in the lower leg and between the radius and ulna in the lower arm.
2. Partly movable joints permit slight movement. Most partly movable joints are cartilaginous joints. Besides the joints between vertebrae, they include the joints between the ribs and sternum (breast bone).
3. Movable joints allow bones to move freely. All movable joints are synovial joints. Besides the knee, they include the shoulder, hip, and elbow. Movable joints are the most common type of joints in the body.

TYPES OF MOVABLE JOINTS

Movable joints can be classified further according to the type of movement they allow. There are six classes of movable joints: pivot, hinge, saddle, plane, condyloid, and ball-and-socket joints. An example of each class, as well as the type of movement it allows, is shown in Figure **7.6.3**.

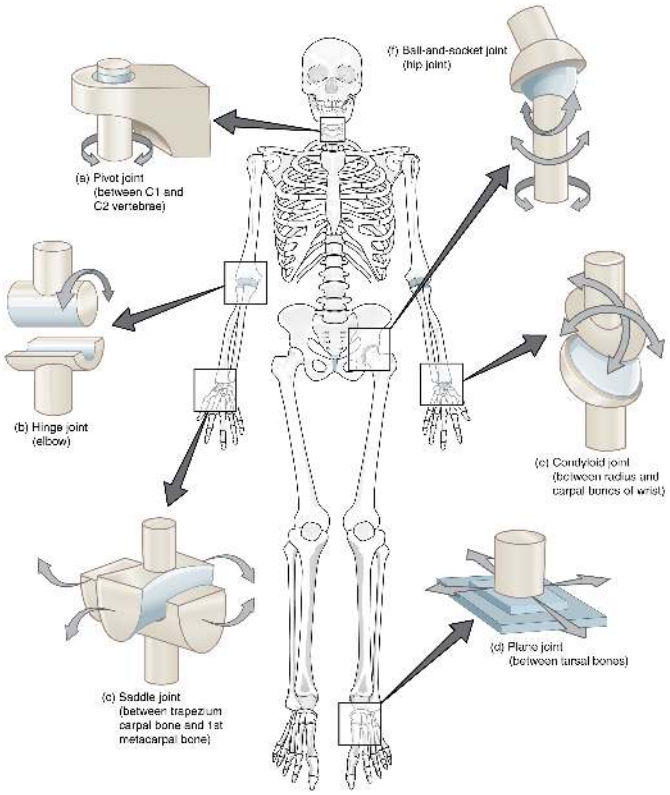


Figure **7.6.3**: This diagram shows the six classes of movable joints in the human body. All of these joints are synovial joints.

- A pivot joint allows one bone to rotate around another. An example of a pivot joint is the joint between the first two vertebrae in the spine. This joint allows the head to rotate from left to right and back again.
- A hinge joint allows back and forth movement like the hinge of a door. An example of a hinge joint is the elbow. This joint allows the arm to bend back and forth.
- A saddle joint allows two different types of movement. An example of a saddle joint is the joint between the first metacarpal bone in the hand and one of the carpal bones in the wrist. This joint allows the thumb to move toward and away from the index finger and also to cross over the palm toward the little finger.
- A plane joint also called a gliding joint, allows two bones that glide over one another. The joints between the tarsals in the ankles and between the carpals in the wrists are mainly gliding joints. In the wrist, this type of joint allows the hand to bend upward at the wrist and also to wave from side to side while the lower arm is held steady.
- A condyloid joint is one in which an oval-shaped head on one bone moves in an elliptical cavity in another bone, allowing movement in all directions except rotation around an axis. The joint between the radius in the lower arm and carpal bones of the wrist is a condyloid joint as is the joint at the base of the index finger.
- A ball-and-socket joint allows the greatest range of movement of any movable joint. It allows forward and backward as well as upward and downward motions. It also allows rotation in a circle. The hip and shoulder are the only two ball-and-socket joints in the human body.

FEATURE: MY HUMAN BODY

Of all the parts of the skeletal system, the joints are generally the most fragile and subject to damage. If the cartilage that cushions bones at joints wears away, it does not grow back. Eventually, all of the cartilage may wear away. This is the cause of osteoarthritis, which can be both painful and debilitating. In serious cases, people may lose the ability to climb stairs, walk long distances, perform routine daily activities, or participate in activities they love such as gardening or playing sports. If you protect your joints, you can reduce your chances of joint damage, pain, and disability. If you already have joint damage, it is equally important to protect your joints and limit further damage. Follow these five tips:

1. Maintain a normal, healthy weight. The higher your weight is, the more force you exert on your joints. When you walk, each knee has to bear a force equal to as much as six times your body weight. If a person weighs 200 pounds, each knee bears more than half a ton of weight with every step. Seven in ten knee replacement surgeries for osteoarthritis can be attributed to obesity.
2. Avoid too much high-impact exercise. Examples of high-impact activities include volleyball, basketball, and tennis. These activities generally involve running or jumping on hard surfaces, which puts tremendous stress on weight-bearing joints, especially the knees. Replace some or all of your high-impact activities with low-impact activities, such as biking, swimming, yoga, or lifting light weights.
3. Reduce your risk of injury. Don't be a weekend warrior, sitting at a desk all week and then crowding all your physical activity into two days. Get involved in a regular, daily exercise routine that keeps your body fit and your muscles toned. Building up muscles will make your joints more stable and spread stress across them. Be sure to do some stretching every day to keep the muscles around joints flexible and less prone to injury.
4. Distribute work over your body, and use your largest, strongest joints. Use your shoulder, elbow, and wrist to lift heavy objects, not just your fingers. Hold small items in the palm of your hand, rather than by the fingers. Carry heavy items in a backpack rather than in your hands. Hold weighty objects close to your body rather than at arms' length. Lift with your hips and knees, not your back.
5. Respect pain. If it hurts, stop doing it. Take a break from the activity at least until the pain stops. Try to use joints only to the point of mild fatigue, not pain.

REVIEW

1. What are the joints?
2. What are the two ways that joints are commonly classified?

3. How are joints classified structurally?
4. Describe the functional classification of joints.
5. How are movable joints classified?
6. Name the six classes of movable joints, and describe how they move.
7. Give an example of a joint in each of the classes of movable joints.
8. *True or False.* The skull is one smooth bone and has no joints.
9. *True or False.* A plane joint is a type of synovial joint.
10. Which specific type of moveable joint do you think your knee joint is? Explain your reasoning.
11. Explain the difference between cartilage in a cartilaginous joint and cartilage in a synovial joint.
12. Why are fibrous joints immovable?
13. Which type of joint has ligaments?

    A. Ball-and-socket
    B. Fibrous
    C. Cartilaginous
    D. None of the above

14. Which type of joint allows for the greatest range of motion?
15. What is the function of synovial fluid?

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7.7: DISORDERS OF THE SKELETAL SYSTEM

DOWAGER'S HUMP

The individual on the right in Figure **7.7.1** has a deformity in her back commonly called dowager's hump because it occurs most often in elderly women. Its medical name is kyphosis, and it is defined as excessive curvature of the spinal column in the thoracic region. The curvature generally results from fractures of thoracic vertebrae. As the inset drawings suggest, these fractures may occur due to a significant decrease in bone mass, which is called osteoporosis. Osteoporosis is one of the most prevalent disorders of the skeletal system.



Figure **7.7.1**: Kyphosis

COMMON SKELETAL SYSTEM DISORDERS

A number of disorders affect the skeletal system, including bone fractures and bone cancers. However, the two most common disorders of the skeletal system are osteoporosis and osteoarthritis. At least ten million people in the United States have osteoporosis, and more than 8 million of them are women. Osteoarthritis is even more common, affecting almost 30 million people in the United States. Because osteoporosis and osteoarthritis are so common, they are the focus of this concept. These two disorders are also good examples to illustrate the structure and function of the skeletal system.

OSTEOPOROSIS

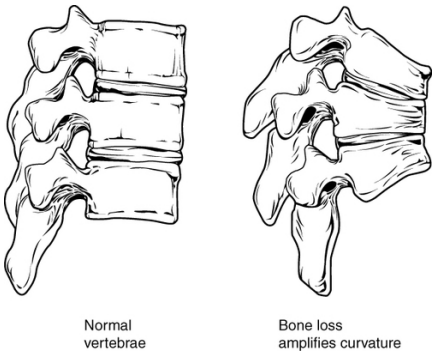


Figure **7.7.2**: Compression fractures of thoracic vertebrae are relatively common in people with osteoporosis.

Osteoporosis is an age-related disorder in which bones lose mass, weaken, and break more easily than normal bones. Bones may weaken so much that a fracture can occur with minor stress — or even spontaneously, without any stress at all. Osteoporosis is the most common cause of broken bones in the elderly, but until a bone fracture occurs, it typically causes no symptoms. The bones that break most often include those in the wrist, hip, shoulder, and spine. When the thoracic vertebrae are affected, there can be a gradual collapse of the vertebrae due to compression fractures, as shown in Figure **7.7.2**. This is what causes kyphosis, as pictured in Figure **7.7.1**.

CHANGES IN BONE MASS WITH AGE

As shown in the graph below, bone mass in both males and females generally peaks when people are in their thirties. Bone mass usually decreases after that, and this tends to occur more rapidly in individuals with XX chromosomes, especially after menopause. This is generally attributable to low levels of estrogen in the post-menopausal years.

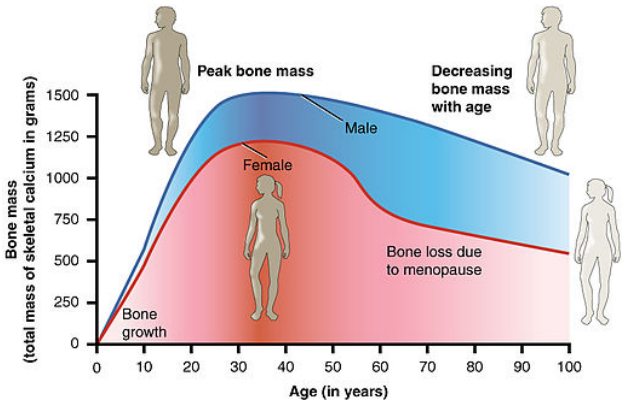


Figure **7.7.3**: Bone mass is a measure of the total mass of calcium in the bones of the skeleton. The chart shows that the bone mass peaks around age 30 in males and females. Then it starts to decrease.

WHAT CAUSES OSTEOPOROSIS?

Osteoporosis is due to an imbalance between bone formation by osteoblasts and bone resorption by osteoclasts. Normally, bones are constantly being remodeled by these two processes, with up to ten percent of all bone mass undergoing remodeling at any point in time. If these two processes are in balance, no net loss of bone occurs. There are three main ways that an imbalance between bone formation and bone resorption can occur and lead to a net loss of bone.

1. **An individual never develops normal peak bone mass during the young adult years:** If the peak level is lower than normal, then there is less bone mass, to begin with, making osteoporosis more likely to develop.
2. **There is greater than normal bone resorption:** Bone resorption normally increases after peak bone mass is reached, but age-related bone resorption may be greater than normal for a variety of reasons. One possible reason is calcium or vitamin D

deficiency, which causes the parathyroid gland to release PTH, the hormone that promotes resorption by osteoclasts.

3. **There is the inadequate formation of new bone by osteoblasts during remodeling:** Lack of estrogen may decrease the normal deposition of new bone. Inadequate levels of calcium and vitamin D also lead to the impaired bone formation by osteoblasts.

An imbalance between bone building and bone destruction leading to bone loss may also occur as a side effect of other disorders. For example, people with alcoholism, anorexia nervosa, or hyperthyroidism have an increased rate of bone loss. Some medications — including anti-seizure medications, chemotherapy drugs, steroid medications, and some antidepressants — also increase the rate of bone loss.

OSTEOPOROTIC FRACTURES

Fractures are the most dangerous aspect of osteoporosis, and osteoporosis is responsible for millions of fractures annually. Debilitating pain among the elderly is often caused by fractures from osteoporosis, and it can lead to further disability and early mortality. Fractures of the long bones (such as the femur) can impair mobility and may require surgery. A hip fracture usually requires immediate surgery, as well. The immobility associated with fractures — especially of the hip — increases the risk of deep vein thrombosis, pulmonary embolism, and pneumonia. Osteoporosis is rarely fatal, but these complications of fractures often are. Older people tend to have more falls than younger people, due to such factors as poor eyesight and balance problems, increasing their risk of fractures even more. The likelihood of falls can be reduced by removing obstacles and loose carpets or rugs in the living environment.

RISK FACTORS FOR OSTEOPOROSIS

There are a number of factors that increase the risk of osteoporosis. Eleven of them are listed below. The first five factors cannot be controlled, but the remaining factors generally can be controlled by changing behaviors.

1. older age
2. XX chromosome
3. European or Asian ancestry
4. family history of osteoporosis
5. short stature and small bones
6. smoking
7. alcohol consumption
8. lack of exercise
9. vitamin D deficiency
10. poor nutrition
11. consumption of soft drinks

TREATMENT AND PREVENTION OF OSTEOPOROSIS

Osteoporosis is often treated with medications that may slow or even reverse bone loss. Medications called bisphosphonates, for example, are commonly prescribed. Bisphosphonates slow down the breakdown of bone, allowing bone rebuilding during remodeling to keep pace. This helps maintain bone density and decreases the risk of fractures. The medications may be more effective in patients who have already broken bones than in those who have not, significantly reducing their risk of another fracture. Generally, patients are not recommended to stay on bisphosphonates for more than three or four years. There is no evidence for continued benefit after this time — in fact, there is a potential for adverse side effects.



Figure **7.7.4**: Hiking is an enjoyable way to help keep bones strong and reduce the risk of osteoporosis.

Preventing osteoporosis includes eliminating any risk factors that can be controlled through changes of behavior. If you smoke, stop. If you drink, reduce your alcohol consumption — or cut it out altogether. Eat a nutritious diet and make sure you are getting adequate amounts of vitamin D. You should also avoid drinking carbonated beverages.

If you're a couch potato, get involved in regular exercise. Aerobic, weight-bearing and resistance exercises can all help maintain or increase bone mineral density. Exercise puts stress on bones, which stimulates bone building. Good weight-bearing exercises for bone-building include weight training, dancing, stair climbing, running, and hiking (Figure **7.7.4**). Biking and swimming are less beneficial because they don't stress the bones. Ideally, you should exercise for at least 30 minutes a day on most days of the week.

OSTEOARTHRITIS

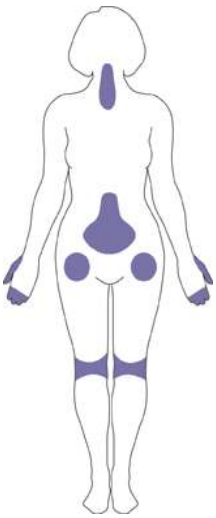


Figure **7.7.5**: The areas shaded in blue indicate the joints most commonly affected by OA.

Osteoarthritis (OA) is a joint disease that results from the breakdown of joint cartilage and bone. The most common symptoms are joint pain and stiffness. Other symptoms may include joint swelling and decreased range of motion. Initially, symptoms may

occur only after exercise or prolonged activity, but over time, they may become constant, negatively affecting work and normal daily activities. As shown in Figure **7.7.5**, the most commonly involved joints are those near the ends of the fingers, at the bases of the thumbs, and in the neck, lower back, hips, and knees. Often, joints on one side of the body are affected more than those on the other side.

WHAT CAUSES OSTEOARTHRITIS?

OA is thought to be caused by mechanical stress on the joints with insufficient self-repair of cartilage. The stress may be exacerbated by low-grade inflammation of the joints, as cells lining the joint attempt to remove breakdown products from cartilage in the synovial space. OA develops over decades as stress and inflammation cause an increasing loss of articular cartilage. Eventually, bones may have no cartilage to separate them, so bones rub against one another at joints. This damages the articular surfaces of the bones and contributes to the pain and other symptoms of OA. Because of the pain, movement may be curtailed, leading to loss of muscle, as well.

DIAGNOSING OSTEOARTHRITIS

Diagnosis of OA is typically made on the basis of signs and symptoms. Signs include joint deformities, such as bony nodules on the finger joints or bunions on the feet (Figure **7.7.6**). Symptoms include joint pain and stiffness. The pain is usually described as a sharp ache or burning sensation, which may be in the muscles and tendons around the affected joints, as well as in the joints themselves. The pain is usually made worse by prolonged activity, and it typically improves with rest. Stiffness is most common when first arising in the morning, and it usually improves quickly as daily activities are undertaken.



Figure **7.7.6**. A bunion is a common sign of osteoarthritis. It is typically located at the base of the big toe.

X-rays or other tests are sometimes used to either support the diagnosis of OA or to rule out other disorders. Blood tests might be done, for example, to look for factors that indicate rheumatoid arthritis (RA), an autoimmune disease in which the immune system attacks the body's joints. If these factors are not present in the blood, then RA is unlikely, and a diagnosis of OA is more likely to be correct.

RISK FACTORS FOR OSTEOARTHRITIS

Age is the chief risk factor for osteoarthritis. By age 65, as many as 80 percent of all people have evidence of osteoarthritis. However, people are more likely to develop OA — especially at younger ages — if they have had a joint injury. A high school football player might have a bad knee injury that damages the joint, leading to OA in the knee by the time he is in his thirties. If people have joints that are misaligned due to congenital malformations or disease, they are also more likely to develop OA. Excess body weight is another factor that increases the risk of OA, because of the added stress it places on weight-bearing joints.

Researchers have found that people with a family history of OA have a heightened risk of developing the disorder, which suggests that genetic factors are also involved in OA. It is likely that many different genes are needed for normal cartilage and cartilage repair. If such genes are defective and cartilage is abnormal or not normally repaired, OA is more likely to result.

TREATMENT AND PREVENTION OF OSTEOARTHRITIS

OA cannot be cured, but the symptoms — especially the pain — can often be treated successfully to maintain a good quality of life for people with OA. Treatments include exercise, efforts to decrease stress on joints, pain medications, and surgery.

DESTRESSING JOINTS

Efforts to decrease stress on joints include resting and using mobility devices such as canes, which reduce the weight placed on weight-bearing joints and also improve stability. In people who are overweight, losing weight may also reduce joint stress.

EXERCISE

Exercise helps maintain joint mobility and also increases muscle strength. Stronger muscles may help keep the bones in joints correctly aligned, and this can reduce joint stress. Good exercises for OA include swimming, water aerobics (see Figure **7.7.7**), and biking. These activities are recommended for OA because they put relatively little stress on the joints.



Figure **7.7.7**: Exercising in water provides buoyancy that places less stress on joints than the same exercises would on the ground or other hard surfaces.

PAIN MEDICATIONS

The first type of pain medication likely to be prescribed for OA is acetaminophen (e.g., Tylenol). When taken as prescribed, it has a relatively low risk of serious side effects. If this medication is inadequate to relieve the pain, non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen) may be prescribed. NSAIDs, however, are more likely to cause serious side effects, such as gastrointestinal bleeding, elevated blood pressure, and increased risk of stroke. Opioids usually are reserved for patients who have suffered serious side effects or for whom other medications have failed to relieve pain. Due to the risk of addiction, the short-term use of opioids is generally recommended.

SURGERY

Joint replacement surgery is the most common treatment for serious OA in the knee or hip. In fact, knee and hip replacement surgeries are among the most common of all surgeries. Although they require a long period of healing and physical rehabilitation, the results are usually worth it. The replacement "parts" are usually pain-free and fully functional for at least a couple of decades. Quality, durability, and customization of artificial joints are constantly improving.

FEATURE: MYTH VS. REALITY

About one out of every two Americans will develop osteoarthritis in his or her lifetime. The more you know about this disease, the more you can do to avoid it or slow its progression. That means knowing the facts, rather than believing the myths about osteoarthritis.

Myth: Cracking my knuckles will cause osteoarthritis.

Reality: Cracking your knuckles may lead to inflammation of your tendons, but it will not cause osteoarthritis.

Myth: My diet has no effect on my joints.

Reality: What and how much you eat *does* affect your body weight, and every pound you gain translates into an additional four pounds (or more!) of stress on your knees. Being overweight, therefore, increases the chances of developing osteoarthritis — and also the rate at which it progresses.

Myth: Exercise causes osteoarthritis or makes it worse, so I should avoid it.

Reality: This is one of the biggest myths about osteoarthritis. Low-impact exercise can actually lessen the pain and improve other symptoms of osteoarthritis. If you don't have osteoarthritis, exercise can reduce your risk of developing it. Low-impact exercise helps keep the muscles around joints strong and flexible, so they can help stabilize and protect the joints.

Myth: If my mom or dad has osteoarthritis, I will also develop it.

Reality: It is true that you are more likely to develop osteoarthritis if a parent has it, but it isn't a sure thing. There are several things you can do to decrease your risk, such as getting regular exercise and maintaining a healthy weight.

Myth: Bad weather causes osteoarthritis.

Reality: Weather conditions do not cause osteoarthritis, although, in some people who already have osteoarthritis, bad weather seems to make the symptoms worse. It is primarily low barometric pressure that increases osteoarthritis pain, probably because it leads to greater pressure inside the joints relative to the outside air pressure. Some people think their osteoarthritis pain is worse in cold weather, but systematic studies have not found convincing evidence for this.

Myth: Joint pain is unavoidable as you get older, so there is no need to see a doctor for it.

Reality: Many people with osteoarthritis think there is nothing that can be done for the pain of osteoarthritis, or that surgery is the only treatment option. In reality, osteoarthritis symptoms often can be improved with a combination of exercise, weight loss, pain management techniques, and pain medications. If osteoarthritis pain interferes with daily life and lasts more than a few days, you should see your doctor.

Myth: Osteoarthritis is inevitable in seniors.

Reality: Although many people over 65 develop osteoarthritis, there are many people who never develop it, no matter how old they live to be. You can reduce your risk of developing osteoarthritis in later life by protecting your joints throughout life.

REVIEW

1. Name the two most common disorders of the skeletal system.
2. What is osteoporosis? What causes it?
3. How is osteoporosis diagnosed?
4. Why is osteoporosis dangerous?
5. Identify risk factors for osteoporosis.
6. How is osteoporosis treated? What can be done to prevent it?
7. What is OA? What are its chief symptoms?
8. What causes OA?
9. Describe how OA is diagnosed.
10. Identify risk factors for OA.
11. How is OA treated?
12. Why is it important to build sufficient bone mass in your young adult years?
13. Explain the difference in the cause of rheumatoid arthritis and osteoarthritis.
14. *True or False:* Osteoarthritis is caused by physical activity, so people who are equally active are equally susceptible to it.
15. *True or False:* Estrogen generally promotes the production of new bone.

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ATTRIBUTIONS

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7.8: CASE STUDY CONCLUSION- HEELS AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: A PAIN IN THE FOOT

You may have seen signs such as the one in Figure **7.8.1** indicating that high-heeled shoes are not allowed on certain walking surfaces because of the risk of injury. High heels affect a person's balance, and wearers can easily twist their ankle on uneven or slippery surfaces, causing a sprain or even a fracture. Besides twisting an ankle, wearing high heels on a regular basis can cause a variety of other negative health consequences—some of which may be long-lasting.



Figure **7.8.1**: No heels

As Amari discovered at the beginning of the chapter, wearing high heels can result in a condition called metatarsalgia. Metatarsalgia is named for the metatarsal bones, which are the five bones that run through the ball of the foot just behind the toes (highlighted in Figure **7.8.2**) Wearing high heels causes excessive pressure on the ball of the foot, as described at the beginning of this chapter. Additionally, the toes are forced to pull upwards in high heels, which moves the fleshy padding away from the ball of the foot, adding to the overall pressure placed on this region. Over time, this can cause inflammation and direct stress on the bones, resulting in pain in the ball of the foot known as metatarsalgia. The pain particularly occurs in weight-bearing positions such as standing, walking, or running—which is what Amari was experiencing. There may also be pain, numbness, or tingling in the toes associated with metatarsalgia.

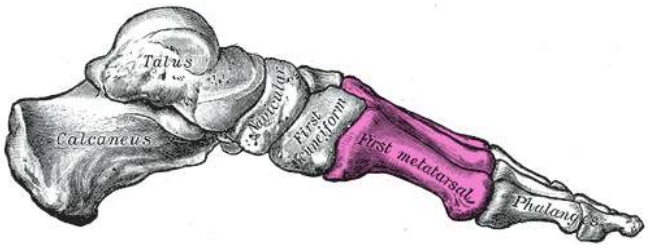


Figure **7.8.2**: Illustration of the bones of the foot, with the metatarsal bones highlighted in pink.

Wearing high heels can also cause stress fractures in the feet, which are tiny breaks in the bone that occur due to repeated mechanical stress. This is due to the excessive pressure that high heels put on some of the bones of the feet. These fractures are somewhat similar to what occurs in osteoporosis when the bone mass decreases to the point where bones can fracture easily as people go about their daily activities. In both cases, a major, noticeable injury is not necessary to create tiny fractures. As you have learned, tiny fractures that accrue over time are the cause of dowager's hump, or kyphosis, which is often seen in women with osteoporosis.

Don't think you are immune to stress fractures just because you don't wear high heels! This injury also commonly occurs in people who participate in sports that involve repetitive striking of the foot on the ground, such as running, tennis, basketball, or gymnastics. Stress fractures may be avoided by taking preventative measures such as ramping up any increase in activity slowly, cross-training by engaging in a variety of different sports or activities, resting if you experience pain, and wearing well-cushioned and supportive running shoes.

Amari learned through their online research that wearing high heels can also lead to foot deformities such as bunions and hammertoes. As you saw in the section *Disorders of the Skeletal System*, a bunion is a protrusion on the side of the foot, most often at the base of the big toe. It can be caused by wearing shoes with a narrow, pointed toe box — a common shape for high heels (see Figure **7.8.3**). The pressure of the shoes on the side of the foot causes an enlargement of bone or inflammation of other tissues in the region, which pushes the big toe towards the other toes.



Figure **7.8.3**: High heels with a narrow, pointed toe box and thin stiletto heels.

Hammertoes are abnormal bend in the middle joint of the second, third, or fourth toe (with the big toe being the first toe), causing the toe to be shaped similar to a hammer as seen in Figure **7.8.4**. The narrow, pointed toe box of many high heels, combined with the way the toes are squished into the front of the shoe as a result of the height of the heel, can cause the toes to become deformed in this manner. Treatments for bunions and hammertoe include wearing shoes with a roomy toe box, padding or taping the toes, and toe exercises and stretches. If the bunion or hammertoe does not respond to these treatments, surgery may be necessary to correct the deformity.



Figure **7.8.4**: X-ray of a hammer toe.

Because the bones of the skeleton are connected and work together with other systems to support the body, wearing high heels can also cause physical problems in areas other than the feet. Wearing high heels shifts a person's posture and alignment and can put a strain on tendons, muscles, and other joints in the body. For instance, research from a team at Stanford University published in 2014 suggests that wearing high heels, particularly if the person is overweight or the heels are very high, may increase the risk of osteoarthritis (OA) in the knee due to added stress on the knee joint as the person walks. As you have learned, OA results from the breakdown of cartilage and bone at the joint. Because it can only be treated to minimize symptoms, not cured, OA could be an unfortunate long-term consequence of wearing high heels.

Amari has decided that wearing high heels regularly is not worth the pain and potential long-term damage to their body. After consulting with their doctor, who confirmed they have metatarsalgia, Amari was able to successfully treat it with ice, rest, and wearing comfortable, supportive shoes instead of heels.

High heels are not the only kind of shoes that can cause problems. Flip-flops, worn-out sneakers, and shoes that are too tight can all cause foot issues. To prevent future problems from shoe choices, Amari is following guidelines recommended by medical experts, which include:

- Wearing shoes that fit well, have plenty of room in the toe box, are supportive, and are comfortable right away. There should be no "break-in" period needed for shoes.
- Avoiding shoes that have high heels, especially ones over two inches in height; narrow, pointed toe boxes; or very thin heels. The shoes in Figure **7.8.3** are an example of a type that should be avoided!
- If high heels must be worn, they should be worn for only a limited period of time.

As you have learned in this chapter, your skeletal system carries out a variety of important functions in your body, including physical support. But even though it is strong, your skeletal system can become damaged and deformed—even through such a seemingly innocuous act as wearing a certain type of shoe. Taking good care of your skeletal system is necessary to help it continue to take good care of the rest of you.

CHAPTER SUMMARY

In this chapter, you learned about the skeletal system. Specifically, you learned that:

- The skeletal system is the organ system that provides an internal framework for the human body. In adults, the skeletal system contains 206 bones.
- Bones are organs made of dense connective tissues, mainly the tough protein collagen. Bones also contain blood vessels, nerves, and other tissues. Bones are hard and rigid due to deposits of calcium and other mineral salts within their living tissues. Besides bones, the skeletal system includes cartilage and ligaments.
- The skeletal system has many different functions, including supporting the body and giving it shape, protecting internal organs, providing attachment surfaces for skeletal muscles, allowing body movements, producing blood cells, storing minerals, helping to maintain mineral homeostasis, and producing endocrine hormones.
- The skeleton is traditionally divided into two major parts: the axial skeleton and the appendicular skeleton.
- The axial skeleton consists of a total of 80 bones. It includes the skull, vertebral column, and rib cage. It also includes the three tiny ossicles in the middle ear and the hyoid bone in the throat.
    - The skull provides a bony framework for the head. It consists of 22 different bones: eight in the cranium, which encloses the brain, and 14 in the face, which includes the upper and lower jaw.
    - The vertebral column is a flexible, S-shaped column of 33 vertebrae that connects the trunk with the skull and encloses the spinal cord. The vertebrae are divided into five regions: cervical, thoracic, lumbar, sacral, and coccygeal regions. The S shape of the vertebral column allows it to absorb shocks and distribute the weight of the body.
    - The rib cage holds and protects the organs of the upper part of the trunk, including the heart and lungs. It includes the 12 thoracic vertebrae, the sternum, and 12 pairs of ribs.
- The appendicular skeleton consists of a total of 126 bones. It includes the bones of the four limbs, shoulder girdle, and pelvic girdle. The girdles attach the appendages to the axial skeleton.
    - Each upper limb consists of 30 bones. There is one bone, called the humerus, in the upper arm, and two bones, called the ulna and radius, in the lower arm. The wrist contains eight carpal bones, the hand contains five metacarpals, and the fingers consist of 14 phalanges. The thumb is opposable to the palm and fingers of the same hand.
    - Each lower limb also consists of 30 bones. There is one bone, called the femur, in the upper leg, and two bones, called the tibia and fibula, in the lower leg. The patella covers the knee joint. The ankle contains seven tarsal bones, and the foot contains five metatarsals. The tarsals and metatarsals form the heel and arch of the foot. The bones in the toes consist of 14 phalanges.

- The shoulder girdle attaches the upper limbs to the trunk of the body. It is connected to the axial skeleton only by muscles, allowing mobility of the upper limbs. Bones of the shoulder girdle include a right and left clavicle and a right and left scapula.
- The pelvic girdle attaches the legs to the trunk of the body and supports the organs of the abdomen. It is connected to the axial skeleton by ligaments. The pelvic girdle consists of two halves that are fused together in adults. Each half consists of three bones: the ilium, pubis, and ischium.

- Bones are organs that consist mainly of bone, or osseous, tissue. Osseous tissue is a type of connective tissue consisting of a collagen matrix that is mineralized with calcium and phosphorus crystals. The combination of flexible collagen and minerals makes bone hard without making it brittle.
  - There are two types of osseous tissues: cortical bone tissue and spongy bone tissue. Cortical bone tissue is smooth and dense. It forms the outer layer of bones. Spongy bone tissue is porous and light. It is found inside many bones.
- Besides osseous tissues, bones also contain nerves, blood vessels, bone marrow, and periosteum.
- Bone tissue is composed of four different types of bone cells: osteoblasts, osteocytes, osteoclasts, and osteogenic cells. Osteoblasts form new collagen matrix and mineralize it, osteoclasts break down bone, osteocytes regulate the formation and breakdown of bone, and osteogenic cells divide and differentiate to form new osteoblasts. Bone is a very active tissue, constantly being remodeled by the work of osteoblasts and osteoclasts.
- There are six types of bones in the human body: long bones such as the limb bones, short bones such as the wrist bones, sesamoid bones such as the patella, sutural bones in the skull, and irregular bones such as the vertebrae.
- Early in the development of a human fetus, the skeleton is made almost entirely of cartilage. The relatively soft cartilage gradually turns into hard bone. This is called ossification. It begins at a primary ossification center in the middle of the bone and later also occurs at secondary ossification centers in the ends of the bone. The bone can no longer grow in length after the areas of ossification meet and fuse at the time of skeletal maturity.
- Throughout life, bone is constantly being replaced in the process of bone remodeling. In this process, osteoclasts resorb bone and osteoblasts make new bone to replace it. Bone remodeling shapes the skeleton, repairs tiny flaws in bones, and helps maintain mineral homeostasis in the blood.
- Bone repair is the natural process in which a bone repairs itself following a bone fracture. This process may take several weeks. In the process, periosteum produces cells that develop into osteoblasts, and the osteoblasts form a new bone matrix to heal the fracture. Bone repair may be affected by diet, age, pre-existing bone disease, or other factors.
- Joints are locations at which bones of the skeleton connect with one another.
- Joints can be classified structurally or functionally, and there is significant overlap between the two types of classifications.
- The structural classification of joints depends on the type of tissue that binds the bones to each other at the joint. There are three types of joints in the structural classification: fibrous, cartilaginous, and synovial joints.
- The functional classification of joints is based on the type and degree of movement that they allow. There are three types of joints in the functional classification: immovable, partly movable, and movable joints.
  - Movable joints can be classified further according to the type of movement they allow. There are six classes of movable joints: pivot, hinge, saddle, plane, condyloid, and ball-and-socket joints.
- A number of disorders affect the skeletal system, including bone fractures and bone cancers. The two most common disorders of the skeletal system are osteoporosis and osteoarthritis.
- Osteoporosis is an age-related disorder in which bones lose mass, weaken, and break more easily than normal bones. The underlying mechanism in all cases of osteoporosis is an imbalance between bone formation and bone resorption in bone remodeling. Osteoporosis may also occur as a side effect of other disorders or certain medications.
  - Osteoporosis is diagnosed by measuring a patient's bone density and comparing it with the normal level of peak bone density. Fractures are the most dangerous aspect of osteoporosis. Osteoporosis is rarely fatal, but complications of fractures often are.
  - Risk factors for osteoporosis include older age, female sex, European or Asian ancestry, family history of osteoporosis, short stature and small bones, smoking, alcohol consumption, lack of exercise, vitamin D deficiency, poor nutrition, and consumption of soft drinks.
  - Osteoporosis is often treated with medications such as bisphosphonates that may slow or even reverse bone loss. Preventing osteoporosis includes eliminating any risk factors that can be controlled through changes of behavior, such as undertaking weight-bearing exercise.
- Osteoarthritis (OA) is a joint disease that results from the breakdown of joint cartilage and bone. The most common symptoms are joint pain and stiffness. OA is thought to be caused by mechanical stress on the joints with insufficient self-repair of cartilage, coupled with low-grade inflammation of the joints.
  - Diagnosis of OA is typically made on the basis of signs and symptoms, such as joint deformities, pain, and stiffness. X-rays or other tests are sometimes used to either support the diagnosis or rule out other disorders. Age is the chief risk factor for OA. Other risk factors include joint injury, excess body weight, and a family history of OA.

- OA cannot be cured, but the symptoms can often be treated successfully. Treatments may include exercise, efforts to decrease stress on joints, pain medications, and surgery to replace affected hip or knee joints.

As you have learned in this chapter, one of the important functions of the skeletal system is to allow movement of the body. But it doesn't do it alone. Movement is caused by the contraction of muscles, which pull on the bones, causing them to move. Read the next chapter to learn about this and other important functions of the muscular system.

CHAPTER SUMMARY REVIEW

1. Hematopoiesis is carried out by:
   A. spongy bone tissue
   B. periosteum
   C. yellow bone marrow
   D. red bone marrow
2. *True or False.* Osteocalcin is a hormone produced by bone cells.
3. *True or False.* Vertebrae make up part of the rib cage.
4. For each of the following bones, indicate whether they are part of the axial or appendicular skeleton.
   A. The ossicles of the middle ear
   B. The femur
   C. The phalanges
   D. The bones of the cranium
   E. The ilium
5. Why does the rib cage need to be flexible and why is it able to be flexible?
6. In general, what do "girdles" in the skeletal system do?
7. Which protein does bone mainly consist of?
   A. Keratin
   B. Collagen
   C. Cellulose
   D. Elastin
8. For each of the descriptions below, identify which process best fits the description. Use each process only once. Processes: bone growth; bone repair; bone remodeling
   A. New osteoblasts form from the periosteum and produce new bone tissue.
   B. Cartilage grows, and the primary and secondary ossification centers move towards each other.
   C. Osteoclasts break down bone tissue and osteoblasts build new bone tissue.
9. For each of the following processes, describe when it occurs.
   A. Bone growth
   B. Bone repair
   C. Bone remodeling
10. Would swimming likely be more effective as an exercise for preventing osteoporosis or as a treatment for osteoarthritis? Explain your answer.
11. *True or False.* Use of anabolic steroids in the teenage years generally makes people taller.
12. *True or False.* The largest joint in the human body is the knee joint.
13. How much of an adult's skeletal mass is broken down and rebuilt each year?
    A. None
    B. 5 percent
    C. 10 percent
    D. 30 percent
14. Explain why some of the vertebrae become misshapen in the condition called dowager's hump, or kyphosis.
15. Explain why osteoarthritis often involves inflammation in the joints.
16. Osteoporosis can involve both excess bone resorption as well as insufficient production of new bone tissue. What are the two main bone cell types that carry out these processes, respectively?
17. *True or False.* Bone mass does not decrease as men age.
18. *True or False.* Ideally, a person's spine would be perfectly straight and rigid.
19. Compare and contrast a tendon and a ligament.
20. Describe two roles that calcium plays in the bones of the body.
21. How many bones are in the adult human skeleton?
    A. 80
    B. 126
    C. 206
    D. 270

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CHAPTER OVERVIEW

8: MUSCULAR SYSTEM

This chapter describes the structure and functions of the muscular system. It compares and contrasts the three major types of muscle tissue and explains in detail how muscles contract according to the sliding filament theory. The chapter also relates physical exercise to fitness and health and describes several musculoskeletal and neuromuscular disorders.

8.1: Case Study- Muscles and Movement

8.2: Introduction to the Muscular System

8.3: Types of Muscle Tissue

8.4: Muscle Contraction

8.5: Physical Exercise

8.6: Disorders of the Muscular System

8.7: Case Study Conclusion- Needing to Relax and Chapter Summary

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8.1: CASE STUDY- MUSCLES AND MOVEMENT

CASE STUDY: NEEDING TO RELAX

The dog in Figure **8.1.3** is expressing his interest in something—perhaps a piece of food—by using the neck muscles to tilt its head in an adorable fashion. Humans also sometimes tilt their heads to express interest. But imagine how disturbing and painful it would be if your neck tilted involuntarily, without you being able to control it! Forty-three-year-old Nasir, unfortunately, knows just how debilitating this can be. Nasir uses they, them, and their pronouns.



Figure **8.1.1**: Curious dog

Nasir has a rare condition called cervical dystonia, which is also called spasmodic torticollis. In this condition, the muscles in the neck contract involuntarily, often causing the person's head to twist to one side. The illustration in Figure **8.1.2** shows one type of abnormal head positioning that can be caused by cervical dystonia. The muscles may contract in a sustained fashion, holding the head and neck in one position, or they may spasm repeatedly, causing jerky movements of the head and neck.

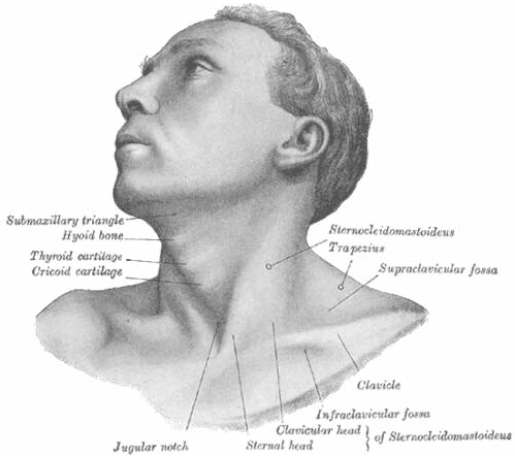


Figure **8.1.2**: Illustration from a medical book written around 1910, showing a person identified as having spasmodic torticollis. The person's neck is permanently tilted to the side.

Cervical dystonia is painful and can significantly interfere with individuals' ability to carry out their usual daily activities. In Nasir's case, they can no longer drive a car, because their uncontrollable head and neck movements and abnormal head positioning prevent them from navigating the road safely. Nasir also has severe neck and shoulder pain much of the time.

Although it can be caused by an injury, there is no known cause of cervical dystonia—and there is also no cure. Fortunately for Nasir and other cervical dystonia sufferers, though, there is a treatment that can significantly reduce symptoms in many people. You may be surprised to learn that this treatment is the same substance that, when injected into the face, is used for cosmetic purposes to reduce wrinkles!

The substance is botulinum toxin, one preparation of which may be familiar to you by its brand name: Botox. It is a neurotoxin produced by the bacterium *Clostridium botulinum*, and can cause a life-threatening illness called botulism. However, when injected in very small amounts by a skilled medical professional, botulinum toxins have some safe and effective uses. In addition to cervical dystonia, botulinum toxins can be used to treat other disorders involving the muscular system, such as strabismus (misalignment of the eyes), eye twitches, excessive muscle contraction due to neurological conditions like cerebral palsy; and even overactive bladder.

Botulinum toxin has its effect on the muscular system by inhibiting muscle contractions. When used to treat wrinkles, it relaxes the muscles of the face, lessening the appearance of wrinkles. When used to treat cervical dystonia and other disorders involving excessive muscle contraction, it reduces abnormal contractions.

In this chapter, you will learn about the muscles of the body, how they contract to produce movements and carry out their functions, and some disorders that affect the muscular system. At the end of the chapter, you will find out if botulinum toxin helped relieve Nasir's cervical dystonia, and how this toxin works to inhibit muscle contraction.

CHAPTER OVERVIEW: MUSCULAR SYSTEM

In this chapter, you will learn about the muscular system, which carries out both voluntary body movements and involuntary contractions of internal organs and structures. Specifically, you will learn about:

- The different types of muscle tissue—skeletal, cardiac, and smooth muscle—and their different characteristics and functions
- How muscle cells are specialized to contract and cause voluntary and involuntary movements
- The ways in which muscle contraction is controlled
- How skeletal muscles can grow or shrink, causing changes in strength
- The structure and organization of skeletal muscles (including the different types of muscle fibers) and how actin and myosin

filaments move across each other, according to the sliding filament theory, to cause muscle contraction
- How cardiac muscle tissue in the heart contracts to pump blood through the body
- Smooth muscle tissue that makes up internal organs and structures, such as the digestive system, blood vessels, and uterus
- The physical and mental health benefits of aerobic and anaerobic exercise, such as running and weight lifting
- How individuals vary in their response to exercise
- Disorders of the muscular system, including musculoskeletal disorders (such as strains and carpal tunnel syndrome) and neuromuscular disorders (such as muscular dystrophy, myasthenia gravis, and Parkinson's disease)

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

1. How is the contraction of skeletal muscles controlled?
2. Botulinum toxin works on the cellular and molecular levels to inhibit muscle contraction. Based on what you learn about how muscle contraction works, can you think of some ways it could potentially be inhibited?
3. What is one disorder involving a lack of sufficient muscle contraction? Why does it occur?

ATTRIBUTIONS

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8.2: INTRODUCTION TO THE MUSCULAR SYSTEM

MARVELOUS MUSCLES

Does the word *muscle* make you think of the well-developed muscles of a weightlifter, like a woman in Figure **8.2.1**? Her name is Natalia Zabolotnaya, and she's a Russian Olympian. The muscles that are used to lift weights are easy to feel and see, but they aren't the only muscles in the human body. Many muscles are deep within the body, where they form the walls of internal organs and other structures. You can flex your biceps at will, but you can't control internal muscles like these. It's a good thing that these internal muscles work without any conscious effort on your part because the movement of these muscles is essential for survival. Muscles are the organs of the muscular system.



Figure **8.2.1**: weightlifter lifting weight over her head.

WHAT IS THE MUSCULAR SYSTEM?



Figure **8.2.2**: Many of the skeletal muscles in the human muscular system are shown in this drawing of the human body.

The **muscular system** consists of all the muscles of the body. The largest percentage of muscles in the muscular system consists of skeletal muscles, which are attached to bones and enable voluntary body movements. There are almost 650 skeletal muscles in the human body, many of them shown in Figure **8.2.2**. Besides skeletal muscles, the muscular system also includes cardiac muscle — which makes up the walls of the heart — and smooth muscles, which control movement in other internal organs and structures.

MUSCLE STRUCTURE AND FUNCTION

Muscles are organs composed mainly of muscle cells, which are also called **muscle fibers** (mainly in skeletal and cardiac muscle) or **myocytes** (mainly in smooth muscle). Muscle cells are long and thin cells that are specialized for the function of contracting. They contain protein filaments that slide over one another using energy in ATP. The sliding filaments increase the tension in — or shorten the length of — muscle cells, causing a contraction. Muscle contractions are responsible for virtually *all* the movements of the body, both inside and out.

Skeletal muscles are attached to the bones of the skeleton. When these muscles contract, they move the body. They allow us to use our limbs in a variety of ways, from walking to turning cartwheels. Skeletal muscles also maintain posture and help keep balance.

Smooth muscles in the walls of blood vessels contract to cause vasoconstriction, which may help conserve body heat. Relaxation of these muscles causes vasodilation, which may help the body lose heat. In the organs of the digestive system, smooth muscles squeeze food through the gastrointestinal tract by contracting in sequence to form a wave of muscle contractions called **peristalsis.** Think of squirting toothpaste through a tube by applying pressure in sequence from the bottom of the tube to the top, and you have a good idea of how food is moved by muscles through the digestive system. Peristalsis of smooth muscles also moves urine through the urinary tract.

Cardiac muscle tissue is found only in the walls of the heart. When cardiac muscle contracts, it makes the heartbeat. The pumping action of the beating heart keeps blood flowing through the cardiovascular system.

MUSCLE HYPERTROPHY AND ATROPHY

Muscles can grow larger, or **hypertrophy.** This generally occurs through increased use, although hormonal or other influences can also play a role. The increase in testosterone during puberty, for example, causes a significant increase in muscle size. Physical exercise that involves weight-bearing or resistance training can increase the size of skeletal muscles in virtually everyone. Exercises (such as running) that increase the heart rate may also increase the size and strength of cardiac muscle. The size of a muscle, in turn, is the main determinant of muscle strength, which may be measured by the amount of force a muscle can exert.

Muscles can also grow smaller, or **atrophy**, which can occur through lack of physical activity or from starvation. People who are immobilized for any length of time — for example, because of a broken bone or surgery — lose muscle mass relatively quickly. People in concentration or famine camps may be so malnourished

that they lose much of their muscle mass, becoming almost literally just “skin and bones.” Astronauts on the International Space Station may also lose significant muscle mass because of weightlessness in space (Figure 8.2.3).

Many diseases, including cancer and AIDS, are often associated with muscle atrophy. Atrophy of muscles also happens with age. As people grow older, there is a gradual decrease in the ability to maintain skeletal muscle mass, known as **sarcopenia.** The exact cause of sarcopenia is not known, but one possible cause is a decrease in sensitivity to growth factors that are needed to maintain muscle mass. Because muscle size determines the strength, muscle atrophy causes a corresponding decline in muscle strength.

In both hypertrophy and atrophy, the number of muscle fibers does not change. What changes the size of the muscle fibers? When muscle hypertrophy happens, the individual fibers become wider. When muscle atrophy happens, the fibers become narrower.

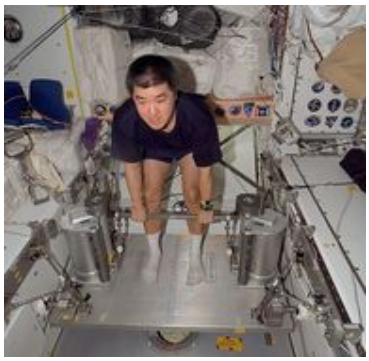


Figure 8.2.3: An astronaut exercising in space. It is important for astronauts to exercise onboard the International Space Station to help counter the loss of muscle mass that occurs because they are weightless without Earth’s gravity.

INTERACTIONS WITH OTHER BODY SYSTEMS

Muscles cannot contract on their own. Skeletal muscles need stimulation from motor neurons in order to contract. The point where a motor neuron attaches to a muscle is called a **neuromuscular junction**. Let’s say you decide to raise your hand in class. Your brain sends electrical messages through motor neurons to your arm and shoulder. The motor neurons, in turn, stimulate muscle fibers in your arm and shoulder to contract, causing your arm to rise.

Involuntary contractions of smooth and cardiac muscles are also controlled by electrical impulses, but in the case of these muscles, the impulses come from the autonomic nervous system (smooth muscle) or specialized cells in the heart (cardiac muscle). Hormones and some other factors also influence involuntary contractions of cardiac and smooth muscles. For example, the fight-or-flight hormone adrenaline increases the rate at which cardiac muscle contracts, thereby speeding up the heartbeat.

Muscles cannot move the body on their own. They need the skeletal system to act upon. The two systems together are often referred to as the **musculoskeletal system**. Skeletal muscles are attached to the skeleton by tough connective tissues called **tendons**. Many skeletal muscles are attached to the ends of bones that meet at a joint. The muscles span the joint and connect the bones. When the muscles contract, they pull on the bones, causing them to move. The skeletal system provides a system of levers that allow body movement. The muscular system provides the force that moves the levers.

REVIEW

1. What is the muscular system?
2. Describe muscle cells and their function.
3. Identify three types of muscle tissue and where each type is found.
4. Define muscle hypertrophy and muscle atrophy.
5. What are the possible causes of muscle hypertrophy?
6. Give three reasons that muscle atrophy may occur.
7. How do muscles change when they increase or decrease in size?
8. How do changes in muscle size affect strength?
9. Explain why astronauts can easily lose muscle mass in space.
10. Describe how the terms *muscle cells*, *muscle fibers*, and *myocytes* relate to each other.
11. Muscle tissue in the stomach is considered _____.

A. cardiac muscle

B. skeletal muscle

C. smooth muscle

D. voluntary muscle

12. Muscle contraction is the _____ of muscle fibers.

A. hypertrophy

B. atrophy

C. lengthening

D. shortening

13. *True or False:* Smooth muscle does not contract.
14. Name two systems in the body that work together with the muscular system to carry out movements.
15. Describe one way in which the muscular system is involved in regulating body temperature.

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8.3: TYPES OF MUSCLE TISSUE

WORK THOSE EYE MUSCLES!

Turn your eyes—a tiny movement, considering the conspicuously large and strong external eye muscles that control eyeball movements. These muscles have been called the strongest muscles in the human body relative to the work they do. However, the external eye muscles actually do a surprising amount of work. Eye movements occur almost constantly during waking hours, especially when we are scanning faces or reading. Eye muscles are also exercised nightly during the phase of sleep called rapid eye movement sleep. External eye muscles can move the eyes because they are made mainly of muscle tissue.



Figure **8.3.1**: Eyes

WHAT IS MUSCLE TISSUE?

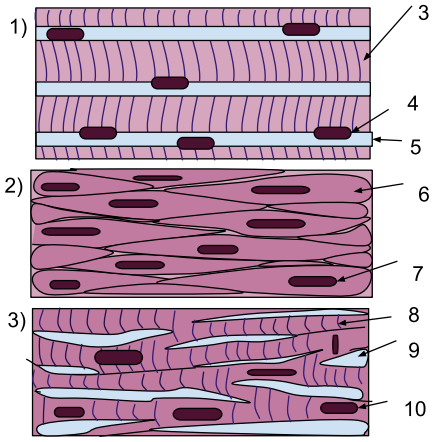


Figure **8.3.2**: Muscle type 1) Skeletal muscle cells are long tubular cells with striations (3) and multiple nuclei (4). The nuclei are embedded in the cell membrane (5) to be just inside the cell. This type of tissue occurs in the muscles that are attached to the skeleton. Skeletal muscles function for the voluntary movements of the body. Muscle type 2) Smooth muscle cells are spindle-shaped (6), and each cell has a single nucleus (7). Unlike skeletal muscle, there are no striations. The smooth muscle acts involuntarily and functions in the movement of substances in the lumens. They are primarily found in blood vessel walls and walls along the digestive tract. Muscle type 3) Cardiac muscle cells branch off from each other, rather than remaining, like the cells in the skeletal and smooth muscle tissues. Because of this, there are junctions between adjacent cells (9). The cells have striations (8), and each cell has a single nucleus (10). This type of tissue occurs in the heart wall, and its primary function is for pumping blood. This is an involuntary action.

Muscle tissue is a soft tissue that makes up most of the tissues in the muscles of the human muscular system. Other tissues in muscles are connective tissues, such as tendons that attach skeletal muscles to bones and sheaths of connective tissues that cover or line muscle tissues. Only muscle tissue per se, however, has cells with the ability to contract.

There are three major types of muscle tissues in the human body: skeletal, smooth, and cardiac muscle tissues. Figure **8.3.2** shows how the three types of muscle tissues appear under a microscope. When you read about each type below, you will learn why the three types appear as they do.

SKELETAL MUSCLE TISSUE

Skeletal muscle is muscle tissue attached to bones by **tendons**, which are bundles of collagen fibers. Whether you are moving your eyes or running a marathon, you are using skeletal muscles. Contractions of skeletal muscles are voluntary or under the conscious control of the central nervous system via the somatic nervous system. Skeletal muscle tissue is the most common type of muscle tissue in the human body. By weight, an average adult male is about 42 percent skeletal muscles, and the average adult female is about 36 percent skeletal muscles. Some of the major skeletal muscles in the human body are labeled in Figures **8.3.3** and Figure **8.3.4** and listed in Table **8.3.1**.

Table 8.3.1: Skeletal muscles. Some muscles are visible from both anterior and posterior views.

Muscles visible in Figure 8.3.3	Muscles visible in Figure 8.3.4
rotator cuff (multiple muscles are part of this group)	levator scapulae
biceps brachii	rhomboids
brachialis	rotator cuff
pronator teres	triceps brachii
brachioradialis	gluteus maximus
adductor muscles	tibialis posterior
tibialis anterior	peroneus longus
deltoid	peroneus brevis
pectoralis major	trapezius
rectus abdominis	deltoid
abdominal external oblique	brachioradialis
iliopsoas	latissimus dorsi
quadriceps femoris	biceps femoris
peroneus longus	semitendinosus
peroneus bravis	semimembranousus
	gastrocnemius
	soleus

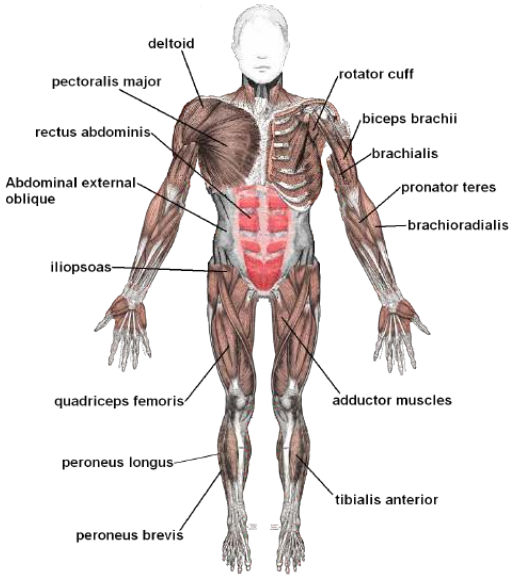


Figure 8.3.3: This figure shows major skeletal muscles in the front (anterior) of the body.

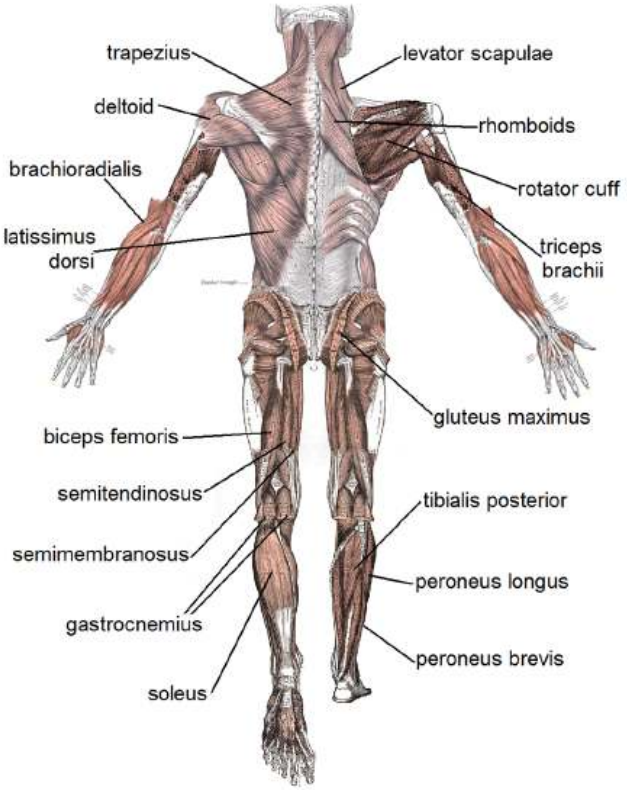


Figure 8.3.4: This figure shows major skeletal muscles in the back (posterior) of the body.

SKELETAL MUSCLE PAIRS

To move bones in opposite directions, skeletal muscles often consist of muscle pairs that work in opposition to one another. For example, when the biceps muscle (on the front of the upper arm) contracts, it can cause the elbow joint to flex or bend the arm, as shown in Figure 8.3.5. When the triceps muscle (on the back of the upper arm) contracts, it can cause the elbow to extend or straighten the arm. The biceps and triceps muscles are examples of a muscle pair where the muscles work in opposition to each other.

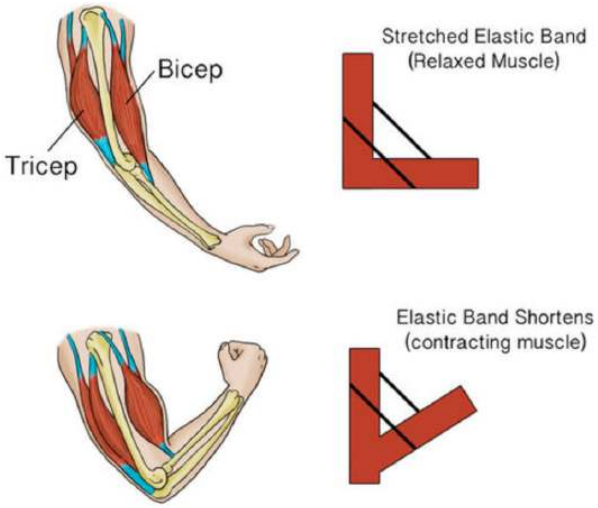


Figure 8.3.5: Triceps and biceps muscles in the upper arm are opposing muscles that move the arm at the elbow in opposite directions.

SKELETAL MUSCLE STRUCTURE

Each skeletal muscle consists of hundreds — or even *thousands* — of skeletal muscle fibers, which are long, string-like cells. As shown in Figure **8.3.6**, skeletal muscle fibers are individually wrapped in connective tissue called **endomysium**. The skeletal muscle fibers are bundled together in units called **muscle fascicles**, surrounded by sheaths of connective tissue called **perimysium**. Each fascicle contains between ten and 100 (or even more!) skeletal muscle fibers. Fascicles, in turn, are bundled together to form individual skeletal muscles, which are wrapped in connective tissue called **epimysium**. The connective tissues in skeletal muscles have a variety of functions. They support and protect muscle fibers, allowing them to withstand contraction forces by distributing the forces applied to the muscle. They also provide pathways for nerves and blood vessels to reach the muscles. Also, the epimysium anchors the muscles to tendons.

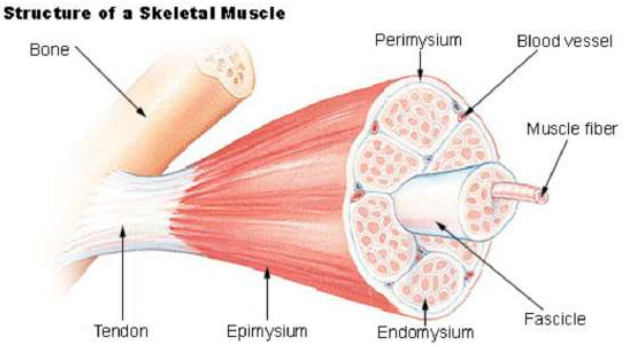


Figure **8.3.6**: Each skeletal muscle has a structure of bundles within bundles. Bundles of muscle fibers make up a muscle fascicle, and fascicles' bundles make up a skeletal muscle. At each level of bundling, a connective tissue membrane surrounds the bundle. The muscle cells, fascicle, and the whole muscle are surrounded by Endomysium, perimysium, and epimysium, respectively. All connective tissues merge together to make a tendon that attaches the muscle to bones.

The same bundles-within-bundles structure is replicated within each muscle fiber. As shown in Figure **8.3.7**, a muscle fiber consists of a bundle of myofibrils, which are themselves bundles of protein filaments. These protein filaments consist of thin filaments of the protein actin, anchored to structures called Z discs — and thick filaments of the protein myosin. The filaments are arranged together within a myofibril in repeating units called **sarcomeres,** which run from one Z disc to the next. The sarcomere is the basic functional unit of skeletal (and cardiac) muscles. It contracts as actin and myosin filaments slide over one another. Skeletal muscle tissue is said to be striated because it appears striped. It has this appearance because of the regular, alternating A (dark) and I (light) bands of filaments arranged in sarcomeres inside the muscle fibers. Other components of a skeletal muscle fiber include multiple nuclei and mitochondria.

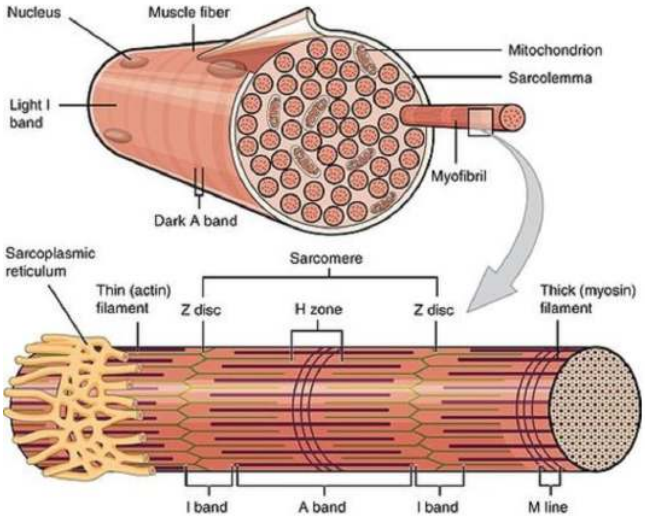


Figure **8.3.7**: Bundles of protein filaments form a myofibril, and bundles of myofibrils make up a single muscle fiber. I and A bands refer to the positioning of myosin and actin fibers in a myofibril. Sarcoplasmic reticulum is a specialized type of endoplasmic reticulum that forms a network around each myofibril. It serves as a reservoir for calcium ions, which are needed for muscle contractions. H zones and Z discs are also involved in muscle contractions, which you can read about in the concept of Muscle Contraction.

SLOW- AND FAST-TWITCH SKELETAL MUSCLE FIBERS

Skeletal muscle fibers can be divided into two types, called slow-twitch (or type I) muscle fibers and fast-twitch (or type II) muscle fibers.

- **Slow-twitch muscle fibers** are dense with capillaries and rich in mitochondria and myoglobin, a protein that stores oxygen until needed for muscle activity. Relative to fast-twitch fibers, slow-twitch fibers can carry more oxygen and sustain aerobic (oxygen-using) activity. Slow-twitch fibers can contract for long periods of time, but not with very much force. They are relied upon primarily in endurance events, such as distance running or cycling.
- **Fast-twitch muscle fibers** contain fewer capillaries and mitochondria and less myoglobin. This type of muscle fiber can contract rapidly and powerfully, but it fatigues very quickly. Fast-twitch fibers can sustain only short, anaerobic (non-oxygen-using) bursts of activity. Relative to slow-twitch fibers, fast-twitch fibers contribute more to muscle strength and have a greater potential for increasing mass. They are relied upon primarily in short, strenuous events, such as sprinting or weight lifting.

Proportions of fiber types vary considerably from muscle to muscle and from person to person. Individuals may be genetically predisposed to have a larger percentage of one type of muscle fiber than the other. Generally, an individual who has more slow-twitch fibers is better suited for activities requiring endurance. In contrast, an individual who has more fast-twitch fibers is better suited for activities requiring short bursts of power.

SMOOTH MUSCLE

Smooth muscle is muscle tissue in the walls of internal organs and other internal structures such as blood vessels. When smooth muscles contract, they help the organs and vessels carry out their functions. When smooth muscles in the stomach wall contract, they squeeze the food inside the stomach, helping to mix and churn the food and break it into smaller pieces. This is an important part of digestion. Contractions of smooth muscles are involuntary, so they are not under conscious control. Instead, they are controlled by the autonomic nervous system, hormones, neurotransmitters, and other physiological factors.

STRUCTURE OF SMOOTH MUSCLE

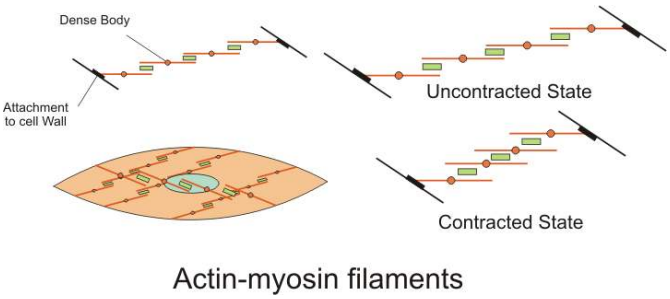


Figure **8.3.8**: The smooth muscle cell is composed of actin and myosin filaments, but they are not arranged in the sarcomere. The arrangement of these filaments is alternate and staggered.

The cells that make up smooth muscle are generally called **myocytes.** Unlike the muscle fibers of striated muscle tissue, the myocytes of smooth muscle tissue do not have their filaments arranged in sarcomeres. Therefore, smooth tissue is not striated. However, the myocytes of smooth muscle contain myofibrils, which contain bundles of myosin and actin filaments. The filaments cause contractions when they slide over each other, as shown in Figure **8.3.8**.

FUNCTIONS OF SMOOTH MUSCLE

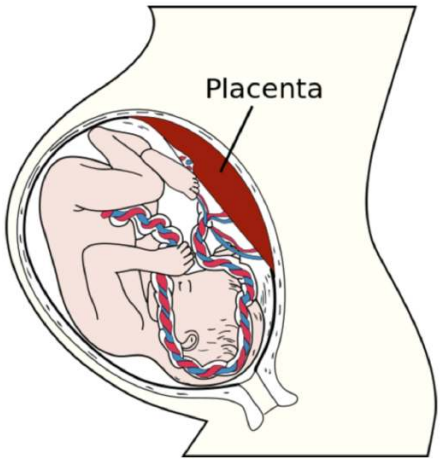


Figure **8.3.9**: The muscular uterine wall stretches to a great extent to accommodate a growing fetus, yet it can still contract with great force during the labor that precedes childbirth. At that time, it can exert up to 100 pounds of force.

Unlike striated muscle, smooth muscle can sustain very long-term contractions. Smooth muscle can also stretch and still maintain its contractile function, which striated muscle cannot. An extracellular matrix secreted by myocytes enhances the elasticity of smooth muscle. The matrix consists of elastin, collagen, and other stretchy fibers. The ability to stretch and still contract is an important attribute of smooth muscle in organs such as the stomach and uterus (Figure **8.3.9**), both of which must stretch considerably as they perform their normal functions.

The following list indicates where many smooth muscles are found, along with some of their specific functions.

- Walls of the gastrointestinal tract (such as the esophagus, stomach, and intestines), moving food through the tract by peristalsis.
- Walls of air passages of the respiratory tract (such as the bronchi), controlling the diameter of the passages and the volume of air that can pass through them
- Walls of organs of the male and female reproductive tracts; in the uterus, for example, pushing a baby out of the uterus and into the birth canal
- Walls of the urinary system structures, including the urinary bladder, allow the bladder to expand so it can hold more urine and then contract as urine is released.
- Walls of blood vessels, controlling the diameter of the vessels and thereby affecting blood flow and blood pressure
- Walls of lymphatic vessels, squeezing the fluid called lymph through the vessels.
- Iris of the eyes, controlling the size of the pupils and thereby the amount of light entering the eyes
- Arrector pili in the skin, raising hairs in hair follicles in the dermis.

CARDIAC MUSCLE

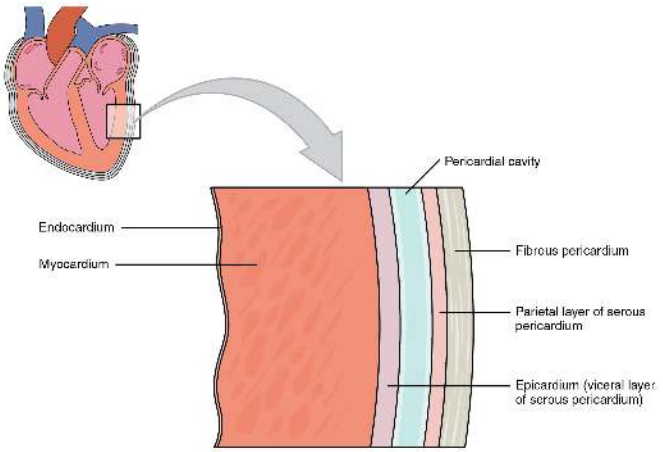


Figure **8.3.10**: The thick wall of the heart consists mainly of cardiac muscle tissue called myocardium. The thin epithelial tissue endocardium covers the chambers of the heart and the epicardium covers the myocardium. The heart is located in the pericardial cavity of the chest. The covering of the pericardial cavity is composed of fibrous and serous layers.

Cardiac muscle is found only in the wall of the heart. It is also called myocardium. As shown in Figure **8.3.10**, the myocardium is enclosed within connective tissues, including the endocardium on

the inside of the heart and pericardium on the outside of the heart. When cardiac muscle contracts, the heart beats and pumps blood. Contractions of cardiac muscle are involuntary, like those of smooth muscles. They are controlled by electrical impulses from specialized cardiac muscle cells in the heart muscle area called the sinoatrial node.

Like skeletal muscle, cardiac muscle is striated because its filaments are arranged in sarcomeres inside the muscle fibers. However, in cardiac muscle, the myofibrils are branched at irregular angles rather than arranged in parallel rows (as they are in skeletal muscle). This explains why cardiac and skeletal muscle tissues look different from one another.

The cells of cardiac muscle tissue are arranged in interconnected networks. This arrangement allows rapid transmission of electrical impulses, which stimulate virtually simultaneous contractions of the cells. This enables the cells to coordinate contractions of the heart muscle.

The heart is the muscle that performs the greatest amount of physical work in a lifetime. Although the heart's power output is much less than the maximum power output of some other muscles in the human body, the heart does its work continuously over an entire lifetime without rest. The cardiac muscle contains many mitochondria, which produce ATP for energy and help the heart resist fatigue.

FEATURE: HUMAN BODY IN THE NEWS

The human heart develops in a sequence of events that are controlled by communication among different types of cells, including cells that will become myocardium (the cardiac muscle that forms the wall of the heart) and cells that will become endocardium (the connective tissue that covers the inside surface of the myocardium). If communication among the cells is abnormal, it can lead to various heart defects, such as cardiac hypertrophy or abnormal enlargement of the heart muscle. Cardiac hypertrophy causes the heart to thicken and weaken over time, so it is less able to pump blood. Eventually, heart failure may develop, causing fluid to build up in the lungs and extremities.

Abnormal cell communication is the mechanism by which a mutation called PTPN11 leads to cardiac hypertrophy in disorder referred to as NSML (Noonan Syndrome with Multiple Lentigines). New research by scientists at Beth Israel Deaconess Medical Center in Boston has determined which type of cell abnormalities occur that lead to NSML. In the research, the scientists engineered mouse models to express the PTPN11 mutation as they developed. The researchers manipulated the mouse models so that the mutation was expressed only in cells that would develop into the myocardium in some of the mice. In contrast, in other mice, the mutation was expressed only in cells that would develop into endocardium. Unexpectedly, the heart's hypertrophy occurred only in the mice that expressed the mutation in endocardial cells, not in myocardial cells, which had long been assumed to be the cells affected. The results of the research suggest potential targets for the treatment of NSML. They may also help scientists understand the causes of other cardiac disorders that are much more common than NSML.

REVIEW

1. What is muscle tissue?
2. Where is the skeletal muscle found, and what is its general function?
3. Why do many skeletal muscles work in pairs?
4. Describe the structure of a skeletal muscle.
5. Relate muscle fiber structure to the functional units of muscles.
6. Why is skeletal muscle tissue striated?
7. Compare and contrast slow-twitch and fast-twitch skeletal muscle fibers.
8. Where is the smooth muscle found? What controls the contraction of smooth muscle?
9. Compare and contrast smooth muscle and striated muscle (such as skeletal muscle).
10. Where is the cardiac muscle found? What controls its contractions?
11. Both cardiac and skeletal muscle tissues are striated, but they look different from one another. Why?
12. The heart muscle is smaller and less powerful than some other muscles in the body. Why is the heart the muscle that performs the greatest amount of physical work in a lifetime? How does the heart resist fatigue?
13. Arrange the following units within a skeletal muscle in order, from smallest to largest: *fascicle; sarcomere; muscle fiber; myofibril*
14. Give one example of connective tissue that is found in muscles. Describe one of its functions.
15. *True or False:* skeletal muscle fibers are cells with multiple nuclei.

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8.4: MUSCLE CONTRACTION

ARM WRESTLING

A sport like arm-wrestling depends on muscle contractions. Arm wrestlers must contract muscles in their hands and arms and *keep* them contracted to resist their opponent's opposing force. The wrestler whose muscles can contract with greater force wins the match.



Figure **8.4.1**: Arm wrestling

MUSCLE CONTRACTION

HOW A SKELETAL MUSCLE CONTRACTION BEGINS

Excluding reflexes, all skeletal muscle contractions occur as a result of conscious effort originating in the brain. The brain sends electrochemical signals through the somatic nervous system to motor neurons that innervate muscle fibers (to review how the brain and neurons function, see the chapter *Nervous System*). A single motor neuron with multiple axon terminals can innervate multiple muscle fibers, thereby causing them to contract at the same time. The connection between a motor neuron axon terminal and a muscle fiber occurs at a neuromuscular junction site**.** This is a chemical synapse where a motor neuron transmits a signal to muscle fiber to initiate a muscle contraction.

The process by which a signal is transmitted at a neuromuscular junction is illustrated in Figure **8.4.2**. The sequence of events begins when an action potential is initiated in the cell body of a motor neuron, and the action potential is propagated along the neuron's axon to the neuromuscular junction. Once the action potential reaches the end of the axon terminal, it causes the neurotransmitter acetylcholine (ACh) from synaptic vesicles in the axon terminal. The ACh molecules diffuse across the synaptic cleft and bind to the muscle fiber receptors, thereby initiating a muscle contraction. Muscle contraction is initiated with the depolarization of the sarcolemma caused by the sodium ions' entrance through the sodium channels associated with the ACh receptors.

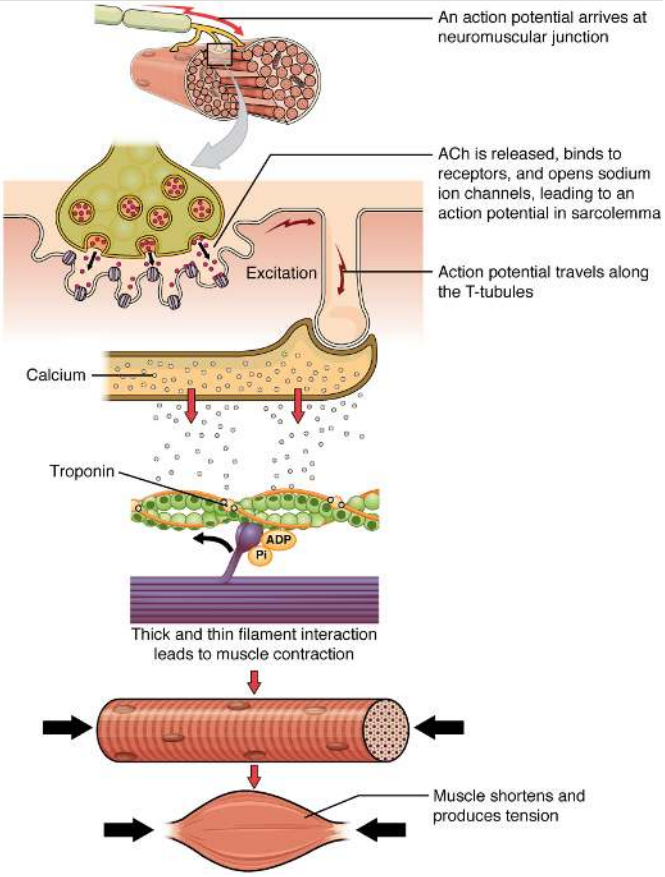


Figure **8.4.2**: This diagram represents the sequence of events that occurs when a motor neuron stimulates a muscle fiber to contract. The action potential travels down the t-tubules and excites the sarcoplasmic reticulum which releases calcium. Calcium when bound to troponin causes conformational changes in the sarcomere. Consequently, the interaction of thick and thin filaments of the sarcomere leads to muscle contraction.

Things happen very quickly in the world of excitable membranes (think about how quickly you can snap your fingers as soon as you decide to do it). Immediately following depolarization of the membrane, it repolarizes, re-establishing the negative membrane potential. Meanwhile, the ACh in the synaptic cleft is degraded by the enzyme acetylcholinesterase (AChE). The ACh cannot rebind to a receptor and reopen its channel, which would cause unwanted extended muscle excitation and contraction.

Propagation of an action potential along the sarcolemma enters the **T-tubules**. For the action potential to reach the membrane of the Sarcoplasmic Reticulum (SR), there are periodic invaginations in the sarcolemma, called **T-tubules** ("T" stands for "transverse"). The arrangement of a T-tubule with the membranes of SR on either side is called a **triad** (Figure **8.4.3**). The triad surrounds the cylindrical structure called a **myofibril**, which contains actin and myosin. The T-tubules carry the action potential into the interior of the cell, which triggers the opening of calcium channels in the membrane of the adjacent SR, causing Ca^{++} to diffuse out of the SR and into the sarcoplasm. It is the arrival of Ca^{++} in the sarcoplasm that initiates

contraction of the muscle fiber by its contractile units, or sarcomeres.

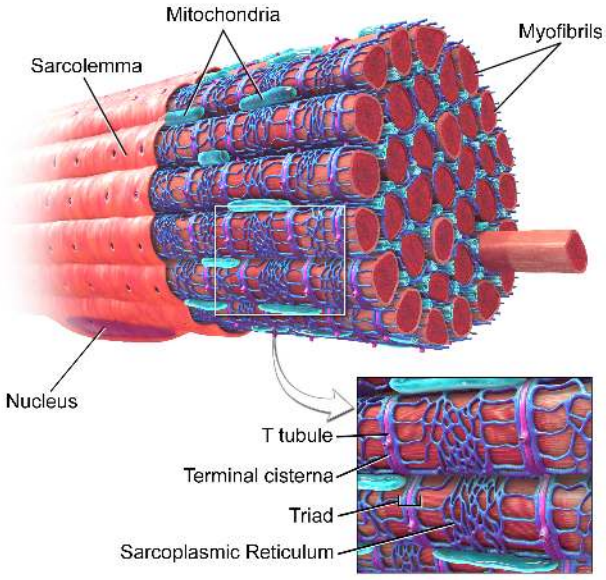


Figure 8.4.3: Narrow T-tubules permit the conduction of electrical impulses. The SR functions to regulate intracellular levels of calcium. Two terminal cisternae (where enlarged SR connects to the T-tubule) and one T-tubule comprise a triad—a "threesome" of membranes, with those of SR on two sides and the T-tubule sandwiched between them.

EXCITATION-CONTRACTION COUPLING

Although the term **excitation-contraction coupling** confuses or scares some students, it comes down to this: for a skeletal muscle fiber to contract, its membrane must first be "excited"—in other words, it must be stimulated to fire an action potential. The muscle fiber action potential, which sweeps along the sarcolemma as a wave, is "coupled" to the actual contraction through the release of calcium ions (Ca^{++}) from the SR. Once released, the Ca^{++} interacts with the shielding proteins, troponin and tropomyosin complex, forcing them to move aside so that the actin-binding sites are available for attachment by myosin heads. The myosin then pulls the actin filaments toward the center, shortening the muscle fiber.

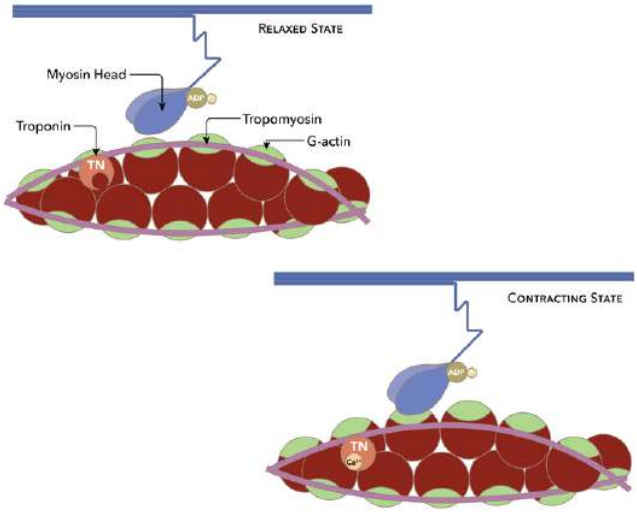


Figure 8.4.4: Tropomyosin Troponin complex shields the cross-bridge sites on actin. Myosin can only bind with actin when this complex is removed with the help of Calcium ions.

In skeletal muscle, this sequence begins with signals from the somatic motor division of the nervous system. In other words, the "excitation" step in skeletal muscles is always triggered by signaling from the nervous system.

SLIDING FILAMENT THEORY OF MUSCLE CONTRACTION

Once the muscle fiber is stimulated by the motor neuron, actin, and myosin protein filaments within the skeletal muscle fiber slide past each other to produce a contraction. The **sliding filament theory** is the most widely accepted explanation for how this occurs. According to this theory, muscle contraction is a cycle of molecular events in which thick myosin filaments repeatedly attach to and pull on thin actin filaments, so they slide over one another. The actin filaments are attached to Z discs, each of which marks the end of a sarcomere. The sliding of the filaments pulls the Z discs of a sarcomere closer together, thus shortening the sarcomere. As this occurs, the muscle contracts.

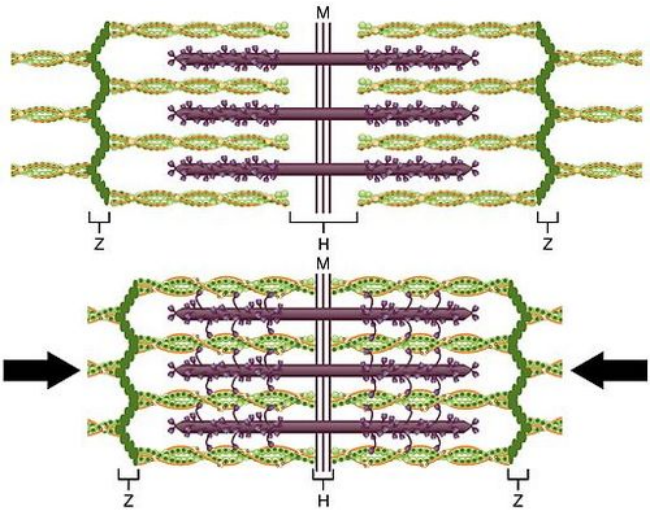


Figure **8.4.5**: The top diagram shows a relaxed sarcomere, and the bottom diagram shows a contracted sarcomere. Please note the z discs, h zone, and M line. In a contracted sarcomere the H zone reduces as compared to relaxed sarcomere because actin fibers (greenish-yellow double helix) move towards the M line.

CROSSBRIDGE CYCLING

Crossbridge cycling is a sequence of molecular events that underlies the sliding filament theory. There are many projections from the thick myosin filaments, each of which consists of two myosin heads (you can see the projections and heads in Figures **8.4.5** and **8.4.3**). Each myosin head has binding sites for ATP (or ATP hydrolysis products: ADP and P_i) and actin. The thin actin filaments also have binding sites for the myosin heads—a cross-bridge forms when a myosin head binds with an actin filament.

The process of cross-bridge cycling is shown in Figure **8.4.6**. A cross-bridge cycle begins when the myosin head binds to an actin filament. ADP and P_i are also bound to the myosin head at this stage. Next, a power stroke moves the actin filament inward toward the sarcomere center, thereby shortening the sarcomere. At the end of the power stroke, ADP and P_i are released from the myosin head, leaving the myosin head attached to the thin filament until another ATP binds to the myosin head. When ATP binds to the myosin head, it causes the myosin head to detach from the actin filament. ATP is again split into ADP and P_i and the energy released is used to move the myosin head into a "cocked" position. Once in this position, the myosin head can bind to the actin filament again, and another cross-bridge cycle begins.

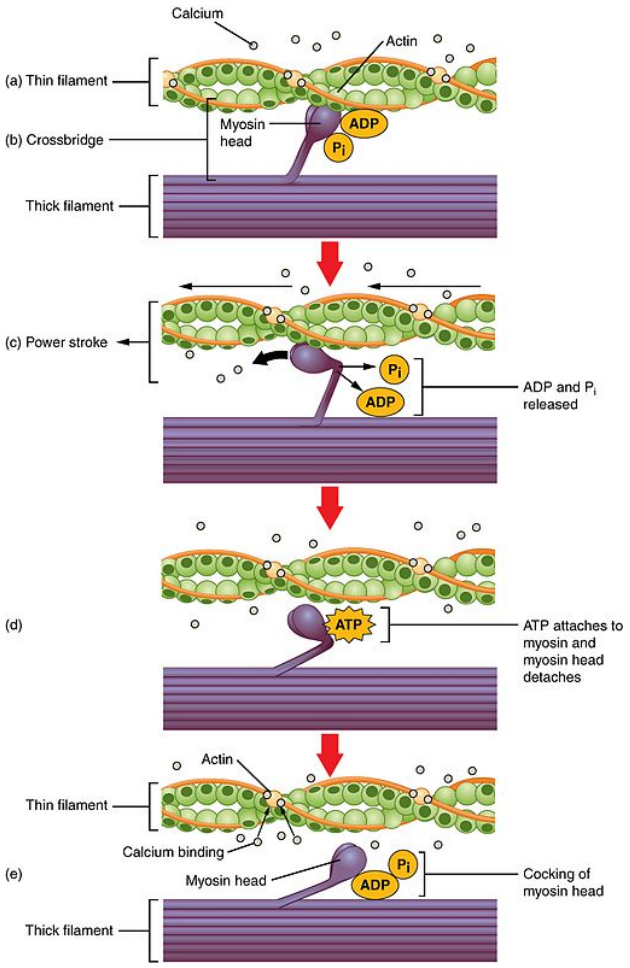


Figure **8.4.6**: Crossbridge cycling

FEATURE: HUMAN BIOLOGY IN THE NEWS

Interesting and hopeful basic research on muscle contraction is often in the news because muscle contractions are involved in so many different body processes and disorders, including heart failure and stroke.

- **Heart failure** is a chronic condition in which cardiac muscle cells cannot contract forcefully enough to keep body cells adequately supplied with oxygen. In 2016, researchers at the University of Texas Southwestern Medical Center identified a potential new target for developing drugs to increase the strength of cardiac muscle contractions in patients with heart failure. The UT researchers found a previously unidentified protein involved in muscle contraction. The minimal protein turns off the “brake” on the heart, so it pumps blood more vigorously. At the molecular level, the protein affects the calcium-ion pump that controls muscle contraction. This result is likely to lead to searches for additional such proteins.
- A **stroke** occurs when a blood clot lodges in an artery in the brain and cuts off blood flow to part of the brain. Damage from the clot would be reduced if the smooth muscles lining brain arteries relaxed following a stroke because the arteries

would dilate and allow greater blood flow to the brain. In a recent study undertaken at the Yale University School of Medicine, researchers determined that the muscles lining blood vessels in the brain actually contract after a stroke. This constricts the vessels, reduces blood flow to the brain, and appears to contribute to permanent brain damage. The hopeful takeaway of this finding is that it suggests a new target for stroke therapy.

REVIEW

1. What is skeletal muscle contraction?
2. Distinguish between isometric and isotonic contractions of skeletal muscle.
3. How does a motor neuron stimulate a skeletal muscle contraction?
4. What is the sliding filament theory?
5. Describe cross-bridge cycling.
6. Where does the ATP needed for a muscle contraction come from?
7. Explain why an action potential in a single motor neuron can cause multiple muscle fibers to contract.
8. The name of the synapse between a motor neuron and a muscle fiber is the _____ _____.
9. If a drug blocks the acetylcholine receptors on muscle fibers, what do you think this would do to muscle contraction? Explain your answer.
10. *True or False:* According to the sliding filament theory, actin filaments actively attach to and pull on myosin filaments.
11. *True or False:* When a motor neuron produces an action potential, the sarcomeres in the muscle fiber that it innervates become shorter as a result.
12. Explain how cross-bridge cycling and sliding filament theory are related to each other.
13. When does anaerobic respiration typically occur in human muscle cells?
14. If there were no ATP available in a muscle, how would this affect cross-bridge cycling? What would this do to muscle contraction?

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8.5: PHYSICAL EXERCISE

STROLLERS

These caregivers are setting a great example for their children by engaging in physical exercise. Adopting a regular physical exercise habit is one of the most important ways to maintain fitness and good health. From higher self-esteem to a healthier heart, physical exercise can positively affect virtually all aspects of health, including physical, mental, and emotional health.



Figure **8.5.1**: Jogging with strollers

WHAT IS PHYSICAL EXERCISE?

Physical exercise is any bodily activity that enhances or maintains physical fitness and overall health and wellness. We generally think of physical exercise as activities that are undertaken for the main purpose of improving physical fitness and health. However, physical activities that are undertaken for other purposes may also count as physical exercise. Scrubbing a floor, raking a lawn, or playing active games with young children or a dog are all activities that can have fitness and health benefits, even though they generally are not done mainly for this purpose.

How much physical exercise should people get? In the United States, both the Centers for Disease Control and Prevention and the Surgeon General have recommended that every adult participates in moderate exercise for a minimum of 30 minutes a day. This might include walking, swimming, and/or household or yard work.

TYPES OF PHYSICAL EXERCISE

Physical exercise can be classified into three types, depending on the effects it has on the body: aerobic exercise, anaerobic exercise, and flexibility exercise. Many specific physical exercise examples (including playing soccer and rock climbing) can be classified as more than one type.

AEROBIC EXERCISE

Aerobic exercise is any physical activity in which muscles are used below their maximum contraction strength, but for long periods of time. Aerobic exercise uses a relatively high percentage of slow-twitch muscle fibers that consume a large amount of oxygen. The main goal of aerobic exercise is to increase cardiovascular endurance, although it can have many other benefits, including muscle toning. Examples of aerobic exercise include cycling, swimming, brisk walking, jumping rope, rowing, hiking, and tennis.

ANAEROBIC EXERCISE

Anaerobic exercise is any physical activity in which muscles are used close to their maximum contraction strength but for relatively short periods of time. Anaerobic exercise uses a relatively high percentage of fast-twitch muscle fibers that consume a small amount of oxygen. The goals of anaerobic exercise include building and strengthening muscles and improving bone strength, balance, and coordination. Examples of anaerobic exercise include push-ups, lunges, sprinting, interval training, resistance training, and weight training (such as biceps curls with a dumbbell, as pictured Figure **8.5.2**).



Figure **8.5.2**: Pitting the biceps muscle in the upper arm against a heavyweight helps build and strengthen this muscle.

FLEXIBILITY EXERCISE

Flexibility exercise is any physical activity that stretches and lengthens muscles. The goals of flexibility exercise include increasing joint flexibility, keeping muscles limber, and improving the range of motion, all of which can reduce the risk of injury. Examples of flexibility exercises include stretching, yoga, and tai chi.

HEALTH BENEFITS OF PHYSICAL EXERCISE

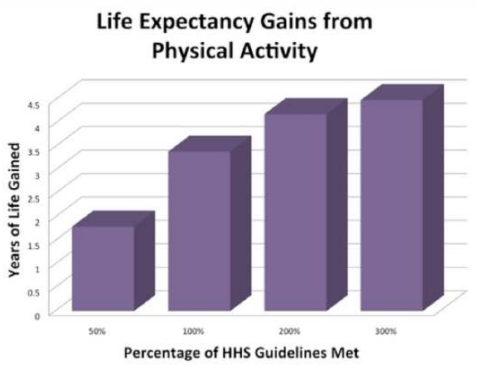


Figure 8.5.3: The U.S. Department of Health and Human Services (HHS) recommends that adults aged 18 to 64 engage in regular aerobic physical activity for 2.5 hours at moderate intensity (1.25 hours at vigorous intensity) each week. Moderate activities are those during which a person could talk but not sing. Vigorous activities are those during which a person could say only a few words without stopping to breathe. When people exercise at 50 percent of the HHS guidelines, they gain an average of 1.5 years of life. Exercising at 100 percent of the HHS guidelines results in a gain of almost four years of life. The gain in life expectancy starts to level off at about 300 percent of the HHS guidelines.

Many studies have shown that physical exercise is positively correlated with a diversity of health benefits. Some of these benefits include maintaining physical fitness, losing weight and maintaining a healthy weight, regulating digestive health, building and maintaining healthy bone density, increasing muscle strength, improving joint mobility, strengthening the immune system, boosting cognitive ability, and promoting psychological well-being. Some studies have also found a significant positive correlation between exercise and quality of life and life expectancy. People who participate in moderate to high levels of physical activity have been shown to have lower mortality rates than people of the same ages who are not physically active. The years of life gained with different amounts of physical activity are shown in the graph in Figure 8.5.3.

The underlying physiological mechanisms explaining why exercise has these positive health benefits are not completely understood. However, developing research suggests that many of the benefits of exercise may come about because of skeletal muscles' role as endocrine organs. Contracting muscles release hormones called **myokines**, which promote tissue repair and the growth of new tissue. Myokines also have anti-inflammatory effects, which, in turn, reduce the risk of developing inflammatory diseases. Exercise also reduces cortisol levels, the adrenal cortex stress hormone that may cause many health problems — both physical and mental — at sustained high levels.

CARDIOVASCULAR BENEFITS OF PHYSICAL EXERCISE

The beneficial effects of exercise on the cardiovascular system are well documented. Physical inactivity has been identified as a risk factor for the development of coronary artery disease. There is also a direct correlation between physical inactivity and cardiovascular disease mortality. Physical exercise, in contrast, has been demonstrated to reduce several risk factors for cardiovascular disease, including hypertension (high blood pressure), "bad" cholesterol (low-density lipoproteins), high total cholesterol, and excess body weight. Physical exercise has also been shown to increase "good" cholesterol (high-density lipoproteins), insulin sensitivity, the mechanical efficiency of the heart, and exercise tolerance, which can perform physical activity without undue stress and fatigue.

COGNITIVE BENEFITS OF PHYSICAL EXERCISE

Physical exercise has been shown to help protect people from developing neurodegenerative disorders, such as dementia. A 30-year study of almost 2,400 men found that those who exercised regularly had a 59 percent reduction in dementia when compared with those who did not exercise. Similarly, a review of cognitive enrichment therapies for the elderly found that physical activity — in particular, aerobic exercise — can enhance the cognitive function of older adults. Anecdotal evidence suggests that frequent exercise may even help reverse alcohol-induced brain damage. There are several possible reasons why exercise is so beneficial for the brain. Physical exercise:

- increases blood flow and oxygen availability to the brain
- increases growth factors that promote new brain cells and new neuronal pathways in the brain
- increases levels of neurotransmitters (such as serotonin), which increase memory retention, information processing, and cognition

MENTAL HEALTH BENEFITS OF PHYSICAL EXERCISE

Numerous studies suggest that regular aerobic exercise works as well as pharmaceutical antidepressants in treating mild-to-moderate depression. A possible reason for this effect is that exercise increases the biosynthesis of at least three neurochemicals that may act as euphoriants. The euphoric effect of exercise is well known. Distance runners may refer to it as "runner's high," and people who participate in the crew (Figure 8.5.4) may refer to it as "rower's high." Because of these effects, health care providers often promote aerobic exercise as a treatment for depression.



Figure 8.5.4: This crew team is competing for the U.S. Army in the lightweight division of the world championships in 2003. They are clearly exerting themselves — and no doubt increasing their euphoriant neurochemicals in the process.

Additional mental health benefits of physical exercise include reducing stress, improving body image, and promoting positive self-esteem. Conversely, there is evidence to suggest that being sedentary is associated with an increased risk of anxiety.

SLEEP BENEFITS OF PHYSICAL EXERCISE

A recent review of published scientific research suggests that exercise generally improves sleep for most people and helps sleep disorders, such as insomnia. Exercise is the most recommended alternative to sleeping pills for people with insomnia. For sleep benefits, the optimum time to exercise is four to eight hours before bedtime, although exercise at any time of day seems to be beneficial. The only possible exception is a heavy exercise undertaken shortly before bedtime, which may actually interfere with sleep.

OTHER BENEFITS OF PHYSICAL EXERCISE

Some studies suggest that physical activity may benefit the immune system. For example, moderate excise is associated with a decreased incidence of upper respiratory tract infections. Evidence from many studies has found a correlation between physical exercise and reduced death rates from cancer, specifically breast cancer and colon cancer. Physical exercise has also been shown to reduce the risk of type 2 diabetes and obesity.

VARIATION IN RESPONSES TO PHYSICAL EXERCISE

Not everyone benefits equally from physical exercise. When participating in aerobic exercise, most people will have a moderate increase in their endurance, but some will double their endurance. On the other hand, some people will show little or no increase in endurance from aerobic exercise. Genetic differences in slow-twitch and fast-twitch skeletal muscle fibers may play a role in these different results. People with more slow-twitch fibers may develop greater endurance because these muscle fibers have more capillaries, mitochondria, and myoglobin than fast-twitch fibers. As a result, slow-twitch fibers can carry more oxygen and sustain aerobic activity for a longer period of time than fast-twitch fibers. Studies show that endurance athletes (like the marathoner in Figure **8.5.5**) generally tend to have a higher proportion of slow-twitch fibers than other people.



Figure **8.5.5**: This winning marathoner is likely to have a relatively high proportion of slow-twitch muscle fibers that increase his endurance.

There is also great variation in individual responses to muscle building as a result of anaerobic exercise. Some people have a much greater capacity to increase muscle size and strength, whereas other people never develop large muscles, no matter how much they exercise them. People who have more fast-twitch than slow-twitch muscle fibers may develop bigger, stronger muscles because fast-twitch muscle fibers contribute more to muscle strength and have greater potential to increase in mass. Evidence suggests that athletes who excel at power activities (such as throwing and jumping) tend to have a higher proportion of fast-twitch fibers than endurance athletes.

CAN YOU "OVERDOSE" ON PHYSICAL EXERCISE?



Figure **8.5.6**: New military recruits may suffer muscle damage from overexertion of unconditioned muscles. The drill instructor pictured here (in an orange shirt) is doing his best to encourage these marine recruits to expend their maximum effort.

Is it possible to exercise too much? Can too much exercise be harmful? Evidence suggests that some adverse effects may occur if exercise is extremely intense and the body is not given proper rest between exercise sessions. Athletes who train for multiple marathons have been shown to develop scarring of the heart and heart rhythm abnormalities. Doing too much exercise without prior conditioning also increases the risk of injuries to muscles and joints. Damage to muscles due to overexertion is often seen in new military recruits (Figure **8.5.6**). Too much exercise in females may cause amenorrhea, which is a cessation of menstrual periods. When this occurs, it generally indicates that a woman is pushing her body too hard.

Many people develop delayed onset muscle soreness (DOMS), which is pain or discomfort in muscles felt one to three days after exercising and generally subsides two or three days later. DOMS was once thought to be caused by the buildup of lactic acid in the muscles. Lactic acid is a product of anaerobic respiration in muscle tissues. However, lactic acid disperses fairly rapidly, so it is unlikely to explain pain experienced several days after exercise. The current theory is that DOMS is caused by tiny tears in muscle fibers, which occur when muscles are used at too high a level of intensity.

FEATURE: MY HUMAN BODY

Most people know that exercise is important for good health, and it's easy to find endless advice about exercise programs and fitness plans. What is not so easy to find is the motivation to start exercising and stick with it. This is the main reason why so many people fail to get regular exercise. Practical concerns like a busy schedule and bad weather can certainly make exercising more of a challenge, but the biggest barriers to adopting a

regular exercise routine are mental. If you want to exercise but find yourself making excuses or getting discouraged and giving up, here are some tips that may help you get started and stay moving:

- **Avoid an all-or-nothing point of view.** Don't think you need to spend hours sweating at the gym or training for a marathon to get healthy. Even a little bit of exercise is better than nothing at all. Start with ten or 15 minutes of moderate activity each day. Taking a walk around your neighborhood is a great way to begin! From there, gradually increase the amount of time until you exercise to at least 30 minutes a day, five days a week.
- **Be kind to yourself, and reinforce positive behaviors with rewards.** Don't be down on yourself because you are overweight or out of shape. Don't beat yourself up because of a supposed lack of willpower. Instead, look at any past failures as opportunities to learn and do better. When you do achieve even small exercise goals, treat yourself to something special. Did you complete your first workout? Reward yourself with a relaxing bath or other treats.
- **Don't make excuses for not exercising.** Common complaints include being too busy or tired or not athletic enough. Such excuses are not valid reasons to avoid exercising, and they will sabotage any plans to improve your fitness. If you can't find a 30-minute period to work out, try to find ten minutes, three times a day. If you're feeling tired, know that exercise can actually reduce fatigue and boost your energy level. If you feel clumsy and uncoordinated, remind yourself that you don't need to be athletic to take a walk or engage in vigorous house or yard work.
- **Find an activity that you truly enjoy doing.** Don't think you have to lift weights or run on a treadmill to exercise your muscles. If you find such activities boring or unpleasant, you won't stick with them. Any activity that increases your heart rate and uses large muscles can provide a workout, especially if you're not in the habit of exercising, so find something you like to do. Do you like to dance? Put on some music and dance up a sweat! Do you enjoy gardening? Get out in the yard and dig up some dirt! Still not interested? Try an activity-based video game, such as Wii or Kinect. You may find it so much fun that it doesn't seem like exercise until you realize you've worked up a sweat.
- **Make yourself accountable.** Tell friends and family members that you're going to start exercising. You'll be letting them — as well as yourself — down if you don't follow through. Some people find that keeping an exercise log to track their progress is a good way to be accountable and stick to an exercise program. Perhaps the best way to keep at it is to find an exercise partner. If you've got someone waiting to exercise with you, you will be less likely to make excuses for not exercising.
- **Add more physical activity to your daily life.** You don't need to follow a structured exercise program to increase your activity level. Do your house or yard work briskly for a workout. Park your car further than necessary from work or the mall, and walk the extra distance. If you live close enough, leave the car at home and walk to and from your destination. Rather than taking elevators or escalators, walk up and downstairs. When you take breaks at work, take a walk instead of sitting. Every time a commercial comes on while you're watching TV, take a quick exercise break — run in place or do some curls with hand weights.

REVIEW

1. How is physical exercise defined?
2. What are the current recommendations for physical exercise for adults?
3. Describe aerobic exercise, and give examples of aerobic exercises.
4. How does anaerobic exercise differ from aerobic exercise, and what are some examples of anaerobic exercises?
5. Define flexibility exercise, and state its benefits. What are two examples of flexibility exercises?
6. In general, how does physical exercise affect health, quality of life, and longevity?
7. What mechanism may underlie many of the general health benefits of physical exercise?
8. Relate physical exercise to cardiovascular disease risk.
9. What may explain the positive benefits of physical exercise on cognition?
10. How does physical exercise compare with antidepressant drugs in the treatment of depression?
11. Identify several other health benefits of physical exercise.
12. Explain how genetics may influence the way individuals respond to physical exercise.
13. Can too much physical exercise be harmful?
14. Lifting hefty weights for a short period of time is likely to:

    A. use a relatively high percentage of fast-twitch muscle fibers

    B. use a relatively high percentage of slow-twitch muscle fibers

    C. be an aerobic exercise

    D. use a large amount of oxygen

15. Walking quickly for an extended period of time is likely to:

    A. use a relatively high percentage of fast-twitch muscle fibers

    B. use a relatively high percentage of slow-twitch muscle fibers

    C. use muscles at close to their maximum contraction

    D. cause the muscles to use only a small amount of oxygen

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8.6: DISORDERS OF THE MUSCULAR SYSTEM

PAIN IN THE NECK

Spending hours each day looking down at hand-held devices is a pain in the neck — literally. The weight of the head bending forward can put a lot of strain on neck muscles, and muscle injuries can be excruciating. Neck pain is one of the most common complaints that bring people to the doctor's office. In any given year, about one in five adults will suffer from neck pain. That's a lot of pain in the neck! Not all of them are due to muscular disorders, but many of them are. Muscular disorders, in turn, generally fall into two general categories: musculoskeletal disorders and neuromuscular disorders.



Figure **8.6.1**: On the phone

MUSCULOSKELETAL DISORDERS

Musculoskeletal disorders are injuries in muscles or associated tissues (such as tendons) because of biomechanical stresses. They may be caused by sudden exertion, over-exertion, repetitive motions, or long periods of maintaining awkward positions. Musculoskeletal disorders often work- or sports-related, and generally, just one or a few muscles are affected. They can often be treated successfully, and full recovery can be very likely. The disorders include muscle strains, tendonitis, and carpal tunnel syndrome.

MUSCLE STRAIN

A **muscle strain** is an injury in which muscle fibers tear as a result of overstretching. A muscle strain is also commonly called a pulled muscle or torn muscle. (Strains are often confused with sprains, which are similar injuries to ligaments.) Depending on the degree of injury to muscle fibers, a muscle strain can range from mildly to extremely painful. Besides pain, typical symptoms include stiffness and bruising in the area of the strained muscle. Figure **8.6.2** shows a large bruise caused by a hamstring muscle strain. Hamstring strains are prevalent in track and field athletes. In sprinters, for example, about one-third of injuries are hamstring injuries. Having a previous hamstring injury puts an athlete at increased risk of having another one.



Figure **8.6.2**: Bleeding in muscle tissue may cause a muscle strain to produce a bruise over the affected muscle, as in this hamstring bruise. The photos show two images of the same leg, both taken four days after the injury occurred.

Proper first aid for a muscle strain includes five steps, which are represented by the acronym PRICE. The PRICE steps should be followed for several days after the injury. The five steps are:

1. **Protection:** Apply soft padding to the strained muscle to minimize impact with objects that might cause further damage.
2. **Rest:** Rest the muscle to accelerate healing and reduce the potential for re-injury.
3. **Ice:** Apply ice for 20 minutes at a time every two hours to reduce swelling and pain.
4. **Compression:** Apply a stretchy bandage to the strained muscle to reduce swelling.
5. **Elevation:** Keep the strained muscle elevated to reduce the chance of blood pooling in the muscle.

Non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen) can help reduce inflammation and relieve pain. However, because such drugs interfere with blood clotting, they should be taken only after bleeding in the muscle has stopped — not immediately after the injury occurs. For severe muscle strains, professional medical care may be needed.

TENDINITIS

Tendinitis is inflammation of a tendon that occurs when it is over-extended or worked too hard without rest. Tendons that are commonly affected include those in the ankle, knee, shoulder, and elbow. The affected tendon depends on the type of use that causes inflammation. Rock climbers tend to develop tendinitis in their fingers, while basketball players are more likely to develop tendonitis in the knees, to name a few examples.

Symptoms of tendinitis may include aching, sharp pain, a burning sensation, or joint stiffness. In some cases, swelling occurs around the inflamed tendon, and the area feels hot and looks red. Treatment includes the PRICE guidelines listed above and the use of NSAIDs to reduce inflammation and pain further. Although symptoms should show improvement within a few days of treatment, full recovery may take several months. A gradual return to exercise or other use of the affected tendon is recommended. Physical or occupational therapy may speed the return to normal activity levels.

CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome is a common biomechanical problem in the wrist when the median nerve becomes compressed between carpal bones (Figure **8.6.3**). This may occur due to repetitive use of the wrist, a tumor, or trauma to the wrist. Two-thirds of the cases are work-related. Computer work, work with vibrating tools and work requiring a strong grip all increase one's risk of developing this problem. Carpal tunnel syndrome occurs more often in women than in men. Other risk factors include obesity, pregnancy, and arthritis. Genetics may also play a role.

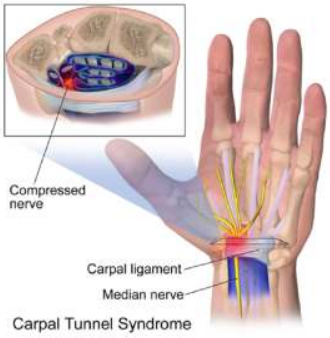


Figure **8.6.3**: Carpal tunnel syndrome occurs when the median nerve in the wrist becomes compressed.

Compression of the median nerve results in the muscles' inadequate nervous stimulation in the thumb and first two fingers of the hand. The main symptoms are pain, numbness, and tingling in these digits. Sometimes, symptoms can be improved by wearing a wrist splint or receiving corticosteroid injections. Surgery to cut the carpal ligament reduces pressure on the median nerve and is generally more effective than nonsurgical treatment. Recurrence of carpal tunnel syndrome after surgery is rare. On the other hand, without treatment, the lack of nervous stimulation by the median nerve may eventually cause the affected muscles of the hand to weaken and waste away.

NEUROMUSCULAR DISORDERS

Neuromuscular disorders are systemic disorders that occur because of problems with the nervous control of muscle contractions or muscle cells themselves. These disorders are often due to faulty genes and not due to biomechanical stresses. Other system-wide problems, such as abnormal immune system responses, may also be involved in neuromuscular disorders.

Unlike musculoskeletal disorders, neuromuscular disorders generally affect most or all of the muscles in the body. The disorders also tend to be progressive and incurable. However, in most cases, treatment is available to slow the disease progression or lessen symptoms. Examples of neuromuscular disorders include muscular dystrophy, myasthenia gravis, and Parkinson's disease.

MUSCULAR DYSTROPHY

Muscular dystrophy is a genetic disorder caused by defective proteins in muscle cells. It is characterized by progressive skeletal muscle weakness and death of muscle cells and tissues. Muscles become increasingly unable to contract in response to nervous stimulation.

There are at least nine major types of muscular dystrophy caused by different gene mutations. Some of the mutations cause autosomal recessive or autosomal dominant disorders, and some cause X-linked disorders. The most common type of childhood muscular dystrophy is Duchenne muscular dystrophy (DMD) due to a mutation in a recessive gene on the X chromosome. As an X-linked recessive disorder, Duchenne muscular dystrophy occurs almost exclusively in males.

Different types of muscular dystrophy affect different major muscle groups. In Duchenne muscular dystrophy, the lower limbs are affected. Signs of the disorder usually first become apparent when a child starts walking. Difficulty walking becomes progressively worse through childhood. By the time a child is ten, braces may be needed for walking — and walking may no longer even be possible by age 12. The lifespan of someone with muscular dystrophy is likely to be shorter than normal because of the disease, ranging from 15 to 45 years.

Duchenne muscular dystrophy (DMD) is a progressive weakening of the skeletal muscles. It is one of several diseases collectively referred to as "muscular dystrophy." DMD is caused by a lack of the protein dystrophin, which helps the thin filaments of myofibrils bind to the sarcolemma. Without sufficient dystrophin, muscle contractions cause the sarcolemma to tear, causing an influx of Ca++, leading to cellular damage and muscle fiber degradation. Over time, as muscle damage accumulates, muscle mass is lost, and greater functional impairments develop.

In some cases, physical therapy, drug therapy, or orthopedic surgery may improve muscular dystrophy signs and symptoms. However, at present, there is no known cure for the disorder. Research is ongoing to find a cure, with financial support from such sources as the Muscular Dystrophy Association (MDA) (see photo below). MDA is a non-profit organization dedicated to curing muscular dystrophy by funding worldwide research.



Figure **8.6.4**: A firefighters from Camp Pendleton, California, who collected donations during their off hours for the Muscular Dystrophy Association (MDA) in 2010.

MYASTHENIA GRAVIS

Myasthenia gravis is an autoimmune disorder in which circulating antibodies block the nicotinic acetylcholine receptors on the neuromuscular junction's motor endplate. This blockage of acetylcholine receptors causes muscle weakness, often first exhibiting drooping eyelids and expanding to include overall muscle

weakness and fatigue. It occurs more commonly in women and generally begins between the ages of 20 and 40. The initial symptom of myasthenia gravis is painless muscle weakness, generally in muscles around the eye (Figure 8.6.5). The disease then progresses to muscles elsewhere in the body, eventually involving most of the muscles. Swallowing and chewing may become difficult as the disease progresses, and speech may become slow and slur. In more advanced cases, myasthenia crises may occur, during which the muscles that control breathing may be affected. Emergency medical care to provide assisted ventilation is required to sustain life. A myasthenia gravis crisis may be triggered by various stressors, such as infection, fever, or stress. Treatment of myasthenia gravis may include medications to counter the mutant gene's effects or suppress the immune system.



Figure 8.6.5: The photograph on the left shows a myasthenia gravis patient with a drooping eyelid. The photo on the right shows the same patient after administering a drug that blocks the breakdown of acetylcholine.

PARKINSON'S DISEASE



Figure 8.6.6: The awkward, stooped gait of this person is typical of people with advanced Parkinson's disease.

Parkinson's disease is a degenerative disorder of the central nervous system that mainly affects the muscular system and movement. Four motor signs and symptoms are considered defining Parkinson's disease: muscle tremor (shaking), muscle rigidity, slowness of movement, and postural instability. Tremor is the most common and obvious symptom, and it most often occurs in a limb at rest, so it disappears during sleep or when the patient moves the limb voluntarily. Difficulty walking eventually develops, and dementia is common in the advanced stages of the disease. Depression is common, as well.

Parkinson's disease is more common in older people, with most cases being diagnosed after 50. Often, the disease occurs for no known reason. Cases like this are called primary Parkinson's disease. Sometimes, the disease has a known or suspected cause, such as exposure to toxins in pesticides or repeated head trauma. In this case, it is called secondary Parkinson's disease. Regardless of the cause, the disease's motor symptoms result from the death of neurons in the midbrain. The cause of cell death is not fully understood, but it appears to involve the buildup in the brain of protein structures called Lewy bodies. Early in the course of the illness, medications can be prescribed to help reduce the motor disturbances. As the disease progresses, however, the medications become ineffective. They also cause a negative side effect of involuntary writhing movements.

FEATURE: HUMAN BIOLOGY IN THE NEWS

On June 3, 2016, media worldwide exploded with news of the death of Muhammad Ali at the age of 74. The world champion boxer and Olympic gold medalist died that day of a respiratory infection complication, but the underlying cause was Parkinson's disease. Ali was diagnosed with Parkinson's in 1984 when he was only 42 years old. Doctors attributed his disease to repeated head trauma from boxing.

In the days following Ali's death, the news was full of stories and images from milestones in the athlete's life, both before and after his diagnosis with Parkinson's disease. Sadly, the news coverage also provided an overview of his gradual decline as the disease progressed. Ali was pictured in 1996, lighting the flame at the Summer Olympics in Atlanta. In 2012, Ali had to be helped to his feet by his wife to stand before the flag he was supposed to carry into the stadium. He was unable to carry it because of the ravages of Parkinson's disease.

Muhammad Ali retired from boxing in 1981 at 39, but he didn't retire from fighting. Until the final year of his life, Ali was a passionate activist for peace and justice and against war and racism. In 1998, he joined Michael J. Fox, who also has Parkinson's disease, to raise awareness and fund research on Parkinson's disease. In 2002, Fox and Ali made a joint appearance before Congress to present their case. In 2005, Ali received the Presidential Medal of Freedom from George W. Bush (Figure 8.6.7) for the many achievements and contributions he made throughout his amazing life, despite Parkinson's disease.



Figure 8.6.7: President George W. Bush gives a congratulatory hug to Muhammad Ali after awarding him a Presidential Medal of Freedom in 2005 as Ali's wife, Lonnie Ali, looks on.

REVIEW

1. What are musculoskeletal disorders? What causes them?
2. How does a muscle strain occur?
3. Define tendinitis. Why does it occur?
4. Identify first-aid steps for treating musculoskeletal disorders such as muscle strains and tendinitis.
5. Describe carpal tunnel syndrome and how it may be treated.
6. Define neuromuscular disorders.
7. Identify the cause and symptoms of muscular dystrophy.

8. Outline the cause and progression of myasthenia gravis.
9. What is Parkinson's disease? List four characteristic signs of the disorder.
10. What are the main differences between musculoskeletal disorders and neuromuscular disorders?
11. Why is the padding of a strained muscle part of the typical treatment?
12. Which disorder would be the most likely to be caused by repeated use of a jackhammer?

    A. Parkinson's disease

    B. Muscular dystrophy

    C. Carpal tunnel syndrome

    D. A neuromuscular disorder

13. *True or False.* Participation in some sports may cause Parkinson's disease.
14. *True or False.* Myasthenia gravis occurs because the body stops making acetylcholine.
15. What are two tissues, other than muscle tissue, that can experience problems that result in muscular system disorders?

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8.7: CASE STUDY CONCLUSION- NEEDING TO RELAX AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: NEEDING TO RELAX

As you learned at the beginning of this chapter, botulinum toxin—one form sold under the brand name Botox—does much more than smooth out wrinkles. It can be used to treat several disorders involving excessive muscle contraction, including cervical dystonia. You also learned that cervical dystonia, from which Nasir suffers, causes abnormal, involuntary muscle contractions of the neck. This results in the head and neck's jerky movements and/or a sustained abnormal tilt to the head. It is often painful and can significantly interfere with a person's life.

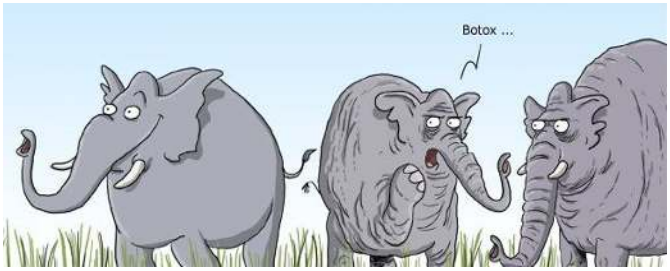


Figure 8.7.1: Botox, he whispered.

How could a toxin actually *help* treat a muscular disorder? The soil bacterium *Clostridium botulinum* produces the botulinum toxin, and it is the cause of the potentially deadly disease called botulism. Botulism is often a foodborne illness, commonly caused by improperly canned foods. Other forms of botulism are caused by wound infections or occur when infants consume the bacteria's spores from soil or honey.

Botulism can be life-threatening because it paralyzes muscles throughout the body, including those involved in breathing. When a minimal amount of botulinum toxin is injected carefully into specific muscles by a trained medical professional, however, it can inhibit unwanted muscle contractions.



Figure 8.7.2: These pickles are jokingly labeled "botulism," but actual botulism is really no joke.

For cosmetic purposes, botulinum toxin injected into the facial muscles relaxes them to reduce wrinkles' appearance. When used to treat cervical dystonia, it is injected into the neck muscles to inhibit excessive muscle contractions. For many patients, this helps relieve the abnormal positioning, movements, and pain associated with the disorder. The effect is temporary, so the injections must be repeated every three to four months to keep the symptoms under control.

How does botulinum toxin inhibit muscle contraction? First, recall how skeletal muscle contraction works. A motor neuron instructs skeletal muscle fibers to contract at a synapse between them called the neuromuscular junction. A nerve impulse called an action potential travels down to the motor neuron's axon terminal, where it causes the release of the neurotransmitter acetylcholine (ACh) from synaptic vesicles. The ACh travels across the synaptic cleft and binds to ACh receptors on the muscle fiber, signaling the muscle fiber to contract. According to the sliding filament theory, muscle fibers' contraction occurs due to the sliding of myosin and actin filaments across each other. This causes the Z discs of the sarcomeres to close together, shortening the sarcomeres and causing the muscle fiber to contract.

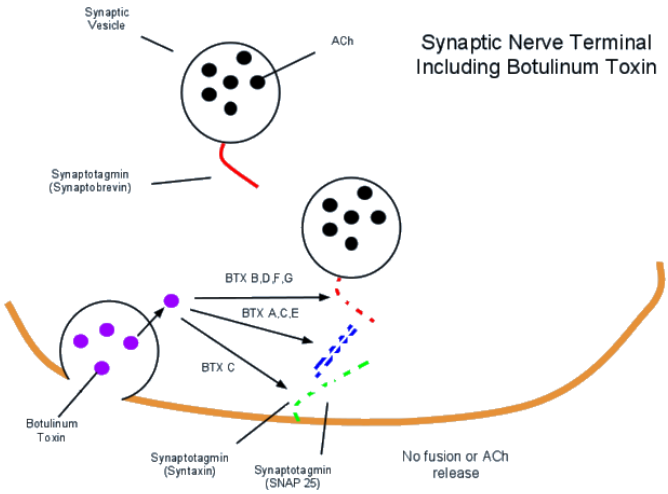


Figure 8.7.3: Botulinum toxins cleave (break down) proteins (depicted here as red, blue, and green lines) that normally allow synaptic vesicles to bind to the membrane of the motor neuron's axon terminal to release the neurotransmitter ACh. Cleavage of these proteins prevents the synaptic vesicles from fusing to the membrane, and therefore ACh release is inhibited. In this illustration, BTX A-G refers to different subtypes of botulinum toxins.

If you wanted to inhibit muscle contraction, at what points could you theoretically interfere with this process? Inhibiting the action potential in the motor neuron, the release of ACh, the activity of ACh receptors, or the sliding filament process in the muscle fiber would all theoretically impair this process and inhibit muscle contraction. For example, in the disease myasthenia gravis, the ACh receptors' function is impaired, causing a lack of sufficient muscle contraction. As you have learned, this results in muscle weakness that can eventually become life-threatening. Botulinum toxin works by inhibiting the release of ACh from the motor neurons, thereby removing the signal instructing the muscles to contract (Figure 8.7.3).

Fortunately, Nasir's excessive muscle contractions and associated pain improved significantly, thanks to botulinum toxin injections.

Although cervical dystonia cannot currently be cured, botulinum toxin injections have improved many patients' quality of life with this and other disorders involving excessive involuntary muscle contractions.

As you have learned in this chapter, our muscular system allows us to make voluntary movements, digest our food, and pump blood through our bodies. Whether in your arm, heart, stomach, or blood vessels, muscle tissue works by contracting. But as you have seen here, too much contraction can be a terrible thing. Fortunately, scientists and physicians have found a way to put a potentially deadly toxin—and wrinkle-reducing treatment—to excellent use as a medical treatment for some muscular system disorders.

CHAPTER SUMMARY

In this chapter, you learned about the muscular system. Specifically, you learned that:

- The muscular system consists of all the muscles of the body. There are three types of muscle: skeletal muscle (which is attached to bones by tendons and enables voluntary body movements), cardiac muscle (which makes up the walls of the heart and makes it beat), and smooth muscle (which is found in the walls of internal organs and other internal structures and controls their movements).
- Muscles are organs composed mainly of muscle cells, which may also be called muscle fibers or myocytes. Muscle cells are specialized for contracting, which occurs when protein filaments inside the cells slide over one another using energy from ATP. Muscle tissue is the only type of tissue that has cells with the ability to contract.
- Muscles can grow larger or hypertrophy. This generally occurs through increased use, although hormonal or other influences can also play a role. Muscles can also grow smaller or atrophy. This may occur through lack of use, starvation, certain diseases, or aging. In both hypertrophy and atrophy, the size—but not the number—of muscle fibers changes. The size of the muscles is the main determinant of muscle strength.
- Skeletal muscles need the stimulus of motor neurons to contract and to move the body; they need the skeletal system to act upon.
- Skeletal muscle is the most common type of muscle tissue in the human body. To move bones in opposite directions, skeletal muscles often consist of pairs of muscles that work in opposition to move bones in different directions at joints.
- Skeletal muscle fibers are bundled together in muscle fascicles, which are bundled together to form individual skeletal muscles. Skeletal muscles also have connective tissue supporting and protecting the muscle tissue.
    - Each skeletal muscle fiber consists of a bundle of myofibrils, which are bundles of protein filaments. The filaments are arranged in repeating units called sarcomeres, which are the skeletal muscles' basic functional units. Skeletal muscle tissue is striated because of the pattern of sarcomeres in its fibers.
    - Skeletal muscle fibers can be divided into two types, called slow-twitch and fast-twitch fibers. Slow-twitch fibers are used mainly in aerobic endurance activities (such as long-distance running). Fast-twitch fibers are used mainly for non-aerobic, strenuous activities (such as sprinting). Proportions of the two types of fibers vary from muscle to muscle and person to person.
- Smooth muscle tissue is found in the walls of internal organs and vessels. When smooth muscles contract, they help the organs and vessels carry out their functions. Contractions of smooth muscles are involuntary and controlled by the autonomic nervous system, hormones, and other substances.
    - Cells of smooth muscle tissue are not striated because they lack sarcomeres, but the cells contract in the same basic way as striated muscle cells. Unlike striated muscle, smooth muscle can sustain very long-term contractions and maintain its contractile function, even when stretched.
- Cardiac muscle tissue is found only in the wall of the heart. When cardiac muscle contracts, the heart beats and pumps blood. Contractions of cardiac muscle are involuntary, like those of smooth muscles. Electrical impulses from specialized cardiac cells control them.
    - Like skeletal muscle, cardiac muscle is striated because its filaments are arranged in sarcomeres. However, the exact arrangement differs, making cardiac and skeletal muscle tissues look different from one another.
    - The heart is the muscle that performs the greatest amount of physical work in a lifetime. Its cells contain many mitochondria to produce ATP for energy and help the heart resist fatigue.
- A muscle contraction is an increase in tension or a decrease in the length of a muscle. A muscle contraction is isometric if muscle tension changes, but muscle length remains the same. It is isotonic if muscle length changes, but muscle tension remains the same.
    - A skeletal muscle contraction begins with the electrochemical stimulation of a muscle fiber by a motor neuron. This occurs at a chemical synapse called a neuromuscular junction. The neurotransmitter acetylcholine diffuses across the synaptic cleft and binds to receptors on the muscle fiber. This initiates a muscle contraction.
    - Once stimulated, the skeletal muscle fibers' protein filaments slide past each other to produce a contraction. The sliding filament theory is the most widely accepted explanation for how this occurs. According to this theory, thick myosin filaments repeatedly attach to and pull on thin actin filaments, thus shortening sarcomeres.
    - Crossbridge cycling is a cycle of molecular events that underlies the sliding filament theory. Using energy in ATP, myosin heads repeatedly bind with and pull on actin filaments. This moves the actin filaments toward the center of

a sarcomere, shortening the sarcomere and causing a muscle contraction.
    - The ATP needed for a muscle contraction comes first from ATP already available in the cell, and more is generated from creatine phosphate. These sources are quickly used up. Glucose and glycogen can be broken down to form ATP and pyruvate. Pyruvate can then be used to produce ATP in aerobic respiration if oxygen is available or used in anaerobic respiration if oxygen is not available.
- Physical exercise is defined as any bodily activity that enhances or maintains physical fitness and overall health. Activities such as household chores may even count as physical exercise! Current recommendations for adults are 30 minutes of moderate exercise a day.
- Aerobic exercise is any physical activity that uses muscles at less than their maximum contraction strength but for long periods of time. This type of exercise uses a relatively high percentage of slow-twitch muscle fibers that consume large amounts of oxygen. Aerobic exercises increase cardiovascular endurance and include cycling and brisk walking.
- Anaerobic exercise is any physical activity that uses muscles at close to their maximum contraction strength, but for short periods of time. This type of exercise uses a relatively high percentage of fast-twitch muscle fibers that consume small amounts of oxygen. Anaerobic exercises increase muscle and bone mass and strength, and they include push-ups and sprinting.
- Flexibility exercise is any physical activity that stretches and lengthens muscles, thereby improving the range of motion and reducing injury risk. Examples include stretching and yoga.
- Many studies have shown that physical exercise is positively correlated with a diversity of physical, mental, and emotional health benefits. Physical exercise also increases the quality of life and life expectancy.
    - Many of the exercise benefits may come about because contracting muscles release hormones called myokines, which promote tissue repair and growth and have anti-inflammatory effects.
    - Physical exercise can reduce risk factors for cardiovascular disease, including hypertension and excess body weight. Physical exercise can also increase cardiovascular health factors, such as the mechanical efficiency of the heart.
    - Physical exercise has been shown to offer protection from dementia and other cognitive problems, perhaps because it increases blood flow or neurotransmitters in the brain, among other potential effects.
    - Numerous studies suggest that regular aerobic exercise works and pharmaceutical antidepressants in treating mild-to-moderate depression, possibly because it increases the synthesis of natural euphoriants in the brain.
    - Research shows that physical exercise generally improves sleep for most people and helps sleep disorders, such as insomnia. Other health benefits of physical exercise include better immune system function and reduced risk of type 2 diabetes and obesity.
- There is great variation in individual responses to exercise, partly due to genetic differences in proportions of slow-twitch and fast-twitch muscle fibers. People with more slow-twitch fibers may be able to develop greater endurance from aerobic exercise. In contrast, people with more fast-twitch fibers may develop greater muscle size and strength from anaerobic exercise.
- Some adverse effects may occur if exercise is extremely intense, and the body is not given proper rest between exercise sessions. Many people who overwork their muscles develop delayed onset muscle soreness (DOMS), caused by tiny tears in muscle fibers.
- Musculoskeletal disorders are injuries in muscles or associated tissues (such as tendons) because of biomechanical stresses. The disorders may be caused by sudden exertion, over-exertion, repetitive motions, and similar stresses.
    - A muscle strain is an injury in which muscle fibers tear as a result of overstretching. First aid for a muscle strain includes the five steps represented by the acronym PRICE (protection, rest, ice, compression, and elevation). Medications for inflammation and pain (such as NSAIDs) may also be used.
    - Tendinitis is inflammation of a tendon that occurs when it is over-extended or worked too hard without rest. Tendinitis may also be treated with PRICE and NSAIDs.
    - Carpal tunnel syndrome is a biomechanical problem in the wrist when the median nerve becomes compressed between carpal bones. It may occur with repetitive use, a tumor, or trauma to the wrist. It may cause pain, numbness, and eventually—if untreated—muscle wasting in the thumb and first two fingers of the hand.
- Neuromuscular disorders are systemic disorders that occur because of problems with the nervous control of muscle contractions or muscle cells themselves.
    - Muscular dystrophy is a genetic disorder caused by defective proteins in muscle cells. It is characterized by progressive skeletal muscle weakness and death of muscle tissues.
    - Myasthenia gravis is a genetic neuromuscular disorder characterized by fluctuating muscle weakness and fatigue. More muscles are affected, and muscles become increasingly weakened, as the disorder progresses. Myasthenia gravis most often occurs because immune system antibodies block acetylcholine receptors on muscle cells because of the actual loss of acetylcholine receptors.
    - Parkinson's disease is a degenerative disorder of the central nervous system that mainly affects the muscular system and movement. It occurs because of the death of neurons in the midbrain. Characteristic signs of the disorder are muscle tremor, muscle rigidity, slowness of movement, and postural instability. Dementia and depression also often characterize advanced stages of the disease.

As you saw in this chapter, muscles need oxygen to provide enough ATP for most of their activities. In fact, all of the body's systems

require oxygen and remove waste products, such as carbon dioxide. In the next chapter, you will learn about how the respiratory system obtains and distributes oxygen throughout the body and how it removes wastes, such as carbon dioxide.

CHAPTER SUMMARY REVIEW

1. *True or False.* Each motor neuron controls one muscle fiber.
2. *True or False.* Peristalsis is a pattern of muscle contraction in smooth muscle tissue.
3. When muscles atrophy:
   A. muscle fibers become narrower
   B. muscle fibers turn into fat cells
   C. muscle fibers are lost
   D. muscle fibers become shorter
4. What are tendons?
5. What is a muscular system disorder involving tendons?
6. Which of the main types of muscle tissue is used when you make a voluntary movement of one of your limbs?
7. Which main types of muscle tissue function independently of conscious control by the brain?
8. Describe the relationship between muscles, muscle fibers, and fascicles.
9. *Choose one.* The (autonomic; somatic) nervous system controls the skeletal muscles.
10. *True or False.* Sarcomeres are the cells of the muscular system.
11. *True or False.* Muscles contain connective tissue as well as muscle tissue.
12. The biceps and triceps muscles are shown in Figure **8.7.4**. Answer the following questions about these arm muscles.
    A. When the biceps contract and become shorter, as in the illustration, what kind of motion does this produce in the arm?
    B. Is the situation described in part more likely to be an isometric or isotonic contraction? Explain your answer.
    C. If the triceps were to then contract, which way would help the arm move?

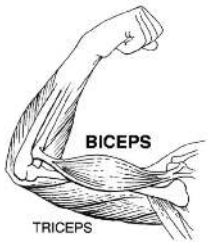


Figure **8.7.4**: biceps

13. Put the following events in order of when they occur during the process of skeletal muscle contraction, from earliest to latest:
    A. Acetylcholine binds to receptors on the muscle fiber
    B. Actin filaments slide, shortening the sarcomere
    C. An action potential is initiated in a motor neuron
    D. Acetylcholine is released from synaptic vesicles
14. What are Z discs, and what happens to them during muscle contraction?
15. *True or False.* Synapses only exist between neurons.
16. *True or False.* Muscles can produce hormones.
17. Which have been called the strongest muscles in the human body, relative to their work?
    A. The heart muscles
    B. The hamstring muscles
    C. The external eye muscles
    D. The stomach muscles
18. What is the function of mitochondria in muscle cells? Which type of muscle fiber has more mitochondria—slow-twitch or fast-twitch?
19. Fast-twitch and slow-twitch are types of which kind of muscle fibers?
    A. skeletal
    B. smooth
    C. cardiac
    D. B and C
20. Myoglobin:
    A. Stores oxygen for anaerobic respiration
    B. Stores oxygen for aerobic respiration
    C. Is present in higher amounts in fast-twitch fibers than slow-twitch fibers
    D. Is where ATP is produced
21. *True or False.* All people have the same proportion of slow-twitch to fast-twitch muscle fibers.
22. *True or False.* A sprain is a tear in the muscle fibers.
23. Which condition directly damages neurons, not muscles?
    A. Myasthenia gravis
    B. Muscular dystrophy
    C. Musculoskeletal disorder
    D. Parkinson's disease
24. What is the difference between primary and secondary Parkinson's disease?
25. Why can carpal tunnel syndrome cause muscle weakness in the hands?
26. *True or False.* The heart consists of smooth muscle tissue.
27. *True or False.* Sprinting is considered an anaerobic exercise

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CHAPTER OVERVIEW

9: NERVOUS SYSTEM

This chapter describes neurons and other cells of the nervous system and compares and contrasts divisions of the nervous system, including central, peripheral, somatic, and autonomic divisions. The chapter explains how nerve impulses occur and how we sense stimuli. It also describes disorders of the nervous system and the effects of psychoactive drugs on the nervous system.

9.1: Case Study- The Control Center of Your Body

9.2: Introduction to the Nervous System

9.3: Neurons

9.4: Nerve Impulses

9.5: Central Nervous System

9.6: Peripheral Nervous System

9.7: Human Senses

9.8: Psychoactive Drugs

9.9: Case Study Conclusion- Memory and Chapter Summary

Thumbnail: Cerebral lobes. (CC BY SA 3.0 Unported; Gutenberg Encyclopedia).

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9.1: CASE STUDY- THE CONTROL CENTER OF YOUR BODY

CASE STUDY: FADING MEMORY

Each of these brightly colored sticky notes represents a piece of information that someone doesn't want to forget. Although we are all forgetful sometimes, most people do not have trouble remembering things that are important or routine to us, such as our friend's name or how to get to class. Our brain, the control center of the nervous system and the rest of the body, normally allows us to retain and recall information. But if the brain becomes damaged, a person may need to rely excessively on external reminders — like this wall of sticky notes — rather than being able to trust their own memory. That is if they are able to remember to write things down in the first place.

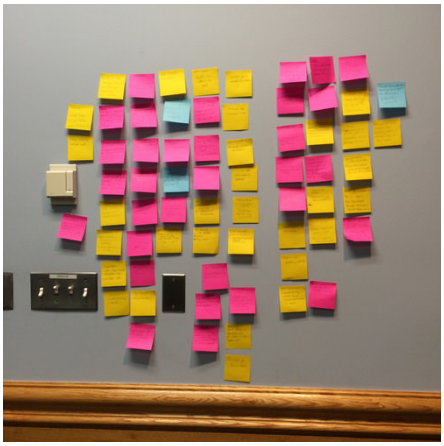


Figure **9.1.1**: Stickies

One person having trouble with their memory is Rosa, who is 68 years old. Rosa has been having difficulty remembering where she has set down objects in her house and forgot about a few doctor's appointments and lunches she planned with friends. Her family began to notice that she would sometimes not recall recent conversations, requiring them to repeat things to her. Rosa would also sometimes struggle to find the right word in a conversation and would put objects in unusual places, such as the milk in a cabinet instead of the refrigerator. While most people do things like this occasionally, it seemed to Rosa and her family that it was happening to her more often recently.

She also had some other symptoms that were impacting her life, such as having trouble paying her bills on time and managing her budget, which she had previously done well. Rosa ascribed these lapses in memory and mental functioning to the normal effects of aging, but her family was concerned. They noticed that she was also more irritable than usual and would sometimes verbally lash out at them, which was not like her. When she became disoriented on a walk around her neighborhood and a neighbor had to escort her home, her family convinced her to see a doctor.

Besides a complete physical exam and lab tests, Rosa's doctor interviewed Rosa and her family about her memory, ability to carry out daily tasks, and mood changes. He also administered a variety of tests to assess her memory and cognitive functioning, such as her ability to solve problems and use numbers and language correctly. Finally, he ordered a scan of her brain to investigate whether a tumor or some other observable cause was causing changes in the functioning of her brain.

Based on the results of these tests, Rosa's doctor came to the conclusion that she most likely has mild Alzheimer's disease (AD). AD results from abnormal changes in the molecules and cells of the brain, characterized by clumps of proteins called amyloid plaques between brain cells and tangled bundles of protein fibers called neurofibrillary tangles within certain brain cells. The affected brain cells stop functioning properly, lose their connections to other brain cells, and eventually will die. The picture below shows part of a cross-section of a brain from a patient who had severe AD compared to a similar section of a healthy brain. You can see how severely shrunken the brain with AD is, due to the death of many brain cells.

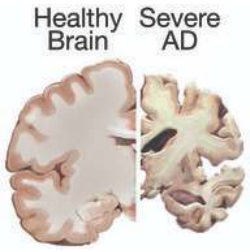


Figure **9.1.2**: The healthy brain is much larger than the brain with AD.

AD is a progressive disease, which means the damage and associated symptoms get worse over time. Clinicians have categorized the progression into three main stages — mild, moderate, and severe AD. Typically, AD cannot be definitively diagnosed until after death when the brain tissue can be directly examined for plaques and tangles. However, based on Rosa's symptoms and the results of her tests, her doctor thinks she most likely has mild AD, when the brain changes and resulting symptoms are not yet severe.

Although there is currently no cure for AD, and Rosa will eventually get worse, her doctor says that medications and behavioral therapies may improve and prolong her functioning and quality of life over the next few years. He prescribes a medication that improves communication between brain cells, which has been shown to help some people with AD.

As you read this chapter, you will learn much more about how the brain and the rest of the nervous system work, and the multitude of functions they control in the body. By the end of the chapter, you will have enough knowledge about the nervous system to learn more about why AD causes the symptoms that it does, how Rosa's medication works, and some promising new approaches that may help physicians diagnose and treat AD patients at earlier stages.

CHAPTER OVERVIEW: NERVOUS SYSTEM

In this chapter, you will learn about the human nervous system, which includes the brain, spinal cord, and nerves. Specifically, you will learn about:

- The organization of the nervous system, including the central and peripheral nervous systems and their organs and subdivisions.
- The cells of the nervous system — neurons and glia — their parts, and their functions.
- How messages are sent by neurons through the nervous system and to and from the rest of the body.
- How these messages, or nerve impulses, are transmitted by electrical changes within neurons, and through chemical molecules to other cells.
- The structure and functions of different parts of the central nervous system, which includes the brain and spinal cord, and some of the things that can go wrong when they are damaged.
- The structure and functions of the peripheral nervous system, which includes the nerves that carry motor and sensory information to and from the body to control voluntary and involuntary activities.
- The human senses and how visual information, sounds, smells, tastes, touch, and balance are detected by sensory receptor cells and then sent to the brain for interpretation.
- How legal and illegal drugs can have psychoactive effects on the brain-altering mood, perceptions, thinking, and behavior — which can sometimes lead to addiction.

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

1. Based on Rosa's symptoms, which parts of her brain may have been affected by Alzheimer's disease?
2. How are messages sent between cells in the nervous system? What molecules are involved in this process? What are the ways in which drugs can alter this process?
3. Why can't Rosa's brain just grow new cells to replace the ones that have died?

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9.2: INTRODUCTION TO THE NERVOUS SYSTEM

IN THE BLINK OF AN EYE

As you drive into a parking lot, a skateboarder suddenly flies in front of your car across your field of vision. You see the skateboarder in the nick of time and react immediately. You slam on the brakes and steer sharply to the right — all in the blink of an eye. You avoid a collision, but just barely. You're shaken up but thankful that no one was hurt. How did you respond so quickly? Such rapid responses are controlled by your nervous system.



Figure **9.2.1**: Skateboarder

OVERVIEW OF THE NERVOUS SYSTEM

The **nervous system**, illustrated in Figure **9.2.2**, is the human organ system that coordinates all of the body's voluntary and involuntary actions by transmitting electrical signals to and from different parts of the body. Specifically, the nervous system extracts information from the internal and external environments using sensory receptors. It then usually sends signals encoding this information to the brain, which processes the information to determine an appropriate response. Finally, the brain sends signals to muscles, organs, or glands to bring about the response. In the example above, your eyes detected the skateboarder, the information traveled to your brain, and your brain instructed your body to act so as to avoid a collision.

SIGNALS OF THE NERVOUS SYSTEM

The signals sent by the nervous system are electrical signals called nerve impulses, and they are transmitted by special nervous system cells named neurons, or nerve cells, like the one in Figure **9.2.3** (all the parts of a neuron are explained in the next section). Dendrites of a neuron receive nerve impulses from other cells. Long projection (called axons) from neurons carries nerve impulses directly to specific target cells. Schwann cells wrapped around the axon are called **glial cells**. They create a myelin sheath which allows the nerve impulse to travel very rapidly through the axons. A cell that receives nerve impulses from a neuron may be excited to perform a function, inhibited from carrying out an action, or otherwise controlled. In this way, the information transmitted by the nervous system is specific to particular cells and is transmitted very rapidly.

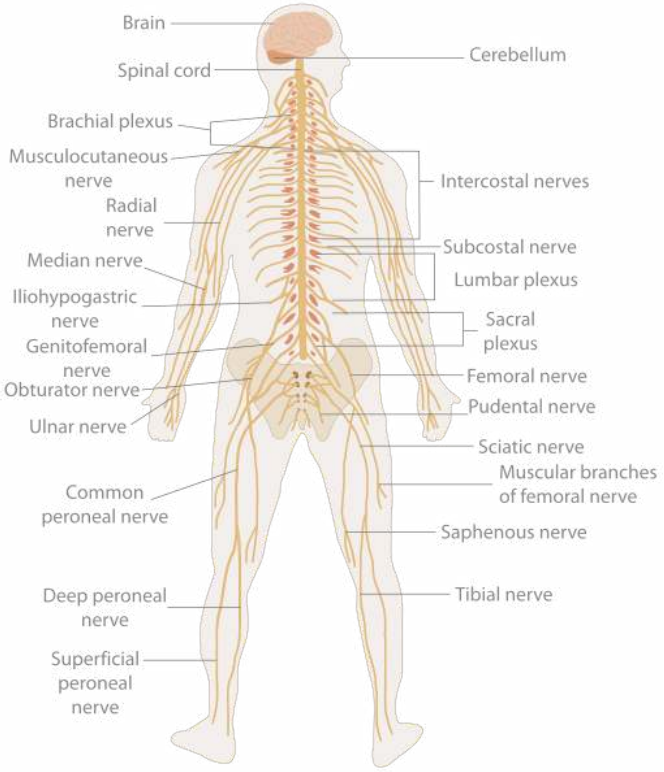


Figure **9.2.2**: The human nervous system consists of the brain and spinal cord (central nervous system) and a network of branching nerves that travel throughout the body (peripheral nervous system). Some of the major nerves in the peripheral system are identified in this drawing.

In fact, the fastest nerve impulses travel at speeds greater than 100 meters per second! Compare this to the chemical messages carried by the hormones that are secreted into the blood by endocrine glands. These hormonal messages are "broadcast" to all the cells of the body, and they can travel only as quickly as the blood flows through the cardiovascular system.

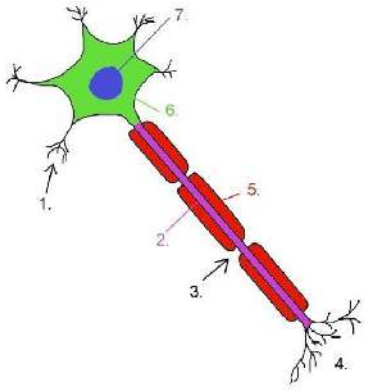


Figure **9.2.3**: This simple model of a neuron shows 1 Dendrite, 2 Axon, 3 Nodes of Ranvier, 4 Axon Terminals, 5 Schwann cell (Myelin Sheath), 6 Cell body, and 7 Nucleus

ORGANIZATION OF THE NERVOUS SYSTEM

As you might predict, the human nervous system is very complex. It has multiple divisions, beginning with its two main parts, the central nervous system (CNS) and the peripheral nervous system (PNS), as shown in Figure **9.2.4**. The CNS includes the brain and spinal cord, and the PNS consists mainly of nerves, which are bundles of axons from neurons. The nerves of the PNS connect the CNS to the rest of the body. You can learn much more about the CNS by reading the concept *Central Nervous System*.

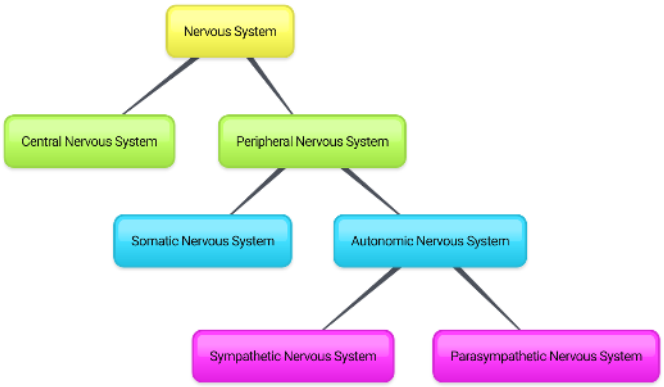


Figure **9.2.4**: The concept map illustrates that the nervous system is divided into the peripheral and central systems. The peripheral nervous system is divided into the autonomic and somatic systems. The autonomic nervous system is divided into the sympathetic and parasympathetic systems.

The PNS is divided into two major parts, called the autonomic and somatic nervous systems. The somatic nervous system controls activities that are under voluntary control, such as turning a steering wheel. The autonomic nervous system controls activities that are not under voluntary control, such as digesting a meal. The autonomic nervous system has two divisions: the sympathetic division, which controls the fight-or-flight response during emergencies, and the parasympathetic division, which controls the routine "housekeeping" functions of the body at other times. You can learn more about the PNS and its subdivisions by reading the concept *Peripheral Nervous System*.

REVIEW

1. List the general steps by which the nervous system generates an appropriate response to information from the internal and external environments.
2. What are neurons?
3. Compare and contrast the central and peripheral nervous systems.
4. Which major division of the peripheral nervous system allows you to walk to class? Which major division of the peripheral nervous system controls your heart rate?
5. Identify the functions of the three divisions of the autonomic nervous system.
6. What is an axon and what is its function?
7. *True or False*. A nerve impulse always causes the target cell to perform an action.
8. *True or False*. The spinal cord is not considered part of the peripheral nervous system.
9. Define nerve impulses.
10. Explain why signals in the nervous system are generally more targeted and specific than signals in the endocrine system.
11. Explain generally how the brain and spinal cord can interact with and control the rest of the body.
12. _____ actions are performed without the person thinking about them.
13. The fight-or-flight response is controlled by the:
    A. autonomic nervous system
    B. somatic nervous system
    C. central nervous system
    D. parasympathetic nervous system
14. How are nerves and neurons related?
15. What type of information from the outside environment do you think is detected by sensory receptors in your ears?

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9.3: NEURONS

LIFE AS ART

This colorful picture could be an abstract work of modern art. You might imagine it hanging in an art museum or art gallery. In fact, the picture illustrates real life rather than an artistic creation. It is a micrograph of human nervous tissue. The neon green structures in the picture are neurons. The neuron is one of two basic types of cells in the nervous system, the other type being the glial cell.

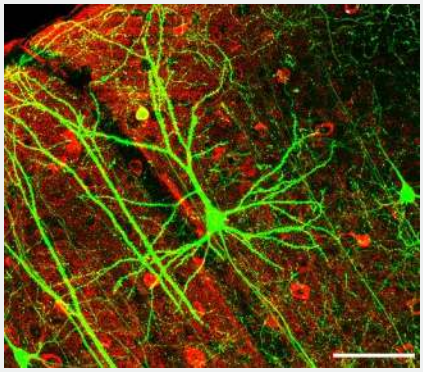


Figure **9.3.1**: Interneurons of Adult Visual Cortex

Neurons, also called nerve cells, are electrically excitable cells that are the main functional units of the nervous system. Their function is to transmit nerve impulses. They are the only type of human cells that can carry out this function.

NEURON STRUCTURE

Figure **9.3.2** shows the structure of a typical neuron. The main parts of a neuron are labeled in the figure and described below.

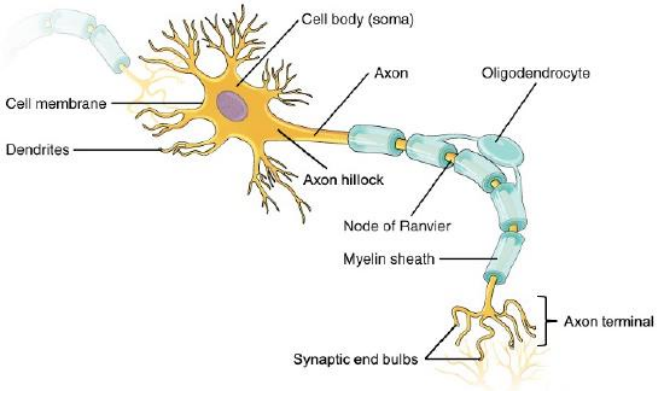


Figure **9.3.2**: Somatic Motor Neuron with cell body, axon, axon, myelin sheath, nodes of Ranvier, axon terminal, dendrites, synaptic end of the bulbs, and other associated structures.

- The **cell body** is the part of a neuron that contains the cell nucleus and other cell organelles. It is usually quite compact, and may not be much wider than the nucleus.
- **Dendrites** are thin structures that are extensions of the cell body. Their function is to receive nerve impulses from other cells and carry them to the cell body. A neuron may have many dendrites, and each dendrite may branch repeatedly to form a dendrite "tree" with more than 1,000 "branches." The end of each branch can receive nerve impulses from another cell, allowing a given neuron to communicate with tens of thousands of other cells.
- The **axon** is a long, thin extension of the cell body. It transmits nerve impulses away from the cell body and toward other cells. The axon branches at the end, forming multiple axon terminals. These are the points where nerve impulses are transmitted to other cells, often to the dendrites of other neurons. An area called a synapse occurs at each axon terminal. Synapses are complex membrane junctions that transmit signals to other cells. An axon may branch hundreds of times, but there is never more than one axon per neuron.
- Spread out along axons, especially the long axons of nerves, are many sections of the **myelin sheath.** These are lipid layers that cover sections of the axon. The myelin sheath is a very good electrical insulator, similar to the plastic or rubber that encases an electrical cord.
- Regularly spaced gaps between sections of myelin sheath occur along the axon. These gaps are called **nodes of Ranvier**, and they allow the transmission of nerve impulses along the axon. Nerve impulses skip from node to node, allowing nerve impulses to travel along the axon very rapidly.
- A Schwann cell (also on an axon) is a type of glial cell. Its function is to produce the myelin sheath that insulates axons in the peripheral nervous system. In the central nervous system, a different type of glial cell, called an oligodendrocyte, produces the myelin sheath.

NEUROGENESIS

Fully differentiated neurons, with all their special structures, cannot divide and form new daughter neurons. Until recently, scientists thought that new neurons could no longer be formed after the brain developed prenatally. In other words, they thought that people were born with all the brain neurons they would ever have, and as neurons died, they would not be replaced. However, new evidence shows that additional neurons can form in the brain, even in adults, from the division of undifferentiated neural stem cells that are found throughout the brain. The production of new neurons is called **neurogenesis.** The extent to which it can occur is not known, but it is not likely to be very great in humans.

NEURONS IN NERVOUS TISSUES

The nervous tissue in the brain and spinal cord consists of gray matter and white matter. Gray matter contains mainly the cell bodies of neurons. It is gray only in cadavers; living gray matter is actually more pink than gray (see image below). White matter consists mainly of axons covered with myelin sheath, which gives them their white color. White matter also makes up nerves of the peripheral nervous system. Nerves consist of long bundles of myelinated axons that extend to muscles, organs, or glands throughout the body. The axons in each nerve are bundled together like wires in a cable.

Axons in nerves may be more than a meter long in an adult. The longest nerve runs from the base of the spine to the toes.

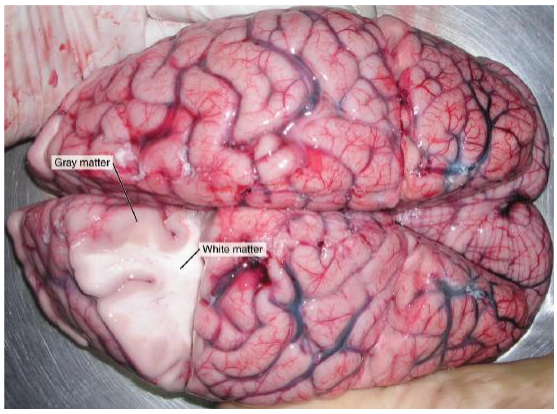


Figure **9.3.3**: You can see the layers of (pinkish) gray matter and white matter in this photo of a brain from a recently deceased human patient

TYPES OF NEURONS

There are hundreds of different types of neurons in the human nervous system. These types exhibit a variety of structures and functions. Nonetheless, many neurons can be classified functionally based on the direction in which they carry nerve impulses.

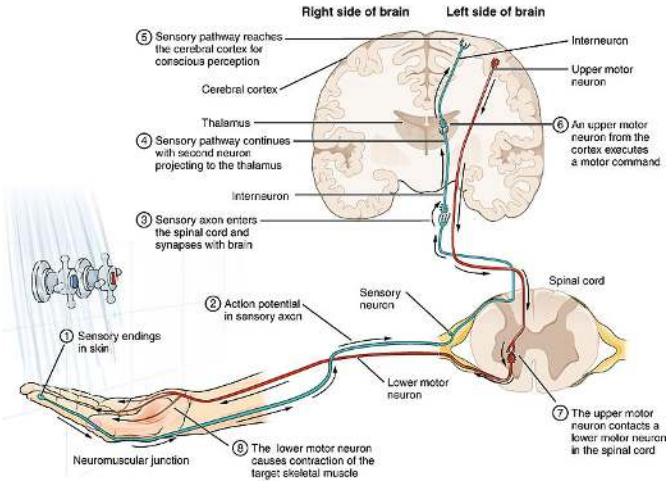


Figure **9.3.4**: Sensory neurons carry information towards the CNS. Motor neurons carry information from the CNS. Interneurons carry information between sensory and motor neurons.

- **Sensory** (also called afferent) **neurons** carry nerve impulses from sensory receptors in tissues and organs to the central nervous system. They change physical stimuli such as touch, light, and sound into nerve impulses.
- **Motor** (also called efferent) **neurons,** like the one in figure **9.3.2**, carry nerve impulses from the central nervous system to muscles and glands. They change nerve signals into the activation of these structures.
- **Interneurons** carry nerve impulses back and forth often between sensory and motor neurons within the spinal cord or brain.

GLIAL CELLS

Besides neurons, nervous tissues also consist of **glial cells** (also called neuroglia). They are now known to play many vital roles in the nervous system. There are several different types of glial cells, each with a different function. Schwann cells and Oligodendrocytes are glial cells that produce myelin sheath.

FEATURE: MY HUMAN BODY

Would you like your brain to make new neurons that could help you become a better learner? What college student wouldn't want a little more brainpower when it comes to learning new things? If research on rats applies to humans, then sustained aerobic exercise such as running can increase neurogenesis in the adult brain, and specifically in the hippocampus, a brain structure important for learning temporally and/or spatially complex tasks as well as memory. Although the research is still at the beginning stages, it suggests that exercise may actually lead to a "smarter" brain. However, even if the research results are not confirmed in the future for humans, it can't hurt to get more aerobic exercise, because it is certainly beneficial for your body if not for your brain.

REVIEW

1. Identify the three main parts of a neuron and their functions.
2. Describe the myelin sheath and nodes of Ranvier. How does their arrangement allow nerve impulses to travel very rapidly along axons?
3. What is a synapse?
4. Define neurogenesis. What is the potential for neurogenesis in the human brain?
5. Relate neurons to different types of nervous tissues.
6. Compare and contrast sensory and motor neurons.
7. Identify the role of interneurons.
8. For each type of neuron below, identify whether it is a sensory neuron, motor neuron, or interneuron.
   A. A neuron in the spinal cord receives touch information and then transmits that information to another spinal cord neuron that controls the movement of an arm muscle.
   B. A neuron that takes taste information from your tongue and sends it to your brain.
   C. A spinal cord neuron stimulates a muscle to contract.
9. The myelin sheath is made by:
   A. Sensory neurons
   B. White neurons
   C. Peripheral nervous system neurons
   D. Glial cells
10. *True or False.* Synapses often exist where a dendrite and an axon terminal meet.
11. *True or False.* There is only one axon terminal per neuron.

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9.4: NERVE IMPULSES

WHEN LIGHTNING STRIKES

This amazing cloud-to-surface lightning occurred when a difference in electrical charge built up in a cloud relative to the ground. When the buildup of charge was great enough, a sudden discharge of electricity occurred. A nerve impulse is similar to a lightning strike. Both a nerve impulse and a lightning strike occur because of differences in electrical charge, and both result in an electric current.



Figure **9.4.1**: Lightning

GENERATING NERVE IMPULSES

A **nerve impulse**, like a lightning strike, is an electrical phenomenon. A nerve impulse occurs because of a difference in electrical charge across the plasma membrane of a neuron. How does this difference in electrical charge come about? The answer involves ions, which are electrically charged atoms or molecules.

RESTING POTENTIAL

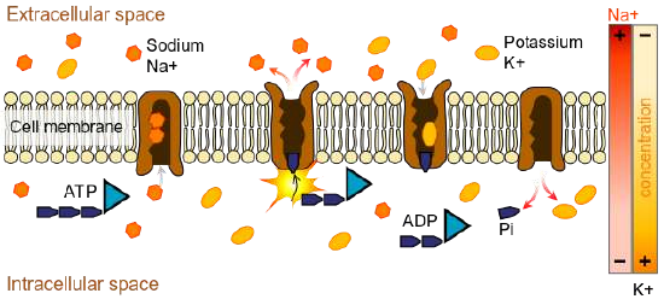


Figure **9.4.2**: The sodium-potassium pump maintains the resting potential of a neuron. There is more negative charge inside than outside the cell membrane. ATP is used to pump sodium out and potassium into the cell. There is more concentration of sodium outside the membrane and more concentration of potassium inside the cell due to the unequal movement of these ions by the pump

When a neuron is not actively transmitting a nerve impulse, it is in a resting state, ready to transmit a nerve impulse. During the resting state, the sodium-potassium pump maintains a difference in charge across the cell membrane of the neuron. The sodium-potassium pump is a mechanism of active transport that moves sodium ions out of cells and potassium ions into cells. The sodium-potassium pump moves both ions from areas of lower to higher concentration, using energy in ATP and carrier proteins in the cell membrane. Figure **9.4.3** shows in greater detail how the sodium-potassium pump works. Sodium is the principal ion in the fluid outside of cells, and potassium is the principal ion in the fluid inside of cells. These differences in concentration create an electrical gradient across the cell membrane, called **resting potential**. Tightly controlling membrane resting potential is critical for the transmission of nerve impulses.

ACTION POTENTIAL

An **action potential**, also called a nerve impulse, is an electrical charge that travels along the membrane of a neuron. It can be generated when a neuron's membrane potential is changed by chemical signals from a nearby cell. In an action potential, the cell membrane potential changes quickly from negative to positive as sodium ions flow into the cell through ion channels, while potassium ions flow out of the cell, as shown in Figure **9.4.3**.

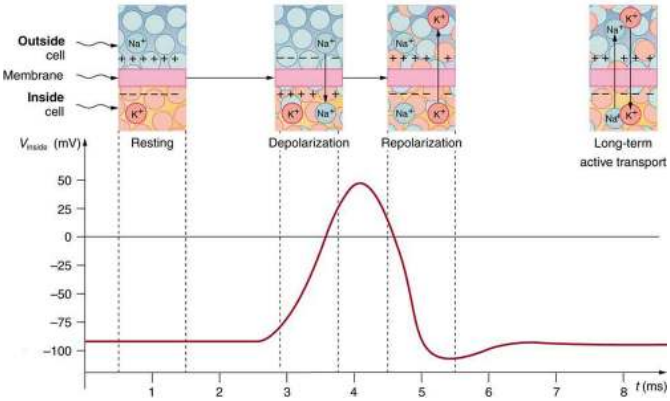


Figure **9.4.3**: An action potential speeds along an axon in milliseconds. Sodium ions flow in and cause the action potential, and then potassium ions flow out to reset the resting potential.

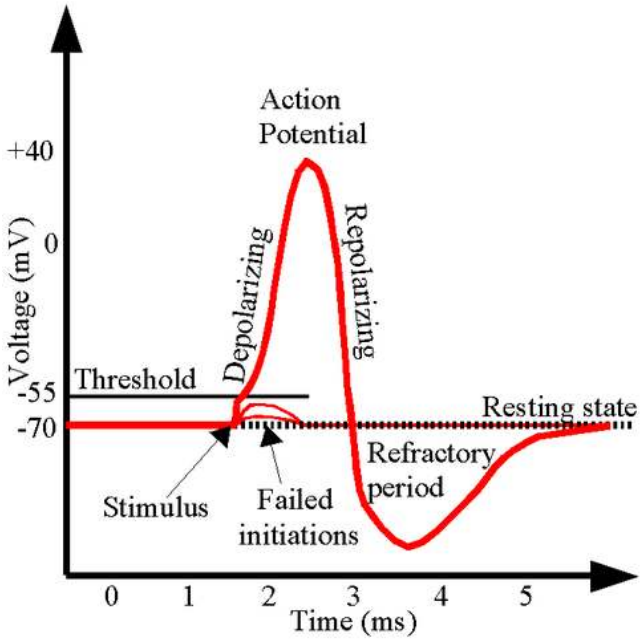


Figure **9.4.4**: An action potential graph of membrane potential over time. A neuron must reach a certain threshold in order to begin the depolarization step of reaching the action potential. The figure also shows the change in potential during the repolarization and refractory periods of the axon.

The change in membrane potential results in the cell becoming depolarized. An action potential works on an all-or-nothing basis. That is, the membrane potential has to reach a certain level of depolarization, called the threshold, otherwise, an action potential will not start. This threshold potential varies but is generally about 15 millivolts (mV) more positive than the cell's resting membrane potential. If a membrane depolarization does not reach the threshold level, an action potential will not happen. You can see in Figure **9.4.4** that two depolarizations did not reach the threshold level of -55mV.

The first channels to open are the sodium ion channels, which allow sodium ions to enter the cell. The resulting increase in positive charge inside the cell (up to about +40 mV) starts the action potential. This is called the depolarization of the membrane. Potassium ion channels then open, allowing potassium ions to flow out of the cell, which ends the action potential. The inside of the membrane becomes negative again. This is called repolarization of the membrane. Both of the ion channels then close, and the sodium-potassium pump restores the resting potential of -70 mV. The action potential will move down the axon toward the synapse like a wave would move along the surface of the water. Figure **9.4.4**shows the change in potential of the axon membrane during an action potential. The nerve goes through a brief refractory period before racing resting potential. During the refractory period, another action potential cannot be generated

In myelinated neurons, ion flows occur only at the nodes of Ranvier. As a result, the action potential signal "jumps" along the axon membrane from node to node rather than spreading smoothly along the membrane, as they do in axons that do not have a myelin sheath. This is due to a clustering of Na+ and K+ ion channels at the Nodes of Ranvier. Unmyelinated axons do not have nodes of Ranvier, and ion channels in these axons are spread over the entire membrane surface.

TRANSMITTING NERVE IMPULSES

The place where an axon terminal meets another cell is called a **synapse.** This is where the transmission of a nerve impulse to another cell occurs. The cell that sends the nerve impulse is called the presynaptic cell, and the cell that receives the nerve impulse is called the postsynaptic cell.

Some synapses are purely electrical and make direct electrical connections between neurons. However, most synapses are chemical synapses. The transmission of nerve impulses across chemical synapses is more complex.

CHEMICAL SYNAPSES

At a chemical synapse, both the presynaptic and postsynaptic areas of the cells are full of the molecular machinery that is involved in the transmission of nerve impulses. As shown in Figure **9.4.5**, the presynaptic area contains many tiny spherical vessels called synaptic vesicles that are packed with chemicals called **neurotransmitters**. When an action potential reaches the axon terminal of the presynaptic cell, it opens channels that allow calcium to enter the terminal. Calcium causes synaptic vesicles to fuse with the membrane, releasing their contents into the narrow space between the presynaptic and postsynaptic membranes. This area is called the synaptic cleft. The neurotransmitter molecules travel across the synaptic cleft and bind to **receptors**, which are proteins that are embedded in the membrane of the postsynaptic cell.

The effect of a neurotransmitter on a postsynaptic cell depends mainly on the type of receptors that it activates, making it possible for a particular neurotransmitter to have different effects on various target cells. A neurotransmitter might excite one set of target cells, inhibit others, and have complex modulatory effects on still others, depending on the type of receptors. However, some neurotransmitters have relatively consistent effects on other cells.

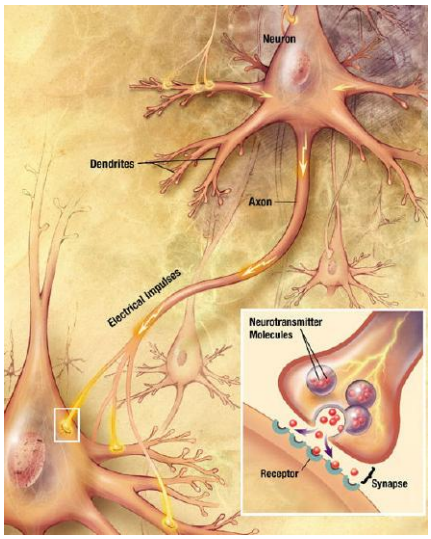


Figure 9.4.5: This diagram shows how an action potential transmits a signal across a synapse to another cell by neurotransmitter molecules. The inset diagram shows the axon terminal, synapse, and receptor of the postsynaptic cell. The neurotransmitters are released from the axon terminal, travel in the synaptic cleft, and attach to the receptors.

REVIEW

1. Define nerve impulse.
2. What is the resting potential of a neuron, and how is it maintained?
3. Explain how and why an action potential occurs.
4. Outline how a signal is transmitted from a presynaptic cell to a postsynaptic cell at a chemical synapse.
5. What generally determines the effects of a neurotransmitter on a postsynaptic cell?
6. Identify three general types of effects neurotransmitters may have on postsynaptic cells.
7. Explain how an electrical signal in a presynaptic neuron causes the transmission of a chemical signal at the synapse.
8. The flow of which type of ion into the neuron results in an action potential?
   A. How do these ions get into the cell?
   B. What does this flow of ions do to the relative charge inside the neuron compared to the outside?
9. The sodium-potassium pump:
   A. is activated by an action potential
   B. requires energy
   C. does not require energy
   D. pumps potassium ions out of cells
10. *True or False.* Some action potentials are larger than others, depending on the amount of stimulation.
11. *True or False.* Synaptic vesicles from the presynaptic cell enter the postsynaptic cell.
12. *True or False.* An action potential in a presynaptic cell can ultimately cause the postsynaptic cell to become inhibited.
13. Name three neurotransmitters.

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9.5: CENTRAL NERVOUS SYSTEM

HOMUNCULUS

Figure **9.5.1** is a very odd-looking drawing and is called a homunculus. The mass represents a cross-sectional wedge of the human brain. The drawing shows some areas of the brain associated with different parts of the body. As you can see, larger areas of the brain in this region are associated with the hands, face, and tongue than the legs and feet. Given the importance of speech, manual dexterity, and face-to-face social interactions in human beings, it is not surprising that relatively large areas of the brain are needed to control these body parts. The brain is the most complex organ in the human body and part of the central nervous system.

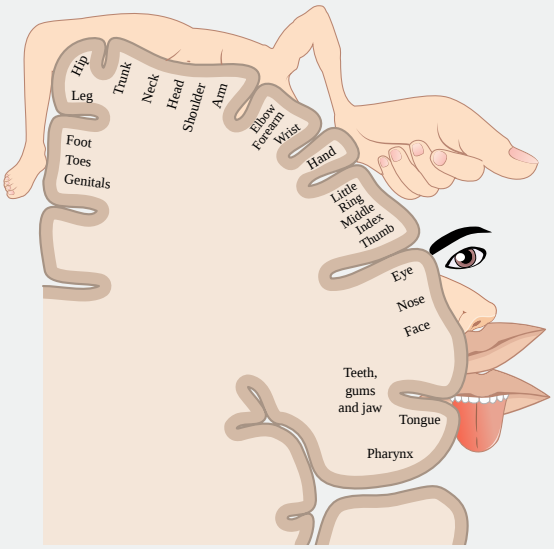


Figure **9.5.1**: Brain-Body Map. There's a map of your body on your brain's cortex, but the map is not proportional to actual space. Sensitive parts like the face and fingers are represented by more areas than less sensitive parts like the legs or back

WHAT IS THE CENTRAL NERVOUS SYSTEM?

The central nervous system (CNS) is the part of the nervous system that includes the brain and spinal cord. Figure **9.5.2** shows the central nervous system as one of the two main divisions of the total nervous system. The other main division is the peripheral nervous system (PNS). The CNS and PNS work together to control virtually all body functions. You can read much more about the PNS in the concept *Peripheral Nervous System*.

The delicate nervous tissues of the central nervous system are protected by major physical and chemical barriers. Physically, the brain and spinal cord are surrounded by tough meninges, a three-layer protective sheath that also contains cushioning cerebrospinal fluid. The bones of the skull and spinal vertebrae also contribute to physically protecting the brain and spinal cord. Chemically, the brain and spinal cord are isolated from the circulation — and most toxins or pathogens in the blood — by the **blood-brain barrier.** The blood-brain barrier is a highly selective membrane formed of endothelial cells (a type of glial cells) that separates the circulating blood from the extracellular fluid in the CNS. The barrier allows water, certain gases, glucose, and some other molecules needed by the brain and spinal cord to cross from the blood into the CNS while keeping out potentially harmful substances. These physical and chemical barriers make the CNS less susceptible to injury. However, damage to the CNS is likely to have more serious consequences.

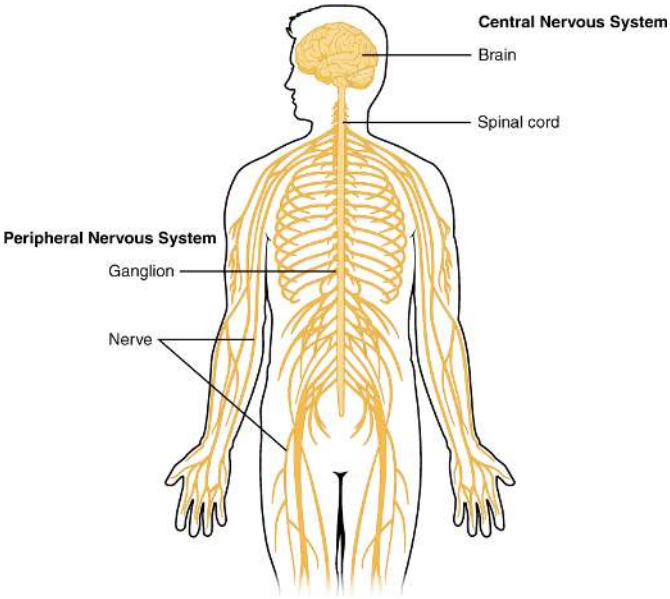


Figure **9.5.2**: The two main parts of the central nervous system are the brain and the spinal cord. Ganglions and nerves are part of the peripheral nerve system.

THE BRAIN

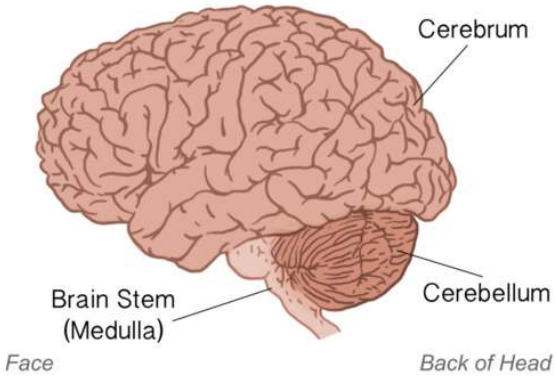


Figure **9.5.3**: Cerebrum, Cerebellum, and Brain Stem are the major parts of the brain. the medulla is part of the brain stem.

The **brain** is the control center not only of the rest of the nervous system but of the entire organism. The adult brain makes up only about 2 percent of the body's weight, but it uses about 20 percent of the body's total energy. The brain contains an estimated one hundred billion neurons, and each neuron has thousands of synaptic connections to other neurons. The brain also has about the same number of glial cells as neurons. No wonder the brain uses so much

energy! In addition, the brain uses mostly glucose for energy. As a result, if the brain is deprived of glucose, it can lead to unconsciousness. The brain is able to store some glucose in the form of glycogen, but in much smaller amounts than are found in the liver and skeletal muscles.

The brain controls such mental processes as reasoning, imagination, memory, and language. It also interprets information from the senses and commands the body how to respond. It controls basic physical processes such as breathing and heartbeat as well as voluntary activities such as walking and writing. The brain has three major parts: the cerebrum, cerebellum, and brain stem (Figure **9.5.3**). The figure shows the brain from the left side of the head. It shows how the brain would appear if the skull and meninges were removed. The brain stem via its medulla links to the spinal cord. The cerebellum is a small section at the back of the brain. The largest part of the brain is the cerebrum.

CEREBRUM

The **cerebrum** is the largest part of the brain. It controls conscious, intellectual functions. For example, it controls reasoning, language, memory, sight, touch, and hearing. When you read a book, play a video game, or recognize a classmate, you are using your cerebrum.

HEMISPHERES AND LATERALIZATION OF THE CEREBRUM

The cerebrum is divided from front to back into two halves called the left and right **hemispheres.** The two hemispheres are connected by a thick bundle of axons, known as the corpus callosum, which lies deep within the brain. The corpus callosum is the main avenue of communication between the two hemispheres. It connects each point in the cerebrum to the mirror-image point in the opposite hemisphere.

The right and left hemispheres of the cerebrum are similar in shape, and most areas of the cerebrum are found in both hemispheres. Some areas, however, show **lateralization,** or a concentration in one hemisphere or the other. For example, in most people, language functions are more concentrated in the left hemisphere, whereas abstract reasoning and visual-spatial abilities are more concentrated in the right hemisphere.

For reasons that are not yet clear, each hemisphere of the brain interacts primarily with the opposite side of the body. The left side of the brain receives messages from and sends commands to the right side of the body, and the right side of the brain receives messages from and sends commands to the left side of the body. Sensory nerves from the spinal cord to the brain and motor nerves from the brain to the spinal cord both cross the midline of the body at the level of the brain stem.

CEREBRAL CORTEX

Most of the information processing in the brain actually takes place in the **cerebral cortex.** This is a rind of gray matter and other tissues just a few millimeters thick that makes up the outer surface of the cerebrum in both hemispheres of the brain. The cerebral cortex has many folds in it that greatly increase the amount of surface area of the brain that can fit within the skull. Because of all the folds in the human cerebral cortex, it has a surface area of about 2,500 cm^2(2.5 ft^2). The size and importance of the cerebral cortex are far greater in the human brain than the brains of any other vertebrates including nonhuman primates.

LOBES OF THE CEREBRAL CORTEX

Each hemisphere of the cerebrum is further divided into the four lobes shown in Figure **9.5.4** and described below.

1. The **frontal lobes** are located at the front of the brain behind the forehead. The frontal lobes are associated with executive functions such as attention, self-control, planning, problem-solving, reasoning, abstract thought, language, and personality.

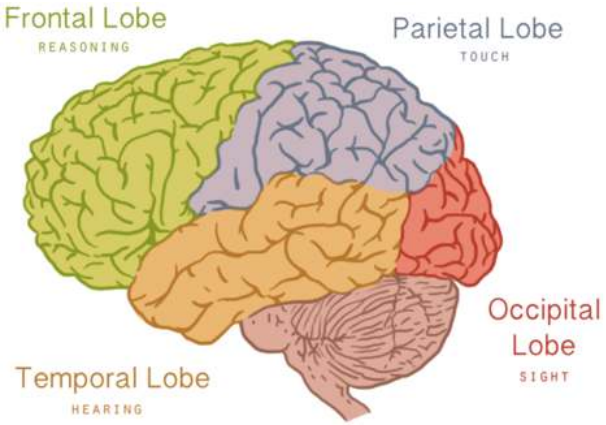


Figure **9.5.4**: Each hemisphere of the cerebrum consists of four parts, called lobes. The lobes are associated with multiple functions. The image shows one function of each lobe. Frontal, Parietal, Occipital, and Temporal lobes are associated with reasoning, touch, sight, and hearing, respectively.

2. The **parietal lobes** are located behind the frontal lobes at the top of the head. The parietal lobes are involved in sensation, including temperature, touch, and taste. Reading and arithmetic are also functions of the parietal lobes.

3. The **temporal lobes** are located at the sides of the head below the frontal and parietal lobes. The temporal lobes enable hearing, the formation and retrieval of memories, and the integration of memories and sensations.

4. The **occipital lobes** are located at the back of the head below the parietal lobes. The occipital lobes are the smallest of the four pairs of lobes. They are dedicated almost solely to vision.

INNER STRUCTURES OF THE BRAIN

Several structures are located deep within the brain and are important for communication between the brain and spinal cord or the rest of the body. These structures include the hypothalamus and thalamus. Figure **9.5.5** shows where these structures are located in the brain. The cerebrum, hypothalamus, and thalamus exist in two halves, one in each hemisphere.

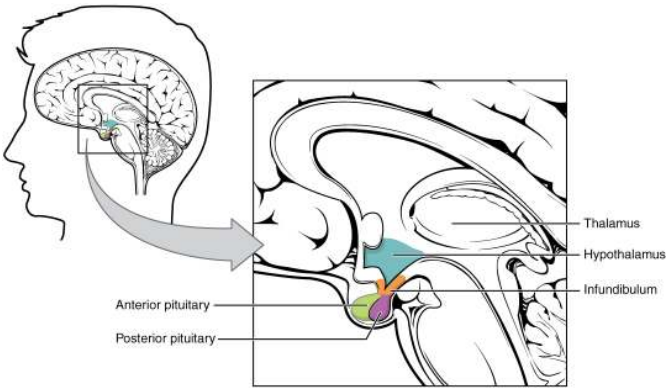


Figure **9.5.5**: Just below the cerebrum is the thalamus. Hypothalamus is located below the thalamus and a little to the anterior. The pituitary gland is attached to the hypothalamus via a tube called the infundibulum.

HYPOTHALAMUS

The **hypothalamus** is located just above the brain stem and is about the size of an almond. The hypothalamus is responsible for certain metabolic processes and other activities of the autonomic nervous system, including body temperature, heart rate, hunger, thirst, fatigue, sleep, wakefulness, and circadian (24-hour) rhythms. The hypothalamus is also an important emotional center of the brain. The hypothalamus can regulate so many body functions because it responds to many different internal and external signals, including messages from the brain, light, steroid hormones, stress, and invading pathogens, among others.

One way the hypothalamus influences body functions is by synthesizing hormones that directly influence body processes. For example, it synthesizes the hormone oxytocin, which stimulates uterine contractions during childbirth and the letdown of milk during lactation. It also synthesizes the hormone vasopressin (also called antidiuretic hormone), which stimulates the kidneys to reabsorb more water and excrete more concentrated urine. These two hormones are sent from the hypothalamus via a stalk-like structure called the infundibulum (see diagram above) directly to the posterior (back) portion of the pituitary gland, which secretes them into the blood.

The main way the hypothalamus influences body functions is by controlling the pituitary gland, known as the master gland of the endocrine system. The hypothalamus synthesizes neurohormones called releasing factors that travel through the infundibulum directly to the anterior (front) part of the pituitary gland. The releasing factors generally either stimulate or inhibit the secretion of anterior pituitary hormones, most of which control other glands of the endocrine system.

THALAMUS

The **thalamus,** which is located near the hypothalamus (Figure **9.5.5**), is a major hub for information traveling back and forth between the spinal cord and cerebrum. It filters sensory information traveling to the cerebrum. It relays sensory signals to the cerebral cortex and motor signals to the spinal cord. It is also involved in the regulation of consciousness, sleep, and alertness.

CEREBELLUM

The **cerebellum** is just below the cerebrum and at the back of the brain behind the brain stem (Figure **9.5.3**). It coordinates body movements and is involved in movements that are learned with repeated practice. For example, when you hit a softball with a bat or touch type on a keyboard you are using the cerebellum. Many nerve pathways link the cerebellum with motor neurons throughout the body.

BRAIN STEM

Sometimes called the “lower brain,” the **brain stem** is the lower part of the brain that is joined to the spinal cord. There are three parts to the brainstem: the midbrain, the pons, and the medulla oblongata, which are shown in Figure **9.5.6** below. The brain stem is primarily involved in the unconscious autonomic functions as well as several types of sensory information. It also helps coordinate large body movements such as walking and running. The **midbrain** deals with sight and sound information and translates these inputs before sending them to the forebrain. The **pons** relays messages to other parts of the brain (primarily the cerebrum and cerebellum) and helps regulate breathing. Some researchers have hypothesized that the pons plays a role in dreaming. Some of the functions of the Pons are shared by the **medulla oblongata,** also called the medulla. The medulla controls several subconscious homeostatic functions such as breathing, heart and blood vessel activity, swallowing, and digestion.

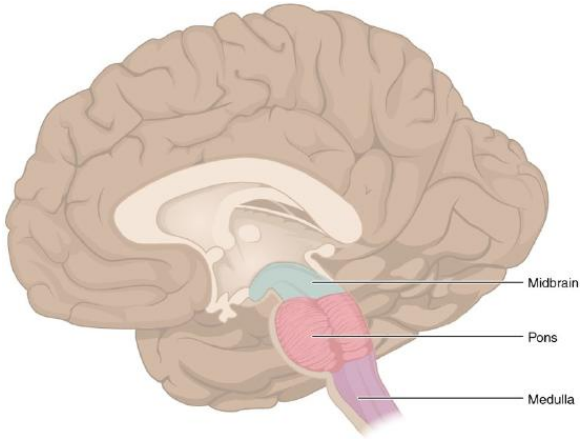


Figure **9.5.6**: Brain stem includes the midbrain, pons, and medulla oblongata

One of the brain stem’s most important roles is that of an “information highway.” That is, all of the information coming from the body to the brain and the information from the cerebrum to the body go through the brain stem. Sensory pathways for such things as pain, temperature, touch, and pressure sensation go upward to the cerebrum, and motor pathways for movement and other body processes go downward to the spinal cord. Most of the axons in the motor pathways cross from one side of the CNS to the other as they pass through the medulla oblongata. As a result, the right side of the brain controls much of the movement on the left side of the body,

and the left side of the brain controls much of the movement on the right side of the body.

SPINAL CORD



Figure **9.5.7**: The spinal cord (yellow) runs from the bottom of the brain to the lower back

The **spinal cord** is a long, thin, tubular bundle of nervous tissues that extends from the brain stem and continues down the center of the back to the pelvis. It is highlighted in yellow in Figure **9.5.7**. The spinal cord is enclosed within but is shorter than, the vertebral column.

STRUCTURE OF THE SPINAL CORD

The center of the spinal cord consists of gray matter, which is made up mainly of cell bodies of neurons, including interneurons and motor neurons. The gray matter is surrounded by white matter that consists mainly of myelinated axons of motor and sensory neurons. Spinal nerves, which connect the spinal cord to the PNS, exit from the spinal cord between vertebrae (Figure **9.5.8**).

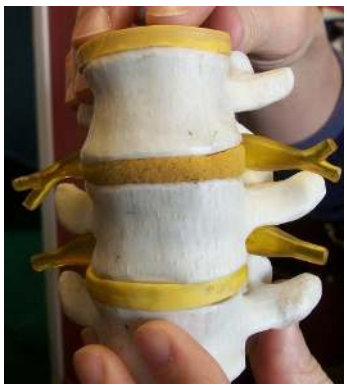


Figure **9.5.8**: This model shows three vertebrae (white) with branching spinal nerves (yellow) emerging from either side of the spinal cord between vertebrae

FUNCTIONS OF THE SPINAL CORD

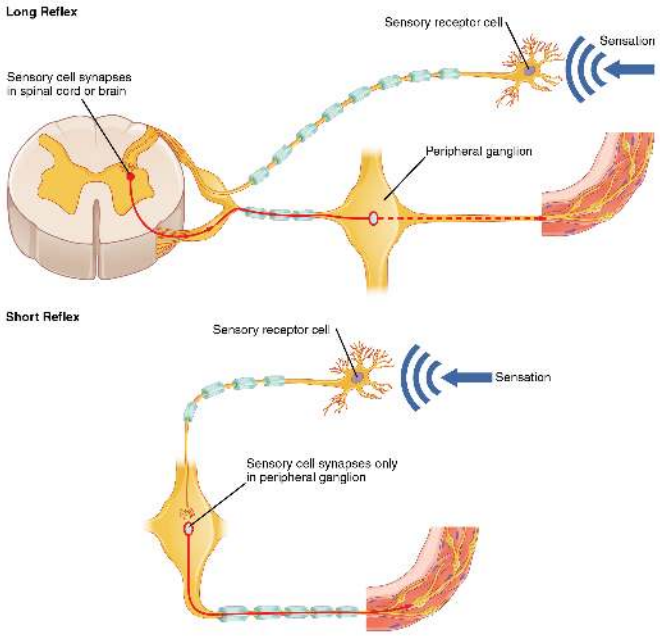


Figure **9.5.9**: This diagram shows what happens in a long reflex (top), in which sensory nerves carry the message all the way to the spinal cord; and in a short reflex (bottom), in which sensory nerves travel only to a ganglion outside the spinal cord. Note that interneurons are involved in reflexes, connecting sensory and motor neurons, but they are not actually shown in the diagram.

The spinal cord serves as an information superhighway. It passes messages from the body to the brain and from the brain to the body. Sensory (afferent) nerves carry nerve impulses to the brain from sensory receptor cells everywhere in and on the body. Motor (efferent) nerves carry nerve impulses away from the brain to glands, organs, or muscles throughout the body.

The spinal cord also independently controls certain rapid responses called **reflexes** without any input from the brain. You can see how this may happen in Figure **9.5.9**. A sensory receptor responds to a sensation and sends a nerve impulse along a sensory nerve to the spinal cord. In the spinal cord, the message passes to an interneuron and from the interneuron to a motor nerve, which carries the impulse to a muscle. The muscle contracts in response. These neuron connections form a reflex arc, which requires no input from the brain. No doubt you have experienced such reflex actions yourself. For example, you may have reached out to touch a pot on the stove, not realizing that it was very hot. Virtually at the same moment that you feel the burning heat, you jerk your arm back and remove your hand from the pot.

INJURIES TO THE SPINAL CORD

Physical damage to the spinal cord may result in **paralysis,** which is a loss of sensation and movement in part of the body. Paralysis generally affects all the areas of the body below the level of the injury because nerve impulses are interrupted and can no longer travel back and forth between the brain and body beyond that point. If an injury to the spinal cord produces nothing more than swelling, the symptoms may be transient. However, if nerve fibers (axons) in

the spinal cord are badly damaged, the loss of function may be permanent. Experimental studies have shown that spinal nerve fibers attempt to regrow, but tissue destruction usually produces scar tissue that cannot be penetrated by the regrowing nerves, as well as other factors that inhibit nerve fiber regrowth in the central nervous system.

FEATURE: MY HUMAN BODY

Each year, many millions of people have a stroke, and stroke is the second leading cause of death in adults. **Stroke,** also known as cerebrovascular accident, occurs when poor blood flow to the brain results in the death of brain cells. There are two main types of strokes:

- Ischemic strokes occur due to a lack of blood flow because of a blood clot in an artery going to the brain.
- Hemorrhagic strokes occur due to bleeding from a broken blood vessel in the brain.

Either type of stroke may result in paralysis, loss of the ability to speak or comprehend speech, loss of bladder control, personality changes, and many other potential effects, depending on the part of the brain that is injured. The effects of a stroke may be mild and transient or more severe and permanent. A stroke may even be fatal. It generally depends on the type of stroke and how extensive it is.

Are you at risk of stroke? The main risk factor for stroke is age: about two-thirds of strokes occur in people over the age of 65. There is nothing you can do about your age, but most other stroke risk factors can be reduced with lifestyle changes or medications. The risk factors include high blood pressure, tobacco smoking, obesity, high blood cholesterol, diabetes mellitus, and atrial fibrillation.

Chances are good that you or someone you know is at risk of a stroke, so it is important to recognize a stroke if one occurs. Stoke is a medical emergency, and the more quickly treatment is given, the better the outcome is likely to be. In the case of ischemic strokes, the use of clot-busting drugs may prevent permanent brain damage if administered within 3 or 4 hours of the stroke. Remembering the signs of a stroke is easy.

They are summed up by the acronym FAST, as explained in the chart below.



Figure 9.5.10: The signs of stroke are abbreviated as FAST. Where F, A, S, and T stand for droopy face, arm weakness, slurry speech, and time to call 911, respectively.

REVIEW

1. What is the central nervous system?
2. How is the central nervous system protected?
3. What is the overall function of the brain?
4. Identify the three main parts of the brain and one function of each part.
5. Describe the hemispheres of the brain.
6. Explain and give examples of lateralization of the brain.
7. Identify one function of each of the four lobes of the cerebrum.
8. Summarize the structure and function of the cerebral cortex.
9. Explain how the hypothalamus controls the endocrine system.
10. Describe the spinal cord.
11. What is the main function of the spinal cord?
12. Explain how reflex actions occur.
13. Why do severe spinal cord injuries usually cause paralysis?
14. What do you think are some possible consequences of severe damage to the brain stem? How might this compare to the consequences of severe damage to the frontal lobe? Explain your answer.
15. Information travels very quickly in the nervous system, but generally, the longer the path between areas, the longer it takes. Based on this, explain why you think reflexes often occur at the spinal cord level and do not require input from the brain.

EXPLORE MORE

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9.6: PERIPHERAL NERVOUS SYSTEM

ONE PIANO, FOUR HANDS

Did you ever see two people play the same piano? How do they coordinate all the movements of their own fingers, let alone synchronize them with those of their partner? The peripheral nervous system plays an important part in this challenge.



Figure **9.6.1**: Two people playing piano together

WHAT IS THE PERIPHERAL NERVOUS SYSTEM?

The *peripheral nervous system (PNS)* consists of all the nervous tissue that lies outside of the central nervous system (CNS). The main function of the PNS is to connect the CNS to the rest of the organism. It serves as a communication relay, going back and forth between the CNS and muscles, organs, and glands throughout the body.

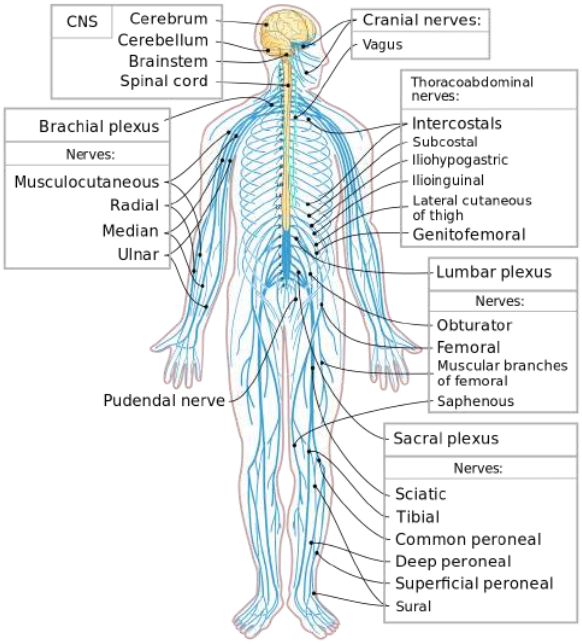


Figure **9.6.2**: The nerves of the peripheral nervous system are shown in blue in this figure.

TISSUES OF THE PERIPHERAL NERVOUS SYSTEM

The tissues that make up the PNS are nerves and ganglia. Ganglia are nervous tissues that act as relay points for messages transmitted through nerves of the PNS. Nerves are cable-like bundles of axons that make up the majority of PNS tissues. Nerves are generally classified on the basis of the direction in which they carry nerve impulses as sensory, motor, or mixed nerves. See examples of sensory and motor never in Figure **9.6.3**.

- **Sensory nerves** transmit information from sensory receptors in the body to the CNS. Sensory nerves are also called afferent nerves.
- **Motor nerves** transmit information from the CNS to muscles, organs, and glands. Motor nerves are also called efferent nerves.
- **Mixed nerves** contain both sensory and motor neurons, so they can transmit information in both directions. They have both afferent and efferent functions.

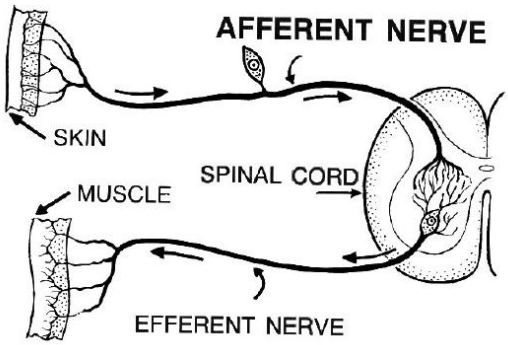


Figure **9.6.3**: An afferent nerve is a sensory nerve. The one pictured here sends nerve impulses from sensory cells in the skin to the CNS. An efferent nerve is a motor nerve. This one sends nerve impulses from the CNS to a muscle.

DIVISIONS OF THE PERIPHERAL NERVOUS SYSTEM

The PNS is divided into two major systems, called the autonomic nervous system and the somatic (or sensory-somatic) nervous system. Both systems of the PNS interact with the CNS and include sensory and motor neurons, but they use different circuits of nerves and ganglia.

SOMATIC NERVOUS SYSTEM

The **somatic nervous system** primarily senses the external environment and controls voluntary activities in which decisions and commands come from the cerebral cortex of the brain. For example, when you feel too warm, decide to turn on the air conditioner, and walk across the room to the thermostat, you are using your somatic nervous system. In general, the somatic nervous system is responsible for all of your conscious perceptions of the outside world and all of the voluntary motor activities you perform in response. Whether it's playing piano, driving a car, or playing basketball, you can thank your somatic nervous system for making it possible.

Structurally, the somatic nervous system consists of 12 pairs of cranial nerves and 31 pairs of spinal nerves (Figure **9.6.2**). Cranial nerves are in the head and neck and connect directly to the brain. Sensory cranial nerves sense smells, tastes, light, sounds, and body position. Motor cranial nerves control muscles of the face, tongue, eyeballs, throat, head, and shoulders. The motor nerves also control the salivary glands and swallowing. Four of the 12 cranial nerves participate in both sensory and motor functions as mixed nerves, having both sensory and motor neurons.

Spinal nerves of the somatic nervous system emanate from the spinal column between vertebrae. All of the spinal nerves are mixed nerves, containing both sensory and motor neurons. Spinal nerves also include motor nerves that stimulate skeletal muscle contraction, allowing for voluntary body movements.

AUTONOMIC NERVOUS SYSTEM

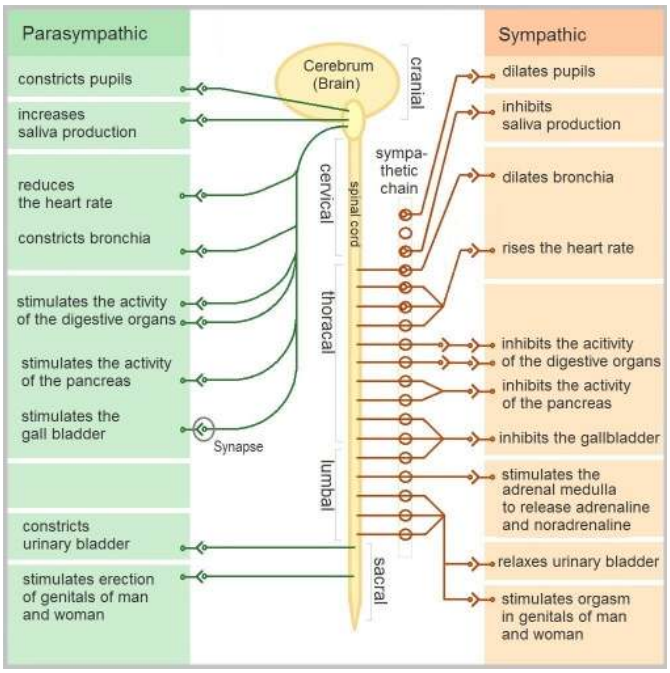


Figure **9.6.4**: This diagram summarizes the structures and functions controlled by the parasympathetic and sympathetic divisions of the autonomic nervous system. The images explained how eyes, salivary gland, bronchi, heart rate, digestive system, bladder, and genitalia are affected in opposite ways by the two systems.

The **autonomic nervous system** primarily senses the internal environment and controls involuntary activities. It is responsible for monitoring conditions in the internal environment and bringing about appropriate changes in them. In general, the autonomic nervous system is responsible for all the activities that go on inside your body without your conscious awareness or voluntary participation.

Structurally, the autonomic nervous system consists of sensory and motor nerves that run between the CNS (especially the hypothalamus in the brain) and internal organs (such as the heart, lungs, and digestive organs) and glands (such as the pancreas and sweat glands). Sensory neurons in the autonomic system detect internal body conditions and send messages to the brain. Motor nerves in the autonomic system function by controlling the contractions of smooth or cardiac muscle or glandular tissue. For example, when sensory nerves of the autonomic system detect a rise in body temperature, motor nerves signal smooth muscles in blood vessels near the body surface to undergo vasodilation, and the sweat glands in the skin secrete more sweat to cool the body.

The autonomic nervous system, in turn, has two subdivisions: the sympathetic division and parasympathetic division. The two subdivisions of the autonomic system are summarized in Figure **9.6.4**. Both affect the same organs and glands, but they generally do so in opposite ways.

- The **sympathetic division** controls the fight-or-flight response. Changes occur in organs and glands throughout the body that prepare the body to fight or flee in response to a perceived danger. For example, the heart rate speeds up, air passages in the

lungs become wider, more blood flows to the skeletal muscles, and the digestive system temporarily shuts down.

- The **parasympathetic division** returns the body to normal after the fight-or-flight response has occurred. For example, it slows down the heart rate, narrows air passages in the lungs, reduces blood flow to the skeletal muscles, and stimulates the digestive system to start working again. The parasympathetic division also maintains the internal homeostasis of the body at other times.

DISORDERS OF THE PERIPHERAL NERVOUS SYSTEM

Unlike the CNS, which is protected by bones, meninges, and cerebrospinal fluid, the PNS has no such protections. The PNS also has no blood-brain barrier to protect it from toxins and pathogens in the blood. Therefore, the PNS is more subject to injury and disease than is the CNS. Causes of nerve injury include diabetes, infectious diseases such as shingles, and poisoning by toxins such as heavy metals. Disorders of the PNS often have symptoms such as loss of feeling, tingling, burning sensations, or muscle weakness. If a traumatic injury results in a nerve being transacted (cut all the way through), it may regenerate, but this is a very slow process and may take many months.

REVIEW

1. Describe the general structure of the peripheral nervous system, and state its primary function.
2. What are ganglia?
3. Identify three types of nerves based on the direction in which they carry nerve impulses.
4. Outline all of the divisions of the peripheral nervous system.
5. Compare and contrast the somatic and autonomic nervous systems.
6. When and how does the sympathetic division of the autonomic nervous system affect the body?
7. What is the function of the parasympathetic division of the autonomic nervous system? What specific effects does it have on the body?
8. Name and describe two disorders of the peripheral nervous system.
9. Give one example of how the CNS interacts with the PNS to control a function in the body.
10. For each of the following types of information, identify whether the neuron carrying it is sensory or motor and whether it is most likely in the somatic or autonomic nervous system.
    A. Visual information
    B. Blood pressure information
    C. Information that causes muscle contraction in digestive organs after eating
    D. Information that causes muscle contraction in skeletal muscles based on the person's decision to make a movement
11. The cranial nerves:
    A. Carry sensory information
    B. Carry motor information
    C. Are part of the somatic nervous system
    D. All of the above
12. *True or False.* All of the spinal nerves carry both sensory and motor information.
13. *True or False.* The sympathetic nervous system enhances digestion to provide more energy for the body.

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9.7: HUMAN SENSES

SEEING IS BELIEVING

Figure **9.7.1** appears at first glance to be just a pattern of colored leaves, but hidden within it is the three-dimensional shape of an ant. Can you see the ant among the leaves? This figure is an example of a stereogram, which is a two-dimensional picture that reveals a three-dimensional object when viewed correctly. If you can't see the hidden image, it doesn't mean that there is anything wrong with your eyes. It's all in how your brain interprets what your eyes are sensing. The eyes are special sensory organs, and vision is one of our special senses.

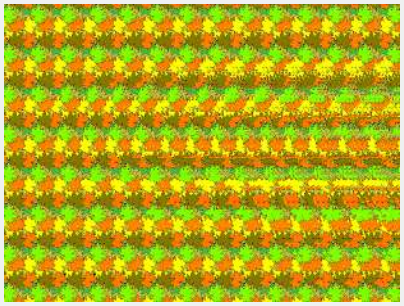


Figure **9.7.1**: Stereogram

SPECIAL AND GENERAL SENSES

The human body has two basic types of senses, called special senses and general senses. **Special senses** have specialized sense organs that gather sensory information and change it into nerve impulses. Special senses include the vision for which the eyes are the specialized sense organs, hearing (ears), balance (ears), taste (tongue), and smell (nasal passages). **General senses,** in contrast, are all associated with the sense of touch and lack special sense organs. Instead, sensory information about touch is gathered by the skin and other body tissues, all of which have important functions besides gathering sensory information. Whether the senses are special or general, however, all of them depend on cells called sensory receptors.

SENSORY RECEPTORS

A **sensory receptor** is a specialized nerve cell that responds to a stimulus in the internal or external environment by generating a nerve impulse. The nerve impulse then travels along with the sensory (afferent) nerve to the central nervous system for processing and to form a response.

There are several different types of sensory receptors that respond to different kinds of stimuli:

- **Mechanoreceptors** respond to mechanical forces such as pressure, roughness, vibration, and stretching. Most mechanoreceptors are found in the skin and are needed for the sense of touch. Mechanoreceptors are also found in the inner ear where they are needed for the senses of hearing and balance.
- **Thermoreceptors** respond to variations in temperature. They are found mostly in the skin and detect temperatures that are above or below body temperature.
- **Nociceptors** respond to potentially damaging stimuli, which are generally perceived as pain. They are found in internal organs as well as on the surface of the body. Different nociceptors are activated depending on the particular stimulus. For example, some detect damaging heat or cold, others detect excessive pressure, and still, others detect painful chemicals such as very hot spices in food.
- **Photoreceptors** detect and respond to light. Most photoreceptors are found in the eyes and are needed for the sense of vision.
- **Chemoreceptors** respond to certain chemicals. They are found mainly in taste buds on the tongue, where they are needed for the sense of taste; and in nasal passages, where they are needed for the sense of smell.

TOUCH

Touch is the ability to sense pressure, vibration, temperature, pain, and other tactile stimuli. These types of stimuli are detected by mechanoreceptors, thermoreceptors, and nociceptors all over the body, but most noticeably in the skin. These receptors are especially concentrated on the tongue, lips, face, palms of the hands, and soles of the feet. Various types of tactile receptors in the skin are shown in Figure **9.7.2**.

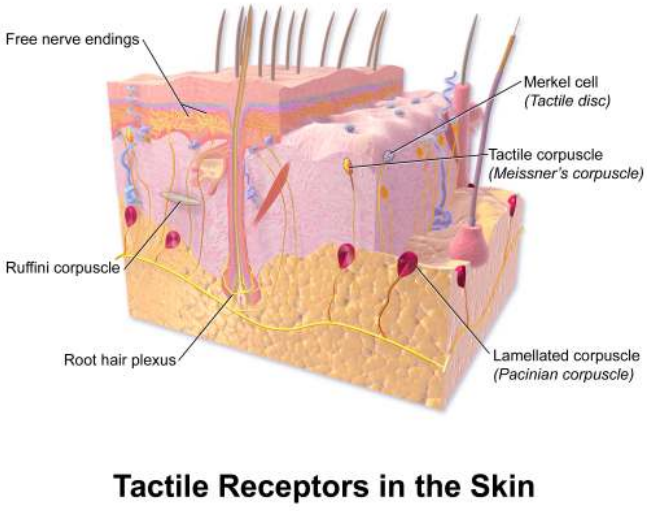


Figure **9.7.2**: Tactile receptors in the skin include free nerve endings, Merkel cells, Meissner's corpuscles, Pacinian corpuscles, root hair plexuses, and Ruffini corpuscles. Each type of sensory receptor responds to a different kind of tactile stimulus. For example, free nerve endings generally respond to pain and temperature variations, whereas Merkel cells are associated with the sense of light touch and the discrimination of shapes and textures.

VISION

Vision, or sight, is the ability to sense light and see. The **eye** is the special sensory organ that collects and focuses light and forms images. However, the eye is not sufficient for us to see. The brain also plays a necessary role in vision.

HOW THE EYE WORKS

Figure **9.7.3** shows the anatomy of the human eye in cross-section. The eye gathers and focuses light to form an image and then changes the image to nerve impulses that travel to the brain. How the eye performs these functions is summarized in the following steps.

1. Light passes first through the cornea, which is a clear outer layer that protects the eye and helps to focus the light by refracting, or bending, it.
2. Light next enters the interior of the eye through an opening called the pupil. The size of this opening is controlled by the colored part of the eye, called the iris, which adjusts the size based on the brightness of the light. The iris causes the pupil to narrow in bright light and widen in dim light.
3. The light then passes through the lens, which refracts the light even more and focuses it on the retina at the back of the eye as an inverted image.
4. The **retina** contains photoreceptor cells of two types, called rods and cones. Rods, which are found mainly in all areas of the retina other than the very center, are particularly sensitive to low levels of light. Cones, which are found mainly in the center of the retina, are sensitive to light of different colors and allow color vision. The rods and cones convert the light that strikes them to nerve impulses.
5. The nerve impulses from the rods and cones travel to the optic nerve via the optic disc, which is a circular area at the back of the eye where the optic nerve connects to the retina.

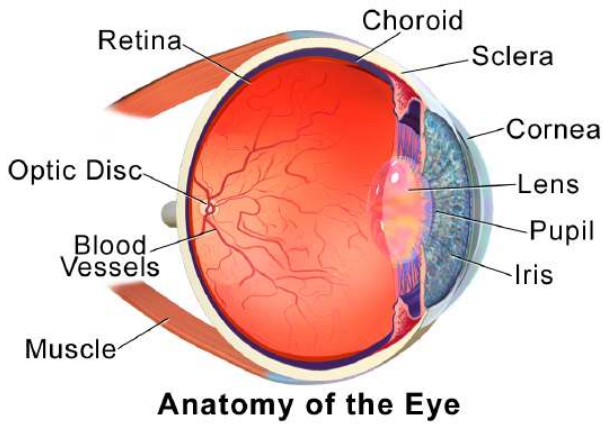


Figure **9.7.3**: In this image, you can see the three layers of the eyeball, the sclera (cornea at the front), choroid, and retina. Lens, pupil, Irish, optic disc, option nerve (not labeled), blood vessels, and eye muscles are also visible. Trace the path of light through the eye as you read about in the five steps described in the text

ROLE OF THE BRAIN IN VISION

The optic nerves from both eyes meet and cross just below the bottom of the hypothalamus in the brain. The information from both eyes is sent to the visual cortex in the occipital lobe of the cerebrum, which is part of the cerebral cortex. The visual cortex is the largest system in the human brain and is responsible for processing visual images. It interprets messages from both eyes and "tells" us what we are seeing.

VISION PROBLEMS

Vision problems are very common. Two of the most common are myopia and hyperopia, and they often start in childhood or adolescence. Another common problem, called presbyopia, occurs in most people beginning in middle adulthood. All three problems result in blurred vision due to the failure of the eyes to focus images correctly on the retina.

MYOPIA

Myopia, or nearsightedness, occurs when the light that comes into the eye does not directly focus on the retina but in front of it, as shown in Figure **9.7.4**. This causes the image of distant objects to be out of focus but does not affect the focus of close objects. Myopia may occur because the eyeball is elongated from front to back or because the cornea is too curved. Myopia can be corrected through the use of corrective lenses, either eyeglasses or contact lenses. Myopia can also be corrected by refractive surgery performed with a laser.

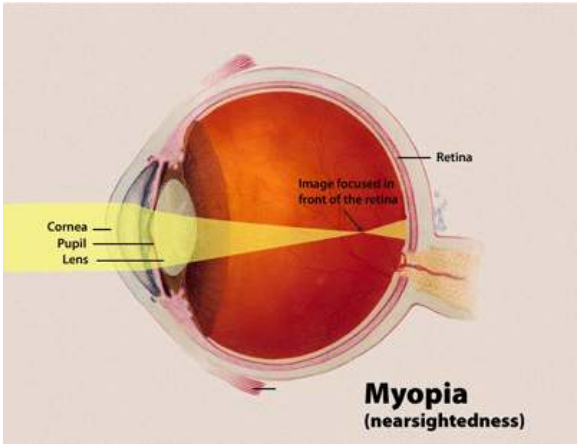


Figure **9.7.4**: In myopia, the focal point of images is in front of the retina because the eyeball is elongated.

HYPEROPIA

Hyperopia, or farsightedness, occurs when the light that comes into the eye does not directly focus on the retina but behind it, as shown in Figure **9.7.5**. This causes the image of close objects to be out of focus but does not affect the focus of distant objects. Hyperopia may occur because the eyeball is too short from front to back or because the lens is not curved enough. Hyperopia can be corrected through the use of corrective lenses or laser surgery.

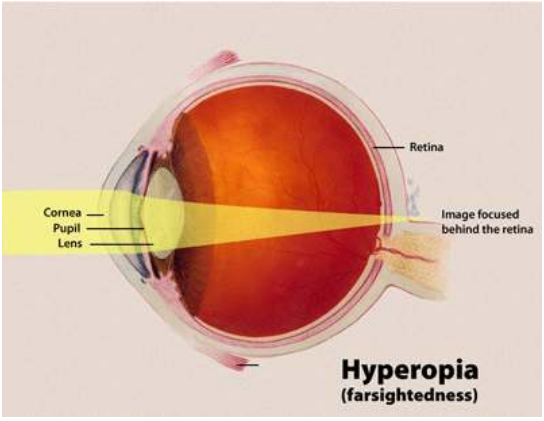


Figure **9.7.5**: In hyperopia, the focal point of images is behind the retina because the eyeball is too short.

PRESBYOPIA

Presbyopia is a vision problem associated with aging in which the eye gradually loses its ability to focus on close objects. The precise cause of presbyopia is not known for certain, but evidence suggests that the lens may become less elastic with age, and the muscles that control the lens may lose power as people grow older. The first signs of presbyopia – eyestrain, difficulty seeing in dim light, problems focusing on small objects, and fine print – are usually first noticed between the ages of 40 and 50. Most older people with this problem use corrective lenses to focus on close objects because surgical procedures to correct presbyopia have not been as successful as those for myopia and hyperopia.

HEARING

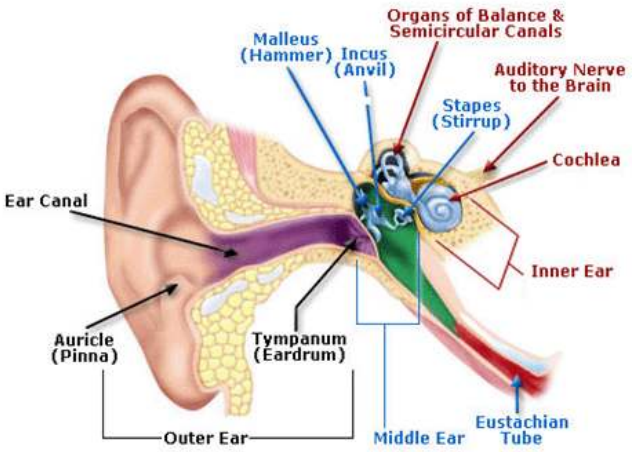


Figure **9.7.6**: The image shows structures of the outer, middle and inner ear. The outer ear has an auricle and an ear canal in it. The eardrum is in the middle of the outer and middle ear. The middle ear contains a hammer, anvil, and stirrup, and the inner ear has a cochlea, vestibule (not labeled), semicircular canal, and Eustachian tube. Most of the structures of the ear are involved in hearing. Only the semicircular canals are not involved in hearing. Instead, they sense head position, which is used to monitor balance.

Hearing is the ability to sense sound waves, and the ear is the organ that senses sound. Sound waves enter the ear through the ear canal and travel to the eardrum (see the diagram of the ear in Figure **9.7.6**). The sound waves strike the eardrum and make it vibrate. The vibrations then travel through the three tiny bones (hammer, anvil, and stirrup) of the middle ear, which amplify the vibrations. From the middle ear, the vibrations pass to the cochlea in the inner ear. The cochlea is a coiled tube filled with liquid. The liquid moves in response to the vibrations, causing tiny hair cells (which are mechanoreceptors) lining the cochlea to bend. In response, the hair cells send nerve impulses to the auditory nerve, which carries the impulses to the brain. The brain interprets the impulses and "tells" us what we are hearing.

TASTE AND SMELL

Taste and smell are both abilities to sense chemicals, so taste and olfactory (odor) receptors are chemoreceptors. Both types of chemoreceptors send nerve impulses to the brain along sensory nerves, and the brain "tells" us what we are tasting or smelling.

Taste receptors are found in tiny bumps on the tongue called **taste buds.** You can see a diagram of a taste receptor cell and related structures in Figure **9.7.7**. Taste receptor cells make contact with chemicals in food through tiny openings called taste pores. When certain chemicals bind with taste receptor cells, it generates nerve impulses that travel through afferent nerves to the CNS. There are separate taste receptors for sweet, salty, sour, bitter, and meaty tastes. The meaty or savory taste is called umami.

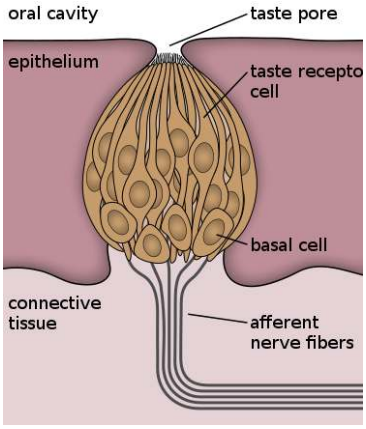


Figure **9.7.7**.Taste receptor cells are in taste buds on the tongue. Taste pore exposes these cells into the oral cavity. Basal cells are not involved in tasting but differentiate into taste receptor cells.

Olfactory receptors line the passages inside the nasal passages (Figure **9.7.8**). There are millions of olfactory receptors, which sense chemicals in the air. Unlike taste receptors, which can sense only five different tastes, olfactory receptors can sense hundreds of different odors and send signals to the olfactory bulb of the brain. Did you ever notice that food seems to have less taste when you have a stuffy nose? This occurs because the sense of smell contributes to the sense of taste, and a stuffy nose interferes with the ability to smell.

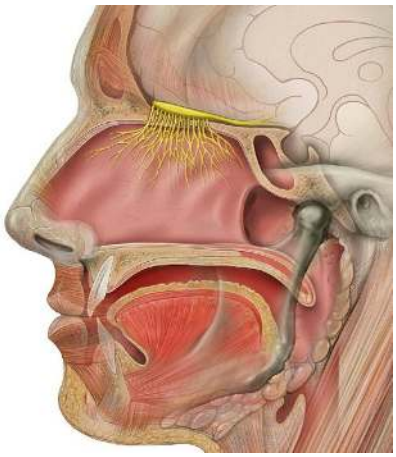


Figure 9.7.8: The yellow structures inside this drawing of the nasal passages are an olfactory nerve with many nerve endings. The nerve endings are located at the roof of the nasal cavity. The nerve endings sense chemicals in the air as it passes through the nasal cavities.

FEATURE: HUMAN BIOLOGY IN THE NEWS

The most common cause of blindness in the Western hemisphere is **age-related macular degeneration (AMD).** About 15 million people in the United States have this type of blindness, and 30 million people are affected worldwide. At present, there is no cure for AMD. The disease occurs with the death of a layer of cells called retinal pigment epithelium, which normally provides nutrients and other support to the macula of the eye. The macula is an oval-shaped pigmented area near the center of the retina that is specialized for high visual acuity and has the retina's greatest concentration of cones. When the epithelial cells die and the macula is no longer supported or nourished, the macula also starts to die. Patients experience a black spot in the center of their vision, and as the disease progresses, the black spot grows outward. Patients eventually lose the ability to read and even to recognize familiar faces before developing total blindness.

In 2016, a landmark surgery was performed as a trial on a patient with severe AMD. In the first-ever operation of its kind, Dr. Pete Coffey of the University of London implanted a tiny patch of cells behind the retina in each of the patient's eyes. The cells were retinal pigmented epithelial cells that had been grown in a lab from **stem cells,** which are undifferentiated cells that have the ability to develop into other cell types. By six months out from the operation, the new cells were still surviving, and the doctor was hopeful that the patient's vision loss would stop and even be reversed. At that point, several other operations had already been planned to test the new procedure. If these cases are a success, Dr. Coffey predicts that the surgery will become as routine as cataract surgery and prevent millions of patients from losing their vision.

REVIEW

1. Compare and contrast special senses and general senses.
2. What are sensory receptors?
3. List five types of sensory receptors and the type of stimulus each detects.
4. Describe the range of tactile stimuli that are detected in the sense of touch.
5. Explain how the eye collects and focuses light to form an image and converts it to nerve impulses.
6. Identify two common vision problems, including both their causes and their effects on vision.
7. Explain how the structures of the ear collect and amplify sound waves and transform them into nerve impulses.
8. What role does the ear play in balance? Which structures of the ear are involved in balance?
9. Describe two ways that the body senses chemicals and the special sense organs that are involved in these senses.
10. Explain why your skin can detect different types of stimuli, such as pressure and temperature.
11. *Choose one.* Sensory information is sent to the central nervous system via (efferent/afferent) nerves.
12. Identify a mechanoreceptor used in two different human senses, and describe the type of mechanical stimuli that each one detects.
13. If a person is blind but their retina is functioning properly, where do you think the damage might be? Explain your answer.
14. When you see colors, what receptor cells are activated? Where are these receptors located? What lobe of the brain is primarily used to process visual information?
15. The auditory nerve carries:

    A. Smell information
    B. Taste information
    C. Balance information
    D. Sound information

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9.8: PSYCHOACTIVE DRUGS

ART IN A CUP

Who knew that a cup of coffee could also be a work of art? A talented barista can make coffee look as good as it tastes. If you are a coffee drinker, you probably know that coffee can also affect your mental state. It can make you more alert and may improve your concentration. That's because the caffeine in coffee is a psychoactive drug. In fact, caffeine is the most widely consumed psychoactive substance in the world. In North America, for example, 90 percent of adults consume caffeine daily.



Figure **9.8.1**: Murano Coffee with decoration on the surface.

Psychoactive drugs are substances that change the function of the brain and result in alterations of mood, thinking, perception, and/or behavior. Psychoactive drugs may be used for many purposes, including therapeutic, ritual, or recreational purposes. Besides caffeine, other examples of psychoactive drugs include cocaine, LSD, alcohol, tobacco, codeine, and morphine. Psychoactive drugs may be legal prescription medications (e.g., codeine and morphine), legal nonprescription drugs (e.g., alcohol and tobacco), or illegal drugs (cocaine and LSD).



Figure **9.8.2**: Advertising for legal psychoactive drugs is ubiquitous.

Cannabis (or marijuana) is also a psychoactive drug, but its status is in flux, at least in the United States. Depending on the jurisdiction, cannabis may be used recreationally and/or medically, and it may be either legal or illegal. Legal prescription medications such as opioids are also used illegally by increasingly large numbers of people. Some legal drugs, such as alcohol and nicotine, are readily available almost everywhere, as illustrated by the sign pictured in Figure **9.8.2**.

CLASSES OF PSYCHOACTIVE DRUGS

Psychoactive drugs are divided into different classes according to their pharmacological effects. Several classes are listed below, along with examples of commonly used drugs in each class.

- Stimulants are drugs that stimulate the brain and increase alertness and wakefulness. Examples of stimulants include caffeine, nicotine, cocaine, and amphetamines such as Adderall.
- Depressants are drugs that calm the brain, reduce anxious feelings, and induce sleepiness. Examples of depressants include ethanol (in alcoholic beverages) and opioids such as codeine and heroin.
- Anxiolytics are drugs that have a tranquilizing effect and inhibit anxiety. Examples of anxiolytic drugs include benzodiazepines such as diazepam (Valium), barbiturates such as phenobarbital, opioids, and antidepressant drugs such as sertraline (Zoloft).
- Euphoriants are drugs that bring about a state of euphoria, or intense feelings of well-being and happiness. Examples of euphoriants include the so-called club drug MDMA (ecstasy), amphetamines, ethanol, and opioids such as morphine.
- Hallucinogens are drugs that can cause hallucinations and other perceptual anomalies. They also cause subjective changes in thoughts, emotions, and consciousness. Examples of hallucinogens include LSD, mescaline, nitrous oxide, and psilocybin.
- Empathogens are drugs that produce feelings of empathy, or sympathy with other people. Examples of empathogens include amphetamines and MDMA.



Figure **9.8.3**: Ecstasy (MDMA) is most commonly taken in tablet form, like the colorful and decorated tablets shown here.

Many psychoactive drugs have multiple effects so they may be placed in more than one class. An example is MDMA, pictured below, which may act both as a euphoriant and as an empathogen. In some people, MDMA may also have stimulant or hallucinogenic effects. As of 2016, MDMA had no accepted medical uses, but it was undergoing testing for use in the treatment of post-traumatic stress disorder and certain other types of anxiety disorders.

MECHANISMS OF ACTION

Psychoactive drugs generally produce their effects by affecting brain chemistry, which in turn may cause changes in a person's mood,

thinking, perception, and/or behavior. Each drug tends to have a specific action on one or more neurotransmitters or neurotransmitter receptors in the brain. Generally, they act as either agonists or antagonists.

- **Agonists** are drugs that increase the activity of particular neurotransmitters. They might act by promoting the synthesis of the neurotransmitters, reducing their reuptake from synapses, or mimicking their action by binding to receptors for the neurotransmitters.
- **Antagonists** are drugs that decrease the activity of particular neurotransmitters. They might act by interfering with the synthesis of the neurotransmitters or by blocking their receptors so the neurotransmitters cannot bind to them.

Consider the example of the neurotransmitter GABA. This is one of the most common neurotransmitters in the brain, and it normally has an inhibitory effect on cells. GABA agonists, which increase its activity, include ethanol, barbiturates, and benzodiazepines, among other psychoactive drugs. All of these drugs work by promoting the activity of GABA receptors in the brain.

USES OF PSYCHOACTIVE DRUGS

You may have been prescribed psychoactive drugs by your doctor. For example, you may have been prescribed an opioid drug such as codeine for pain (most likely in the form of Tylenol with added codeine). Chances are you also use nonprescription psychoactive drugs, such as caffeine for mental alertness. These are just two of the many possible uses of psychoactive drugs.

MEDICAL USES



Figure **9.8.4**: This child is being prepared to receive a general anesthetic prior to surgery

Medical uses of psychoactive drugs include general anesthesia, in which pain is blocked and unconsciousness is induced. General anesthetics are most often used during surgical procedures and may be administered in gaseous form, as in the photo below. General anesthetics include the drugs halothane and ketamine. Other psychoactive drugs are used to manage pain without affecting consciousness. They may be prescribed either for acute pain in cases of trauma such as broken bones; or for chronic pain such as pain caused by arthritis, cancer, or fibromyalgia. Most often, the drugs used for pain control are opioids, such as morphine and codeine.

Many psychiatric disorders are also managed with psychoactive drugs. For example, antidepressants such as sertraline are used to treat depression, anxiety, and eating disorders. Anxiety disorders may also be treated with anxiolytics, such as buspirone and diazepam. Stimulants such as amphetamines are used to treat attention deficit disorder. Antipsychotics such as clozapine and risperidone, as well as mood stabilizers such as lithium, are used to treat schizophrenia and bipolar disorder.

RITUAL USES

Certain psychoactive drugs, particularly hallucinogens, have been used for ritual purposes since prehistoric times. For example, Native Americans have used the mescaline-containing peyote cactus (pictured below) for religious ceremonies for as long as 5,700 years. In prehistoric Europe, the mushroom *Amanita muscaria*, which contains a hallucinogenic drug called muscimol, was used for similar purposes. Various other psychoactive drugs — including jimsonweed, psilocybin mushrooms, and cannabis — have also been used by various peoples for ritual purposes for millennia.



Figure **9.8.5**: The peyote cactus contains a hallucinogenic drug that is still used by some Native Americans for religious rituals.

RECREATIONAL USES

The recreational use of psychoactive drugs generally has the purpose of altering one's consciousness and creating a feeling of euphoria commonly called a "high." Some of the drugs used most commonly for recreational purposes include cannabis, ethanol, opioids, and stimulants such as nicotine. Hallucinogens are also used recreationally, primarily for the alterations in thinking and perception that they cause.

Some investigators have suggested that the urge to alter one's state of consciousness is a universal human drive, similar to the drive to satiate thirst, hunger, or sexual desire. They think that the drive to alter one's state of mind is even present in children, who may attain an altered state by repetitive motions such as spinning or swinging. Some nonhuman animals also exhibit a drive to experience altered states. For example, they may consume fermented berries or fruit and become intoxicated. The way cats respond to catnip (Figure **9.8.6**) is another example.



Figure **9.8.6**: This cat is holding a catnip toy and apparently enjoying its psychoactive effects.

ADDICTION, DEPENDENCE, AND REHABILITATION

Psychoactive substances often bring about subjective changes that the user may find pleasant (for example, euphoria) or advantageous (for example, increased alertness). These changes are rewarding and positively reinforcing, so they have the potential for misuse, addiction, and dependence. **Addiction** refers to the compulsive use of a drug despite the negative consequences that such use may entail. Sustained use of an addictive drug may produce dependence on the drug. **Dependence** may be physical and/or psychological. It occurs when cessation of drug use produces withdrawal symptoms. Physical dependence produces physical withdrawal symptoms, which may include tremors, pain, seizures, or insomnia. Psychological dependence produces psychological withdrawal symptoms, such as anxiety, depression, paranoia, or hallucinations.

Rehabilitation for drug dependence and addiction typically involves psychotherapy, which may include both individual and group therapy. Organizations such as Alcoholics Anonymous (AA) and Narcotics Anonymous (NA) may also be helpful for people trying to recover from addiction. These groups are self-described as international mutual aid fellowships with the primary purpose of helping addicts achieve and maintain sobriety. In some cases, rehabilitation is aided by the temporary use of psychoactive substances that reduce cravings and withdrawal symptoms without creating addiction themselves. For example, the drug methadone is commonly used in the treatment of heroin addiction.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Currently, in the United States, a lot of media attention is being given to a rising tide of opioid addiction and overdose deaths. **Opioids** are drugs derived from the opium poppy or synthetic versions of such drugs. They include illegal drug heroin and prescription painkillers such as codeine, morphine, hydrocodone, oxycodone, and fentanyl. In 2016, fentanyl received wide media attention when it was announced that an accidental fentanyl overdose was responsible for the death of rock-music icon Prince. Fentanyl is an extremely strong and dangerous drug, said to be 50 to 100 times stronger than morphine, making the risk of overdose death from fentanyl very high.

The dramatic increase in opioid addiction and overdose deaths has been called an opioid epidemic. It is considered to be the worst drug crisis in American history. Consider the following facts:

- In 1999, there were more than twice as many accidental deaths from motor vehicle crashes than from drug overdoses. By 2014, these causes of accidental death were reversed, with close to 40 percent more accidental deaths from drug overdoses than car crashes. The majority of these drug overdose deaths were from heroin and opioid painkillers.
- In 1999, the stimulant drug cocaine killed about twice as many people as did heroin. By 2014, deaths from heroin were up by 439 percent. During the same interval, deaths from cocaine also rose slightly but were a much smaller proportion of all drug deaths than those caused by heroin.

The opioid epidemic in the United States has occurred in all demographic groups, including every ethnic, age, gender, and socioeconomic category. What has caused this epidemic? The answer appears to be an equally dramatic increase in the medical use of prescription painkillers. In 1991, about 76 million prescriptions were written for painkillers. In 2011, the number of prescriptions for these drugs had risen to 219 million, an almost three-fold increase. During these same two decades, Mexican drug cartels began shipping huge amounts of heroin to the United States. Heroin became cheaper and easier to buy than prescription painkillers. Many people who became addicted to prescription opioids switched to heroin. About 80 percent of new heroin users in 2014 reported started out misusing prescription painkillers.

Doctors, public health professionals, and politicians have all called for new policies, funding, programs, and laws to address the opioid epidemic. Changes that have already been made include a shift from criminalizing to medicalizing the problem, an increase in treatment programs, and more widespread distribution and use of the opioid-overdose antidote naloxone (Narcan). Opioids can slow or stop a person's breathing, which is what usually causes overdose deaths. Naloxone helps the person wake up and keeps them breathing until emergency medical treatment can be provided.

REVIEW

1. What are psychoactive drugs?
2. Identify six classes of psychoactive drugs and an example of a drug in each class.
3. Compare and contrast psychoactive drugs that are agonists and psychoactive drugs that are antagonists.
4. Describe two medical uses of psychoactive drugs.
5. Give an example of a ritual use of a psychoactive drug.
6. Why do people generally use psychoactive drugs recreationally?

7. Define addiction.
8. Identify possible withdrawal symptoms associated with physical dependence on a psychoactive drug.
9. Why might a person with a heroin addiction be prescribed the psychoactive drug methadone?
10. The prescription drug Prozac inhibits the reuptake of the neurotransmitter serotonin, causing more serotonin to be present in the synapse. Prozac can elevate mood, which is why it is sometimes used to treat depression. Answer the following questions about Prozac.
    A. Is Prozac an agonist or an antagonist for serotonin? Explain your answer.
    B. Is Prozac a psychoactive drug? Explain your answer.
11. Name 3 classes of psychoactive drugs that include opioids.
12. *True or False.* All psychoactive drugs are either illegal or available by prescription only.
13. *True or False.* Anxiolytics might be prescribed by a physician.
14. Name two drugs that activate receptors for the neurotransmitter GABA. Why do you think these drugs generally have a depressant effect?

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9.9: CASE STUDY CONCLUSION- MEMORY AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: FADING MEMORY

Figure 9.9.1 illustrates some of the molecular and cellular changes that occur in **Alzheimer's disease** (AD), which Rosa was diagnosed with at the beginning of this chapter, after experiencing memory problems and other changes in her cognitive functioning, mood, and personality. These abnormal changes in the brain include the development of amyloid plaques between brain cells and neurofibrillary tangles inside of neurons. These hallmark characteristics of AD are associated with the loss of synapses between neurons, and ultimately the death of neurons.

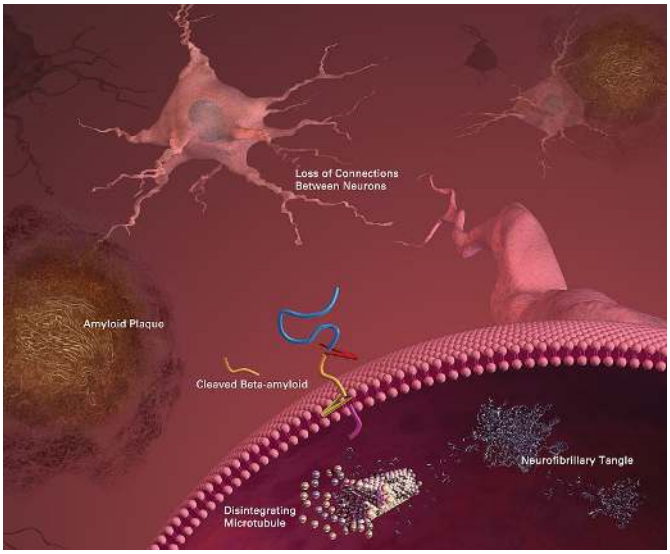


Figure 9.9.1: Characteristics of Alzheimer's disease. On a microscopic level, some of the changes that happen are depicted above. For example, the neurons lose connections, plaque accumulates, microtubes disintegrate, and much more.

After reading this chapter, you should have a good appreciation for the importance of keeping neurons alive and communicating with each other at synapses. The nervous system coordinates all of the body's voluntary and involuntary activities. It interprets information from the outside world through sensory systems and makes appropriate responses through the motor system, through communication between the PNS and CNS. The brain directs the rest of the nervous system and controls everything from basic vital functions such as heart rate and breathing to high-level functions such as problem-solving and abstract thought. The nervous system is able to perform these important functions by generating action potentials in neurons in response to stimulation and sending messages between cells at synapses, typically using chemical neurotransmitter molecules. When neurons are not functioning properly, lose their synapses, or die, they cannot carry out the signaling that is essential for the proper functioning of the nervous system.

AD is a progressive neurodegenerative disease, meaning that the damage to the brain becomes more extensive as time goes on. Figure 9.9.2 illustrates how the damage progresses from before AD is diagnosed (preclinical AD), to mild and moderate AD, and finally to severe AD.

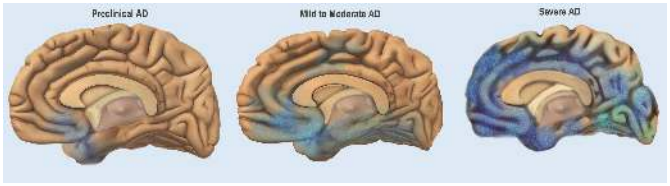


Figure 9.9.2: Illustration showing the areas of the brain that become damaged as Alzheimer's disease (AD) progresses. This is a side view along the middle of the brain, with the front of the brain shown to the left. Damaged are (blue shade) is widespread in severe AD.

You can see that the damage starts in a relatively small location towards the bottom of the brain. One of the earliest brain areas to be affected by AD is the hippocampus. The hippocampus is important for learning and memory. This explains why many of Rosa's symptoms of mild AD involve deficits in memory, such as trouble remembering where she placed objects, recent conversations, and appointments.

As AD progresses, more of the brain is affected, including areas involved in emotional regulation, social behavior, planning, language, spatial navigation, and higher-level thought. Rosa is beginning to show signs of problems in these areas, including irritability, lashing out at family members, getting lost in her neighborhood, problems finding the right words, putting objects in unusual locations, and difficulty in managing her finances. You can see that as AD progresses, damage spreads further across the cerebrum, which you now know controls conscious functions such as reasoning, language, and interpretation of sensory stimuli. You can also see how the frontal lobe, which controls executive functions such as planning, self-control, and abstract thought, becomes increasingly damaged.

Increasing damage to the brain causes corresponding deficits in functioning. In moderate AD, patients have increased memory, language, and cognitive deficits compared to mild AD. They may not recognize their own family members, and may wander and get lost, engage in inappropriate behaviors, become easily agitated, and have trouble carrying out daily activities such as dressing. In severe AD, much of the brain is affected. Patients usually cannot recognize family members or communicate and are fully dependent on others for their care. They begin to lose the ability to control their basic functions, such as bladder and bowel control and proper swallowing. Eventually, AD causes death, usually as a result of this loss of basic functions.

For now, Rosa only has mild AD is still able to function relatively well with care from her family. The medication her doctor gave her has helped improve some of her symptoms. It is a cholinesterase inhibitor, which blocks an enzyme that normally degrades the neurotransmitter acetylcholine. With more of the neurotransmitter available, more of it can bind to neurotransmitter receptors on postsynaptic cells. Therefore, this drug acts as an agonist for

acetylcholine, which enhances communication between neurons in Rosa's brain. This increase in neuronal communication can help restore some of the functions lost in early Alzheimer's disease and may slow the progression of symptoms.

But medication such as this is only a short-term measure and does not halt the progression of the underlying disease. Ideally, the damaged or dead neurons would be replaced by new, functioning neurons. Why does this not happen automatically in the body? As you have learned, neurogenesis is very limited in adult humans, so once neurons in the brain die, they are not normally replaced to any significant extent. However, scientists are studying the ways in which neurogenesis might be able to be increased in cases of disease or injury to the brain. Also, they are investigating the possibility of using stem cell transplants to replace damaged or dead neurons with new neurons. But this research is in very early stages and is not currently a treatment for AD.

One promising area of research is in the development of methods to allow earlier detection and treatment of AD, given that the changes in the brain may actually start 10 to 20 years before the diagnosis of AD. For example, a radiolabeled chemical called Pittsburgh Compound B (PiB) binds to amyloid plaques in the brain and in the future may be used in conjunction with brain imaging techniques to detect early signs of AD. Scientists are also looking for biomarkers in bodily fluids such as blood and cerebrospinal fluid that might indicate the presence of AD before symptoms appear. Finally, researchers are also investigating possible early and subtle symptoms, such as changes in how people move or a loss of smell, to see whether they can be used to identify people who will go on to develop AD. This research is in the early stages, but the hope is that patients can be identified earlier to provide earlier and possibly more effective treatment and to allow families more time to plan.

Scientists are also still trying to fully understand the causes of AD, which affects more than 5 million Americans. Some genetic mutations have been identified that play a role, but environmental factors also appear to be important. With more research into the causes and mechanisms of AD, hopefully, a cure can be found, and people like Rosa can live a longer and better life.

CHAPTER SUMMARY

In this chapter, you learned about the human nervous system. Specifically, you learned that:

- The nervous system is the organ system that coordinates all of the body's voluntary and involuntary actions by transmitting signals to and from different parts of the body. It has two major divisions, the central nervous system (CNS) and the peripheral nervous system (PNS).
- The CNS includes the brain and spinal cord.
- The PNS consists mainly of nerves that connect the CNS with the rest of the body. It has two major divisions: the somatic nervous system and the autonomic nervous system. The somatic system controls activities that are under voluntary control. The autonomic system controls activities that are involuntary.
- The autonomic nervous system is further divided into the sympathetic division, which controls the fight-or-flight response; the parasympathetic division, which controls most routine involuntary responses; and the enteric division, which provides local control for digestive processes.
- Signals sent by the nervous system are electrical signals called nerve impulses. They are transmitted by special, electrically excitable cells called neurons, which are one of two major types of cells in the nervous system.
- Glial cells are the other major type of nervous system cells. There are many types of glial cells, and they have many specific functions. In general, glial cells function to support, protect, and nourish neurons.
- The main parts of a neuron include the cell body, dendrites, and axon. The cell body contains the nucleus. Dendrites receive nerve impulses from other cells, and the axon transmits nerve impulses to other cells at axon terminals. A synapse is a complex membrane junction at the end of an axon terminal that transmits signals to another cell.
- Axons are often wrapped in an electrically-insulating myelin sheath, which is produced by glial cells. Electrical impulses called action potentials occur at gaps in the myelin sheath, called nodes of Ranvier, which speeds the conduction of nerve impulses down the axon.
- Neurogenesis, or the formation of new neurons by cell division, may occur in a mature human brain but only to a limited extent.
- The nervous tissue in the brain and spinal cord consists of gray matter, which contains mainly the cell bodies of neurons; and white matter, which contains mainly myelinated axons of neurons. Nerves of the peripheral nervous system consist of long bundles of myelinated axons that extend throughout the body.
- There are hundreds of types of neurons in the human nervous system, but many can be classified on the basis of the direction in which they carry nerve impulses. Sensory neurons carry nerve impulses away from the body and toward the central nervous system, motor neurons carry them away from the central nervous system and toward the body, and interneurons often carry them between sensory and motor neurons.
- A nerve impulse is an electrical phenomenon that occurs because of a difference in electrical charge across the plasma membrane of a neuron.
- The sodium-potassium pump maintains an electrical gradient across the plasma membrane of a neuron when it is not actively transmitting a nerve impulse. This gradient is called the resting potential of the neuron.
- An action potential is a sudden reversal of the electrical gradient across the plasma membrane of a resting neuron. It begins when the neuron receives a chemical signal from another cell or some other type of stimulus. The action potential travels rapidly down the neuron's axon as an electric current.
- A nerve impulse is transmitted to another cell at either an electrical or a chemical synapse. At a chemical synapse, neurotransmitter chemicals are released from the presynaptic cell

into the synaptic cleft between cells. The chemicals travel across the cleft to the postsynaptic cell and bind to receptors embedded in its membrane.

- There are many different types of neurotransmitters. Their effects on the postsynaptic cell generally depend on the type of receptor they bind to. The effects may be excitatory, inhibitory, or modulatory in more complex ways. Both physical and mental disorders may occur if there are problems with neurotransmitters or their receptors.
- The CNS includes the brain and spinal cord. It is physically protected by bones, meninges, and cerebrospinal fluid. It is chemically protected by the blood-brain barrier.
- The brain is the control center of the nervous system and of the entire organism. The brain uses a relatively large proportion of the body's energy, primarily in the form of glucose.
- The brain is divided into three major parts, each with different functions: brain stem, cerebellum, and cerebrum. The cerebrum is further divided into left and right hemispheres. Each hemisphere has four lobes: frontal, parietal, temporal, and occipital. Each lobe is associated with specific senses or other functions.
- The cerebrum has a thin outer layer called the cerebral cortex. Its many folds give it a large surface area. This is where most information processing takes place.
- Inner structures of the brain include the hypothalamus, which controls the endocrine system via the pituitary gland; and the thalamus, which has several involuntary functions.
- The spinal cord is a tubular bundle of nervous tissues that extends from the head down the middle of the back to the pelvis. It functions mainly to connect the brain with the PNS. It also controls certain rapid responses called reflexes without input from the brain.
- A spinal cord injury may lead to paralysis (loss of sensation and movement) of the body below the level of the injury because nerve impulses can no longer travel up and down the spinal cord beyond that point.
- The PNS consists of all the nervous tissue that lies outside of the CNS. Its main function is to connect the CNS to the rest of the organism.
- The tissues that make up the PNS are nerves and ganglia. Ganglia act as relay points for messages that are transmitted through nerves. Nerves are classified as sensory, motor, or a mix of the two.
- The PNS is not as well protected physically or chemically as the CNS, so it is more prone to injury and disease. PNS problems include injury from diabetes, shingles, and heavy metal poisoning. Two disorders of the PNS are Guillain-Barre syndrome and Charcot-Marie-Tooth disease.
- The human body has two major types of senses, special senses, and general senses. Special senses have specialized sense organs and include vision (eyes), hearing (ears), balance (ears), taste (tongue), and smell (nasal passages). General senses are all associated with touch and lack special sense organs. Touch receptors are found throughout the body but particularly in the skin.
- All senses depend on sensory receptor cells to detect sensory stimuli and transform them into nerve impulses. Types of sensory receptors include mechanoreceptors (mechanical forces), thermoreceptors (temperature), nociceptors (pain), photoreceptors (light), and chemoreceptors (chemicals).
- Touch includes the ability to sense pressure, vibration, temperature, pain, and other tactile stimuli. The skin includes several different types of touch receptor cells.
- Vision is the ability to sense light and see. The eye is the special sensory organ that collects and focuses light, forms images, and changes them to nerve impulses. Optic nerves send information from the eyes to the brain, which processes the visual information and "tells" us what we are seeing.
- Common vision problems include myopia (nearsightedness), hyperopia (farsightedness), and presbyopia (age-related decline in close vision).
- Hearing is the ability to sense sound waves, and the ear is the organ that senses sound. It changes sound waves to vibrations that trigger nerve impulses, which travel to the brain through the auditory nerve. The brain processes the information and "tells" us what we are hearing.
- The ear is also the organ that is responsible for the sense of balance, which is the ability to sense and maintain an appropriate body position. The ears send impulses on head position to the brain, which sends messages to skeletal muscle via the peripheral nervous system. The muscles respond by contracting to maintain balance.
- Taste and smell are both abilities to sense chemicals. Taste receptors in taste buds on the tongue sense chemicals in food and olfactory receptors in the nasal passages sense chemicals in the air. The sense of smell contributes significantly to the sense of taste.
- Psychoactive drugs are substances that change the function of the brain and result in alterations of mood, thinking, perception, and/or behavior. They include prescription medications such as opioid painkillers, legal substances such as nicotine and alcohol, and illegal drugs such as LSD and heroin.
- Psychoactive drugs are divided into different classes according to their pharmacological effects. They include stimulants, depressants, anxiolytics, euphoriants, hallucinogens, and empathogens. Many psychoactive drugs have multiple effects so they may be placed in more than one class.
- Psychoactive drugs generally produce their effects by affecting brain chemistry. Generally, they act either as agonists, which enhance the activity of particular neurotransmitters; or as antagonists, which decrease the activity of particular neurotransmitters.
- Psychoactive drugs are used for various purposes, including medical, ritual, and recreational purposes.
- Misuse of psychoactive drugs may lead to addiction, which is the compulsive use of a drug despite negative consequences.

Sustained use of an addictive drug may produce physical or psychological dependence on the drug. Rehabilitation typically involves psychotherapy and sometimes the temporary use of other psychoactive drugs.

In addition to the nervous system, there is another system of the body that is important for coordinating and regulating many different functions – the endocrine system. You will learn about the endocrine system in the next chapter.

CHAPTER SUMMARY REVIEW

1. Imagine that you decide to make a movement. To carry out this decision, a neuron in the cerebral cortex of your brain (neuron A) fires a nerve impulse that is sent to a neuron in your spinal cord (neuron B). Neuron B then sends the signal to a muscle cell, causing it to contract, resulting in movement. Answer the following questions about this pathway.
   a. Which part of the brain is neuron A located in — the cerebellum, cerebrum, or brain stem? Explain how you know.
   b. The cell body of neuron A is located in a lobe of the brain that is involved in abstract thought, problem-solving and planning. Which lobe is this?
   c. Part of neuron A travels all the way down to the spinal cord to meet neuron B. Which part of neuron A travels to the spinal cord?
   d. Neuron A forms a chemical synapse with neuron B in the spinal cord. How is the signal from neuron A transmitted to neuron B?
   e. Is neuron A in the central nervous system (CNS) or peripheral nervous system (PNS)?
   f. The axon of neuron B travels in a nerve to a skeletal muscle cell. Is the nerve part of the CNS or PNS? Is this an afferent nerve or an efferent nerve?
   g. What part of the PNS is involved in this pathway — the autonomic nervous system or the somatic nervous system? Explain your answer.
2. What are the differences between a neurotransmitter receptor and a sensory receptor?
3. Which part of a postsynaptic neuron typically receives the signals from a presynaptic neuron?
   A. The axon terminal
   B. The nodes of Ranvier
   C. The dendrites
   D. The cell body
4. *True or False.* Glial cells produce action potentials.
5. *True or False.* The spinal cord consists of white matter only.
6. *True or False.* Axons may be more than a meter long in adult humans.
7. If a person has a stroke and as a result has trouble using language correctly, which hemisphere of their brain was most likely damaged? Explain your answer.
8. The right side of the brain generally controls the which side of the body?
   A. right side
   B. left side
   C. head region
   D. trunk and leg regions
9. Electrical gradients are responsible for the resting potential and action potential in neurons. Answer the following questions about the electrical characteristics of neurons.
   a. Define what an electrical gradient is, in the context of a cell.
   b. What is responsible for maintaining the electrical gradient that results in the resting potential?
   c. Compare and contrast the resting potential and the action potential.
   d. Where along a myelinated axon does the action potential occur? Why does it happen here?
10. What does it mean that the action potential is “all-or-none?”
11. What determines whether a neurotransmitter has an excitatory or inhibitory effect? Choose the best answer.
    A. The neurotransmitter itself
    B. The specific receptor for the neurotransmitter on the postsynaptic cell
    C. The number of synaptic vesicles in the axon terminal
    D. Whether it is in a sensory neuron or a motor neuron
12. Compare and contrast Schwann cells and oligodendrocytes.
13. *True or False.* The cerebellum makes up most of the brain and is divided into four lobes.
14. *True or False.* The hypothalamus is part of the brain.
15. Which lobe of the brain processes touch information?
    A. Parietal
    B. Occipital
    C. Cochlea
    D. Temporal
16. Information about sounds is mainly sent to which lobe of the brain?
    A. Parietal
    B. Occipital
    C. Cochlea
    D. Temporal
17. Rods and cones in the retina are:
    A. Mechanoreceptors
    B. Nociceptors
    C. Photoreceptors
    D. Chemoreceptors
18. For the senses of smell and hearing, name their respective sensory receptor cells, what type of receptor cells they are, and what stimuli they detect.
19. *True or False.* Sensory information such as smell, taste, and sound, are carried to the CNS by cranial nerves.
20. *True or False.* The parasympathetic nervous system is a division of the central nervous system.

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CHAPTER OVERVIEW

10: DNA AND PROTEIN SYNTHESIS

This chapter contains information on DNA discovery, the central dogma of biology, DNA replication, transcription, and how proteins are synthesized through the process of translation. Additionally, the chapter highlights gene regulation. This chapter also discusses the types of mutations and their causes. The other topics of this chapter include biotechnology and the Human Genome Project. In order to understand personalized medicine, we need to know what genes do, how they interact and learn all the differences in DNA between people. As you read this chapter, think about how an understanding of the human genome and genetics is essential for discovering how medicines may affect each of us individually.

10.1: Case Study- Why do we need to sequence everybody's genome?

10.2: DNA and RNA

10.3: Chromosomes and Genes

10.4: Protein Synthesis

10.5: Genetic Code

10.6: Mutations

10.7: Regulation of Gene Expression

10.8: Biotechnology

10.9: The Human Genome

10.10: Case Study Conclusion- Parmacogenomics and Chapter Summary

Thumbnail: DNA double helix. (public domain; NIH - Genome Research Institute).

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10.1: CASE STUDY- WHY DO WE NEED TO SEQUENCE EVERYBODY'S GENOME?

CASE STUDY: PHARMACOGENOMICS, A PERSONALIZED MEDICINE

Arya is 50-year-old and morbidly obese. Arya uses gender-neutral pronouns, such as they, them, and theirs. They have high blood pressure and cardiovascular disease. Recently, they lost 10 pounds of weight in a month without trying. They also get thirsty very easily and make frequent visits to the restroom. Their doctor diagnosed them with insulin-dependent type 2 diabetes after some physical and blood tests. Type 2 diabetes, also called diabetes mellitus, is a condition in which either the beta cells of a person's pancreas stop secreting insulin due to the high demand of insulin by an overweight person, or the body cells become insensitive to insulin. Insulin is a hormone that activates all the cells of the body to uptake glucose from the bloodstream. Cells need glucose to acquire energy (ATP) through cellular respiration to perform various metabolic activities. High levels of blood glucose in the absence of insulin may lead to high blood glucose and eventually may lead to the symptoms that Arya is experiencing.

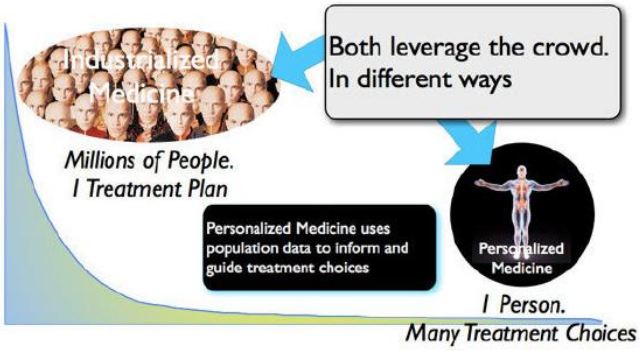


Figure **10.1.1**: Personalized Medicine is the long tail of Health Care. Usually, one treatment plan is prescribed to many individuals. However, one medicine does not work for all due to genetic variation. In personalized medicine, public data and genetic testing is used to prescribe custom treatment plan to an individual patient.

Arya's doctor prescribed gliclazide. Gliclazide belongs to the sulfonylurea category of drugs. Sulfonylureas stimulate the beta cells of the pancreas to secrete insulin. Arya started this treatment and experienced an adverse reaction after taking their second dose. They experienced feelings of hunger, sweating, shakiness, and weakness a few minutes after taking the medication. They called 911. When they recovered, they went back to their doctor. Their doctor told them that they had experienced hypoglycemia, which is one of the major side effects of sulfonylurea-based medicines. The doctor noted that due to the other complications that Arya has, such as cardiovascular disease, gliclazide was the best choice. The doctor explained that not everyone responds to medications in the same way. A drug that works well for one person may not be effective for another. The dose of a drug that cures a disease in one individual may be inadequate for someone else. Some people may experience side effects from a given medication, whereas other people do not. This variation in responses to medications can be due to differences in our genes. That's where the field of pharmacogenetics comes in. News media have hailed it as the "new frontier in medicine." It certainly seems to hold promise for improving the pharmaceutical treatment of patients.

Pharmacogenomics is based on a special kind of genetic testing. It looks for small genetic variations that influence a person's ability to activate and deactivate drugs. Results of the tests can help doctors choose the best drug and most effective dose for a given patient. Many drugs need to be activated by the patient's own enzymes, and inherited variations in enzymes may affect how quickly or efficiently this happens. For example, if a patient's enzymes break down a particular drug too slowly, then standard doses of the drug may not work very well for that patient. Drugs also must be deactivated to reduce their effects on healthy cells. If a patient's enzymes deactivate a drug too slowly, then the drug may remain at high levels and cause side effects. Arya experienced a high release of insulin due to the variations in their genotype.

The doctor recommended that Arya goes through genetic testing for a better treatment plan. One of the main benefits of pharmacogenomics is greater patient safety. Pharmacogenomic testing may help identify patients who are likely to experience adverse reactions to drugs so that different, safer drugs can be prescribed. Another benefit of pharmacogenomics is eliminating the trial-and-error approach that is often used to find appropriate medications and doses for a given patient. This saves time and money as well as improving patient outcomes. This is more like a personalized medicine as demonstrated in the picture above.

Because pharmacogenomics is a new field, some insurance companies do not cover it, and it can be very expensive. Also, not all of the genetic tests are yet widely available. In addition, there may be ethical and legal issues associated with genetic testing, including concerns about privacy issues. Because Arya is concerned, they have many questions for their doctor.

In order to understand personalized medicine, we need to know what genes do, how they interact, and learn all the differences in DNA between people. As you read this chapter, think about how an understanding of the human genome and genetics is essential for discovering how medicines may affect each of us individually.

AS YOU READ THIS CHAPTER, TRY TO ANSWER THE FOLLOWING QUESTIONS:

- What is a gene?
- Enzymes are proteins. How are enzymes synthesized?
- What is the relationship between an enzyme and DNA?
- Why do people differ genetically?
- How are the genes sequenced?

CHAPTER OVERVIEW: IN THIS CHAPTER, YOU WILL LEARN THE FOLLOWING:

- How genes, and their different alleles, are located on chromosomes.
- The 23 pairs of human chromosomes, which include autosomal and sex chromosomes.
- How DNA was discovered to be the inherited genetic material.
- The structure of DNA and how DNA replication occurs.
- The central dogma of molecular biology, which describes how DNA is transcribed into RNA, and then translated into proteins.
- The structure, functions, and possible evolutionary history of RNA.
- How genes code for proteins using codons made of the sequence of nitrogen bases within RNA and DNA.
- How proteins are synthesized through the transcription of RNA from DNA and the translation of protein from RNA, including how RNA and proteins can be modified, and the roles of the different types of RNA.
- What mutations are, what causes them, different specific types of mutations, and the importance of mutations in evolution and to human health.
- How the expression of genes into proteins is regulated and why problems in this process can cause diseases such as cancer.
- What is Biotechnology and how it is applied?
- What is Pharmacogenomics?

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10.2: DNA AND RNA

WHAT MAKES YOU...YOU?

This person has naturally red hair. Why is this hair red instead of some other color? And, in general, what causes specific traits to occur? There is a molecule in human beings and most other living things that is largely responsible for their traits. The molecule is large and has a spiral structure in eukaryotes. What molecule is it? With these hints, you probably know that the molecule is DNA.



Figure **10.2.1**: Red hair

INTRODUCING DNA

Today, it is commonly known that DNA is the genetic material that is passed from parents to offspring and determines our traits. For a long time, scientists knew such molecules existed, that is, they were aware that genetic information is contained within biochemical molecules. However, they didn't know which molecules play this role. In fact, for many decades, scientists thought that proteins were the molecules that contain genetic information.

DISCOVERY THAT DNA IS THE GENETIC MATERIAL

Determining that DNA is the genetic material was an important milestone in biology. It took many scientists undertaking creative experiments over several decades to show with certainty that DNA is the molecule that determines the traits of organisms. This research began in the early part of the 20th century.

GRIFFITH'S EXPERIMENTS WITH MICE

The first important discovery was made in the 1920s. An American scientist named Frederick Griffith was studying mice and two different strains of a bacterium called R (rough) strain and S (smooth) strain. He injected the two bacterial strains into mice. The S strain was virulent and killed the mice, whereas the R strain was not virulent and did not kill the mice. You can see these details in Figure **10.2.2**. Griffith also injected mice with S-strain bacteria that had been killed by heat. As expected, the dead bacteria did not harm the mice. However, when the dead S-strain bacteria were mixed with live R-strain bacteria and injected, the mice died.

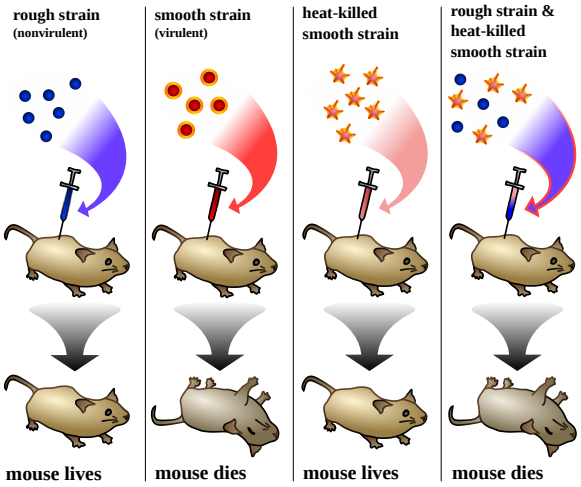


Figure **10.2.2**: Griffith's experiment discovering a "transforming principle" in heat-killed virulent smooth *pneumococcus* that enables the transformation of rough non-virulent rough pneumococcal bacteria.

Based on his observations, Griffith deduced that something in the dead S-strain was transferred to the previously harmless R-strain, making the R-strain deadly. What was this "something?" What type of substance could change the characteristics of the organism that received it?

AVERY AND HIS COLLEAGUES MAKE A MAJOR CONTRIBUTION

In the early 1940s, a team of scientists led by Oswald Avery tried to answer the question raised by Griffith's research results. First, they inactivated various substances in the S-strain bacteria. Then they killed the S-strain bacteria and mixed the remains with live R-strain bacteria. (Keep in mind that the R-strain bacteria normally did not harm the mice.) When they inactivated proteins, the R-strain was deadly to the injected mice. This ruled out proteins as genetic material. Why? Even without the S-strain proteins, the R-strain was changed or transformed into a deadly strain. However, when the researchers inactivated DNA in the S-strain, the R-strain remained harmless. This led to the conclusion that DNA — and not protein — is the substance that controls the characteristics of organisms. In other words, DNA is the genetic material.

HERSHEY AND CHASE CONFIRM THE RESULTS

The conclusion that DNA is the genetic material was not widely accepted until it was confirmed by additional research. In the 1950s, Alfred Hershey and Martha Chase did experiments with viruses and bacteria. Viruses are not cells. Instead, they are basically DNA (or RNA) inside a protein coat. To reproduce, a virus must insert its own genetic material into a cell (such as a bacterium). Then it uses the cell's machinery to make more viruses. The researchers used different radioactive elements to label the DNA and proteins in DNA viruses. This allowed them to identify which molecule the viruses

inserted into bacterial cells. DNA was the molecule they identified. This confirmed that DNA is the genetic material.

CHARGAFF FOCUSES ON DNA BASES

Erwin Chargaff (1905-2002), an Austrian-American biochemist from Columbia University, analyzed the base composition of the DNA of various species. This led him to propose two main rules that have been appropriately named **Chargaff's rules**.

RULE 1

Chargaff determined that in DNA, the amount of one base, a purine, always approximately equals the amount of a particular second base, a pyrimidine. Specifically, in any double-stranded DNA, the number of guanine units equals approximately the number of cytosine units and the number of adenine units equals approximately the number of thymine units.

Human DNA is 30.9% A and 29.4% T, 19.9% G and 19.8% C. The rule constitutes the basis of **base pairs** in the DNA double helix: A always pairs with T, and G always pairs with C. He also demonstrated that the number of purines (A+G) always approximates the number of pyrimidines (T+C), an obvious consequence of the base-pairing nature of the DNA double helix.

RULE 2

In 1947 Chargaff showed that the composition of DNA, in terms of the relative amounts of the A, C, G, and T bases, varied from one species to another. This molecular diversity added to the evidence that DNA could be the genetic material.

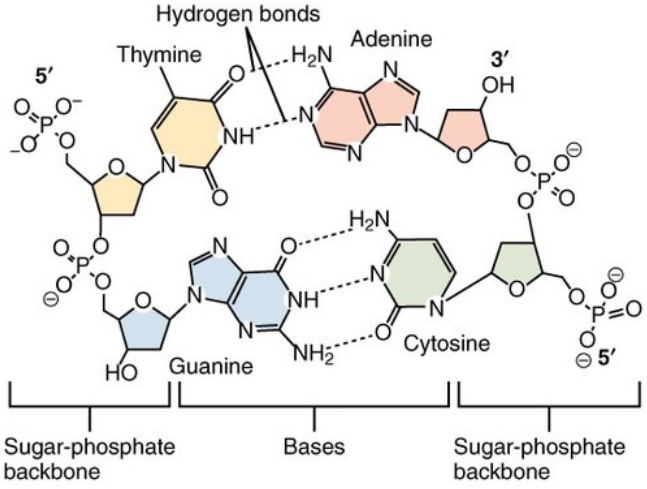


Figure **10.2.3**: Chemical structure of the four nitrogenous bases in the two strands of DNA. Notice how the purines (A and G) are composed of two ring structures, whereas the pyrimidines (T and C) are composed of one ring structure. The DNA of all species has the same four nitrogen bases. The figure also illustrates that Adenine pairs with Thymine and Guanine pairs with cytosine.

DISCOVERY OF THE DOUBLE HELIX

After DNA was shown to be the genetic material, scientists wanted to learn more about it, including its structure. James Watson and Francis Crick are usually given credit for discovering that DNA has a double-helix shape like a spiral staircase, as shown in Figure **10.2.4**. In fact, Watson and Crick's discovery of the double helix depended heavily on the prior work of Rosalind Franklin and other scientists, who had used X-rays to learn more about DNA's structure. Unfortunately, Franklin and these other scientists have not usually been given credit for their important contributions to the discovery of the double helix.

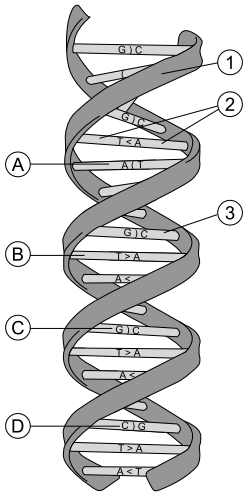


Figure **10.2.4**: Double helix structure of DNA resembles a twisted staircase. In this image A. Adenine B. Thymine C. Guanine D. Cytosine 1. Sugar, Phosphate, Backbone 2. Base pair 3. Nitrogenous base. This image also shows the application of 2 rules of Chargaff.

The double-helix shape of DNA, together with Chargaff's rules, led to a better understanding of DNA. As a nucleic acid, DNA is made from nucleotide monomers. Long chains of nucleotides form polynucleotides, and the DNA double helix consists of two polynucleotide chains. Each nucleotide consists of a sugar (deoxyribose), a phosphate group, and one of the four bases (adenine, cytosine, guanine, or thymine). The sugar and phosphate molecules in adjacent nucleotides bond together and form the "backbone" of each polynucleotide chain.

Scientists concluded that bonds between the bases hold together the two polynucleotide chains of DNA. Moreover, adenine always bonds with thymine, and cytosine always bonds with guanine. That's why these pairs of bases are called **complementary base pairs.** If you look at the nitrogen bases in Figure **10.2.3**, you will see why the bases bond together only in these pairings. Adenine and guanine have a two-ring structure, whereas cytosine and thymine have just one ring. If adenine were to bond with guanine as well as thymine, for example, the distance between the two DNA chains would be variable. However, when a one-ring molecule (such as thymine) always bonds with a two-ring molecule (such as adenine), the distance between the two chains remains constant. This maintains the uniform shape of the DNA double helix. The bonded base pairs (A-T and G-C) stick into the middle of the double helix, forming, in essence, the steps of the spiral staircase.

DNA REPLICATION

Knowledge of DNA's structure helped scientists understand how DNA replicates. **DNA replication** is the process in which DNA is copied. It occurs during the synthesis (S) phase of the eukaryotic cell

cycle. DNA must be copied so that, after cell division occurs, each daughter cell will have a complete set of chromosomes.

DNA replication begins when an enzyme breaks the bonds between complementary bases in the molecule. This exposes the bases inside the molecule so they can be “read” by another enzyme and used to build two new DNA strands with complementary bases. The two daughter molecules that result each contain one strand from the parent molecule and one new strand that is complementary to it. As a result, the two daughter molecules are both identical to the parent molecule. This is a semi-conservative process (see Figure **10.2.5**.)

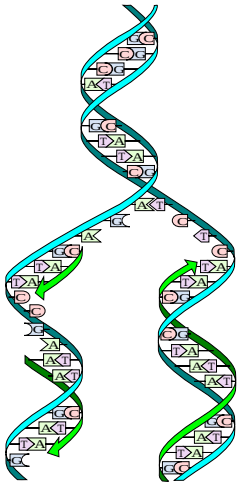


Figure **10.2.5**: DNA Replication. DNA replication is a semi-conservative process. Half of the parent DNA molecule is conserved in each of the two daughter DNA molecules. The blue strand belongs to the parent cell, and the green DNA strand represents a brand new DNA strand.

HELICASE AND POLYMERASE

DNA replication begins as an enzyme, **DNA helicase**, breaks the hydrogen bonds holding the two strands together and forms a **replication fork** (see Figure **10.2.6**. The resulting structure has two branching strands of DNA backbone with exposed bases. These exposed bases allow the DNA to be “read” by another enzyme, **DNA polymerase**, which then builds the complementary DNA strand. As DNA helicase continues to open the double helix, the replication fork grows.

LEADING AND LAGGING STRANDS

Two DNA polymerase enzymes work at a Replication fork. This enzyme can only build new DNA in the 5' → 3' direction. It also needs a **primer** built by **primase** to start building DNA. Therefore, the two new strands, the l**eading strand** and the **lagging strand**, of DNA are “built” in opposite directions. The leading strand is the DNA strand that DNA polymerase constructs in the 5' → 3' direction. This strand of DNA is made in a continuous manner, moving as the replication fork grows. The "lagging” strand is synthesized in short segments known as **Okazaki fragments**. On the lagging strand, **primase** builds a short RNA primer. DNA polymerase is then able to use the free 3'-OH group on the RNA primer to make DNA in the 5' → 3' direction till it reaches to end of the template strand. DNA polymerase of the lagging strand then jumps to go further into the replication fork to make another Okazaki fragment. The RNA fragments are then degraded and new DNA nucleotides are added to fill the gaps where the RNA was present. Another enzyme, **DNA ligase**, is then able to attach (ligate) the DNA nucleotides together, completing the synthesis of the lagging strand (Figure **10.2.6**).

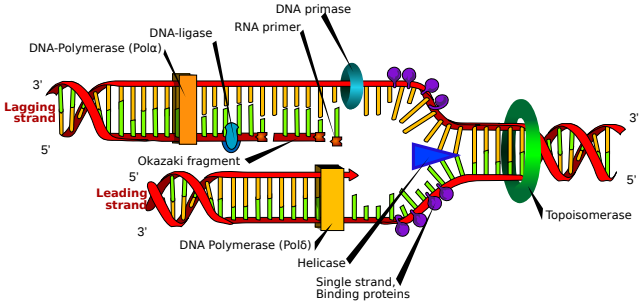


Figure **10.2.6**: DNA replication. The two DNA strands are opened by helicase. The strands are held open by a single strand of binding proteins, preventing premature reannealing. Topoisomerase solves the problem caused by the tension generated by the winding/unwinding of DNA. This enzyme wraps around DNA and makes a cut permitting the helix to spin and relax. Once DNA is relaxed, topoisomerase reconnects broken strands. DNA primase synthesizes a short RNA primer that initiates the Okazaki fragment and leading strand. DNA polymerase synthesizes the leading strand and Okazaki fragments. Okazaki fragments are attached by DNA ligase after the primers are removed.

WHAT IS RNA?

RNA structure differs from the DNA structure in three specific ways. Both are nucleic acids and made out of **nucleotides**; however, RNA is single-stranded while DNA is double-stranded. RNA nucleotides, like those from DNA, have three parts: a 5-carbon sugar, a phosphate group, and a base. RNA contains the 5-carbon sugar **ribose**, whereas, in DNA, the sugar is **deoxyribose**. The difference between ribose and deoxyribose is the lack of a hydroxyl group attached to the pentose ring in the 2' position of deoxyribose (see figure Figure **10.2.7**.

Table **10.2.1**: comparison of RNA and DNA

	RNA	DNA
Strands	single stranded	double stranded
Specific Base	contains uracil	contains thymine
Sugar	ribose	deoxyribose
Size	relatively small	big (chromosomes)
Location	moves to cytoplasm	stays in nucleus
Types	3 types: mRNA, tRNA, rRNA	generally 1 type

Though both RNA and DNA contain the nitrogenous bases adenine, guanine, and cytosine, RNA contains the nitrogenous base **uracil** instead of thymine. Uracil pairs with adenine in RNA, just as thymine pairs with adenine in DNA. Uracil and thymine have very similar structures; uracil is an unmethylated form of thymine.

The nucleotide sequence of RNA, which is complementary to the DNA sequence, allows RNA to encode genetic information. RNA

though carries the genetic information of just one gene. Hence, compared to DNA, RNA molecules are relatively small.

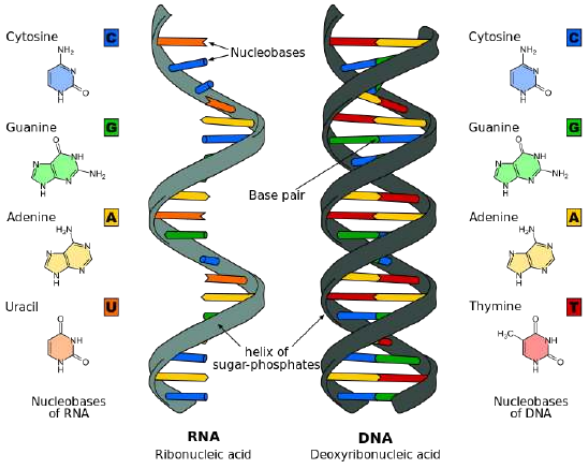


Figure 10.2.7. Comparison of a single-stranded RNA and a double-stranded DNA with their corresponding nucleobases. Also, refer to Table 10.2.1 as your read this image.

REVIEW

1. Outline the discoveries that led to the determination that DNA, and not protein, is the biochemical molecule that contains genetic information.
2. State Chargaff's rules. Explain how the rules are related to the structure of the DNA molecule.
3. Explain how the structure of a DNA molecule is like a spiral staircase. Which parts of the staircase represent the various parts of the molecule?
4. Describe the process of DNA replication.
5. When does DNA replication occur, and why is the process said to be semi-conservative?
6. Why do you think dead S strain bacteria injected into mice does not harm the mice but kills them when mixed with living (and normally harmless) R strain bacteria?
7. In Griffith's experiment, do you think the heat treatment that killed the bacteria also inactivated the bacterial DNA? Why or why not?
8. Give one example of a specific piece of evidence that helped rule out proteins as the genetic material.
9. *True or False.* Two-ring bases always bind to each other.
10. *True or False.* DNA replication involves the breaking of one of the polynucleotide chains into individual nucleotides.
11. *True or False.* In DNA, each nucleotide has a sugar.
12. What would the complementary strand of this stretch of DNA bases be? GTTAC
13. Which scientists detected labeled DNA that was transferred from one organism to another?

    A. Hershey and Chase
    B. Chargaff
    C. Avery
    D. Griffith

14. Which enzyme break the bonds between complementary bases and add new complementary nucleotides to the parental strands during DNA replication?

    A. Phosphates
    B. Enzymes
    C. Viruses
    D. RNA molecules

15. Describe the differences between DNA and RNA.
16. How is DNA replicated? Why is DNA replication called a "semi-conservative" process?
17. What are the roles of the following enzymes?

    A. DNA polymerase
    B. DNA helicase
    C. DNA ligase
    D. primase

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10.3: CHROMOSOMES AND GENES

IDENTICAL TWINS, IDENTICAL GENES

You probably can tell by their close resemblance that these two individuals are identical twins. Identical twins develop from the same fertilized egg, so they inherited copies of the same chromosomes and have all the same genes. Unless you have an identical twin, no one else in the world has exactly the same genes as you. What are genes? How are they related to chromosomes? And how do genes make you the person you are?



Figure **10.3.1**: Identical twins

Chromosomes are coiled structures made of DNA and proteins. Chromosomes are encoded with genetic instructions for making proteins. These instructions are organized into units called **genes**. Most genes contain the instructions for a single protein. There may be hundreds or even thousands of genes on a single chromosome.

HUMAN CHROMOSOMES

Each species is characterized by a set number of chromosomes. The human number is 23. Human cells normally have two sets of chromosomes in each of their cells, one set inherited from each parent. There are 23 chromosomes in each set, for a total of 46 chromosomes per cell. Each chromosome in one set is matched by a chromosome of the same type in the other set, so there are actually 23 pairs of chromosomes per cell. Each pair consists of chromosomes of the same size and shape, and they also contain the same genes. The chromosomes in a pair are known as **homologous chromosomes**. As see in Figure **10.3.2**, there are two types of chromosomes, autosomal and sex chromosomes. Read more about this in the genetics chapter.

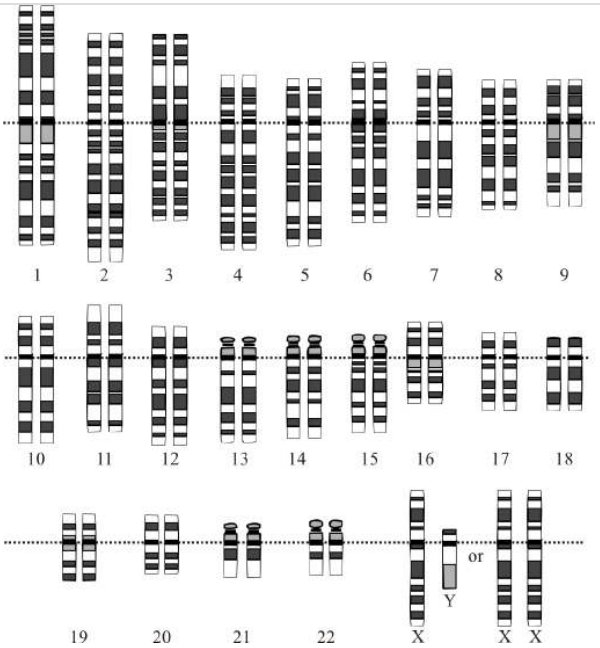


Figure **10.3.2**: All human cells (except gametes, which are sperm and egg cells) have the 23 pairs of chromosomes shown here. There are two types of chromosomes, autosomal (pairs 1-22) and sex (23rd pair). The chromosomes are numbered according to their size, the first chromosome pair being the longest and the twenty-second chromosome pair being the shortest. The 23rd pair is not always homologous. It can be XY or XX. The X chromosome is significantly longer than the Y chromosome. The stripes on the chromosomes represent genes.

HUMAN GENES

Humans have an estimated 25,000 genes. This may sound like a lot, but it really isn't. Far simpler species have almost as many genes as humans. However, human cells use splicing and other processes to make multiple proteins from the instructions encoded in a single gene. Only about 25 percent of the nitrogen base pairs of DNA in human chromosomes make up genes and their regulatory elements. Out of this 25 percent, only two percent code for genes. The functions of many of the other base pairs are still unclear.

The majority of human genes have two or more possible versions, called alleles. Differences in alleles account for the considerable genetic variation among people. In fact, most human genetic variation is the result of differences in individual DNA base pairs within alleles.

LINKAGE

Genes that are located on the same chromosome are called **linked genes**. Linkage explains why certain characteristics are frequently inherited together. For example, genes for hair color and eye color are linked, so certain hair and eye colors tend to be inherited together, such as blonde hair with blue eyes and brown hair with brown eyes. Can you think of other human traits that seem to occur together? Do you think they might be controlled by linked genes?

Genes located on the sex chromosomes are called **sex-linked genes**. Most sex-linked genes are on the X chromosome because the Y chromosome has relatively few genes. Strictly speaking, genes on the X chromosome are **X-linked genes**, but the term sex-linked is often used to refer to them. Figure **10.3.3** is called a linkage map. A linkage map shows the locations of specific genes on a chromosome. It shows the locations of a few of the genes on the human X chromosome, such as a blood group protein gene, Lethyosis (a skin disease gene), ocular albinism gene, and many more.

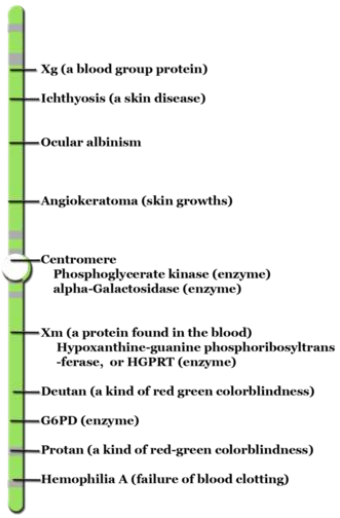


Figure **10.3.3**: Linkage Map for the Human X Chromosome. This linkage map shows the locations of several genes on the X chromosome. Some of the genes code for normal proteins. Others code for abnormal proteins that lead to genetic disorders.

CHROMOSOMES AND GENES

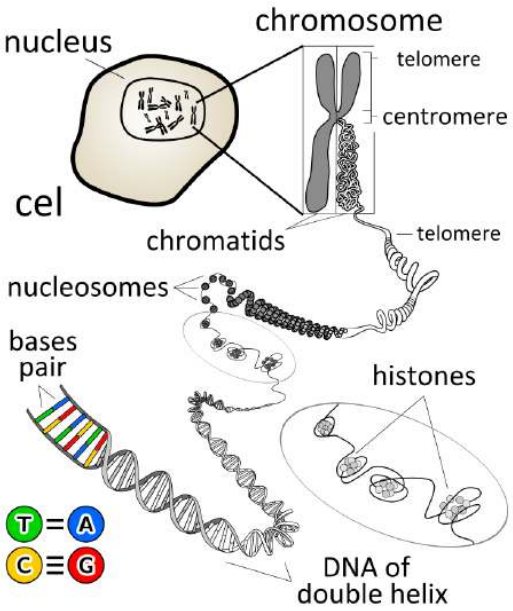


Figure **10.3.4**: Graphic decomposition of a chromosome (found in the cell nucleus), to the bases pair of the DNA. Chromosomes are located in the nucleus of the cell. A duplicated chromosome has two chromatids, double-helix DNA is wrapped in histone proteins to form nucleosomes. This allows DNA to organize into chromosomes.

REVIEW

1. What are chromosomes and genes, and how are the two related?
2. Describe human chromosomes and genes.
3. Explain the difference between autosomes and sex chromosomes.
4. What are linked genes, and what does a linkage map show?
5. Explain why females are considered the default sex in humans.
6. *True or False.* Humans have 46 pairs of chromosomes.
7. *True or False.* Autosomes refer to any chromosome other than sex chromosomes.
8. *True or False.* The majority of human DNA does not encode for proteins.
9. Explain the relationship between genes and alleles.
10. Put the following in order of size, from smallest to largest: chromosome; gene; base pair
11. Sex-linked genes are usually found on which chromosome? Explain why these genes are called sex-linked.
12. Which of the following are considered homologous chromosomes?
    A. Chromosome 22 and the X chromosome
    B. The two copies of chromosome 22 that make up a pair
    C. All of the chromosomes in a skin cell and all of the chromosomes in a muscle cell
    D. Chromosomes 21 and 22
13. What is the one chromosome that is different between genetic males and females? Explain your answer.
14. Most males and females have two sex chromosomes. Explain why then, do only females have Barr bodies.

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10.4: PROTEIN SYNTHESIS

THE CENTRAL DOGMA OF BIOLOGY

Your **DNA**, or deoxyribonucleic acid, contains the genes that determine who you are. How can this organic molecule control your characteristics? DNA contains instructions for all the proteins your body makes. **Proteins**, in turn, determine the structure and function of all your cells. What determines a **protein**'s structure? It begins with the sequence of **amino acids** that make up the protein. Instructions for making proteins with the correct sequence of amino acids are encoded in DNA.



Figure **10.4.1**: Transcription and translation (Protein synthesis) in a cell.

DNA is found in chromosomes. In eukaryotic cells, chromosomes always remain in the nucleus, but proteins are made at ribosomes in the cytoplasm or on the rough endoplasmic reticulum (RER). How do the instructions in DNA get to the site of protein synthesis outside the nucleus? Another type of nucleic acid is responsible. This nucleic acid is **RNA** or ribonucleic acid. RNA is a small molecule that can squeeze through pores in the nuclear membrane. It carries the information from DNA in the nucleus to a ribosome in the cytoplasm and then helps assemble the protein. In short:

DNA → RNA → Protein

Discovering this sequence of events was a major milestone in molecular biology. It is called the **central dogma of biology**. The two processes involved in the central dogma are **transcription** and **translation.**

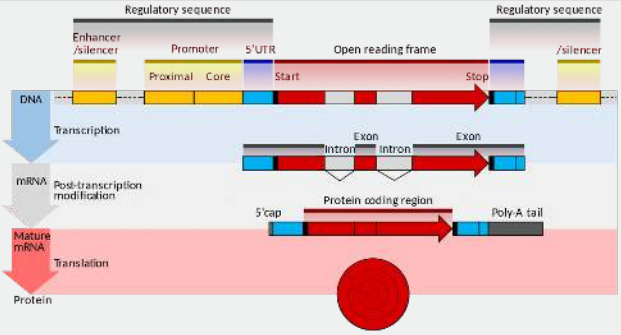


Figure **10.4.2**: An overview of transcription and translation. The top panel shows a gene. A gene is composed of the open reading frame (aka coding sequence) that is flanked by regulatory sequences. At the beginning of the gene, the regulatory sequence contains a promoter where RNA polymerase attaches and starts transcription. At the end of the open reading frame, the regulatory sequence contains a terminator (not shown.)The middle panel shows a pre mRNA which is modified by excising introns and keeping exons. This is called post transcription modification. A mature mRNA contains a 5' cap and poly-A tail. The bottom panel shows a synthesis of protein via translation.

TRANSCRIPTION

Transcription is the first part of the central dogma of molecular biology: **DNA → RNA**. It is the transfer of genetic instructions in DNA to mRNA. Transcription happens in the nucleus of the cell. During transcription, a strand of mRNA is made that is complementary to a strand of DNA called a gene. A gene can easily be identified from the DNA sequence. A gene contains the basic three regions, promoter, coding sequence (reading frame), and terminator. There are more parts of a gene which are illustrated in Figure **10.4.3**.

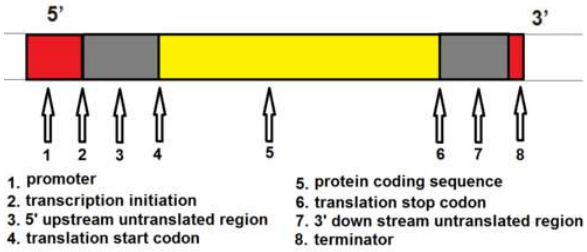


Figure **10.4.3**: The major components of a gene. 1. promoter, 2. transcription initiation, 3. 5' upstream untranslated region, 4. translation start codon site, 5. protein-coding sequence, 6. translation stop codon region, 7. 3' downstream untranslated region, and 8. terminator.

STEPS OF TRANSCRIPTION

Transcription takes place in three steps, called initiation, elongation, and termination. The steps are illustrated in Figure **10.4.4**.

1. Initiation is the beginning of transcription. It occurs when the enzyme RNA polymerase binds to a region of a gene called the **promoter**. This signals the DNA to unwind so the enzyme can "read" the bases in one of the DNA strands. The enzyme is ready

to make a strand of mRNA with a complementary sequence of bases. The promoter is not part of the resulting mRNA

2. Elongation is the addition of nucleotides to the mRNA strand.
3. Termination is the ending of transcription. As RNA polymerase transcribes the terminator, it detaches from DNA. The mRNA strand is complete after this step.

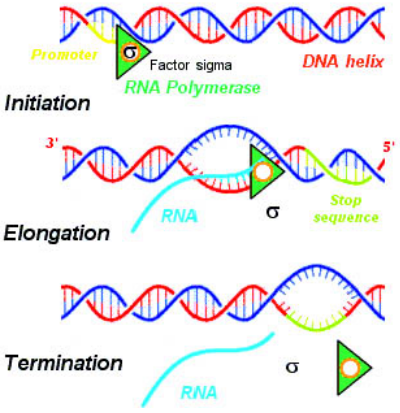


Figure **10.4.4**: Transcription occurs in the three steps - initiation, elongation, and termination

PROCESSING MRNA

In eukaryotes, the new mRNA is not yet ready for translation. At this stage, it is called pre-mRNA, and it must go through more processing before it leaves the nucleus as mature mRNA. The processing may include the addition of a 5' cap, splicing, editing, and 3' polyadenylation (poly-A) tail. These processes modify the mRNA in various ways. Such modifications allow a single gene to be used to make more than one protein. See Figure **10.4.5** as you read below:

- 5' cap protects mRNA in the cytoplasm and helps in the attachment of mRNA with the ribosome for translation.
- Splicing removes introns from the protein-coding sequence of mRNA. **Introns** are regions that do not code for the protein. The remaining mRNA consists only of regions called **exons** that do code for the protein.
- Editing changes some of the nucleotides in mRNA. For example, a human protein called APOB, which helps transport lipids in the blood, has two different forms because of editing. One form is smaller than the other because editing adds an earlier stop signal in mRNA.
- Polyadenylation adds a “tail” to the mRNA. The tail consists of a string of As (adenine bases). It signals the end of mRNA. It is also involved in exporting mRNA from the nucleus, and it protects mRNA from enzymes that might break it down.

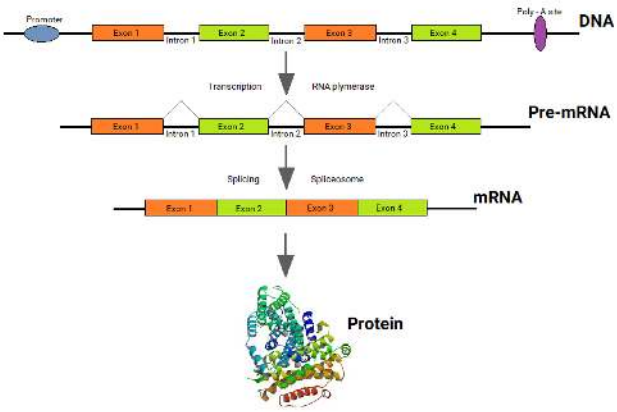


Figure **10.4.5**: Splicing removes introns from mRNA. Mature mRNA is translated to protein.

TRANSLATION

The translation is the second part of the central dogma of molecular biology: **RNA --> Protein**. It is the process in which the genetic code in mRNA is read to make a protein. The translation is illustrated in Figure **10.4.6**. After mRNA leaves the nucleus, it moves to a ribosome, which consists of rRNA and proteins. Translation happens on the ribosomes floating in the cytosol, or on the ribosomes attached to the rough endoplasmic reticulum. The ribosome reads the sequence of codons in mRNA, and molecules of tRNA bring amino acids to the ribosome in the correct sequence.

To understand the role of tRNA, you need to know more about its structure. Each tRNA molecule has an anticodon for the amino acid it carries. An **anticodon** is complementary to the codon for an amino acid. For example, the amino acid lysine has the codon AAG, so the anticodon is UUC. Therefore, lysine would be carried by a tRNA molecule with the anticodon UUC. Wherever the codon AAG appears in mRNA, a UUC anticodon of tRNA temporarily binds. While bound to mRNA, tRNA gives up its amino acid. With the help of rRNA, bonds form between the amino acids as they are brought one by one to the ribosome, creating a polypeptide chain. The chain of amino acids keeps growing until a stop codon is reached.

Ribosomes, which are just made out of rRNA (ribosomal RNA) and protein, have been classified as ribozymes because the rRNA has enzymatic activity. The rRNA is important for the peptidyl transferase activity that bonds amino acids. Ribosomes have two subunits of rRNA and protein. The large subunit has three active sites called E, P, and A sites. These sites are important in the catalytic activity of ribosomes.

Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination. In addition to the mRNA template, many other molecules contribute to the process of translation, such as ribosomes, tRNAs, and various enzymatic factors

Translation Initiation: The small subunit binds to a site upstream (on the 5' side) of the start of the mRNA. It proceeds to scan the mRNA in the 5'-->3' direction until it encounters the START codon

(AUG). The large subunit attaches and the initiator tRNA, which carries methionine (Met), binds to the P site on the ribosome.

Translation Elongation: 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. The energy for each bond between amino acids is derived from GTP, a molecule similar to ATP. Briefly, the ribosomes interact with other RNA molecules to make chains of amino acids called polypeptide chains, due to the peptide bond that forms between individual amino acids. Inside the ribosome, three sites participate in the translation process, the A, P, and E sites. Amazingly, the E. coli translation apparatus takes only 0.05 seconds to add each amino acid, meaning that a 200-amino acid polypeptide could be translated in just 10 seconds.

Translation Termination: Termination of translation occurs when a stop codon (UAA, UAG, or UGA) is encountered (see Figure **10.4.7**. When the ribosome encounters the stop codon, the growing polypeptide is released with the help of various releasing factors 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.

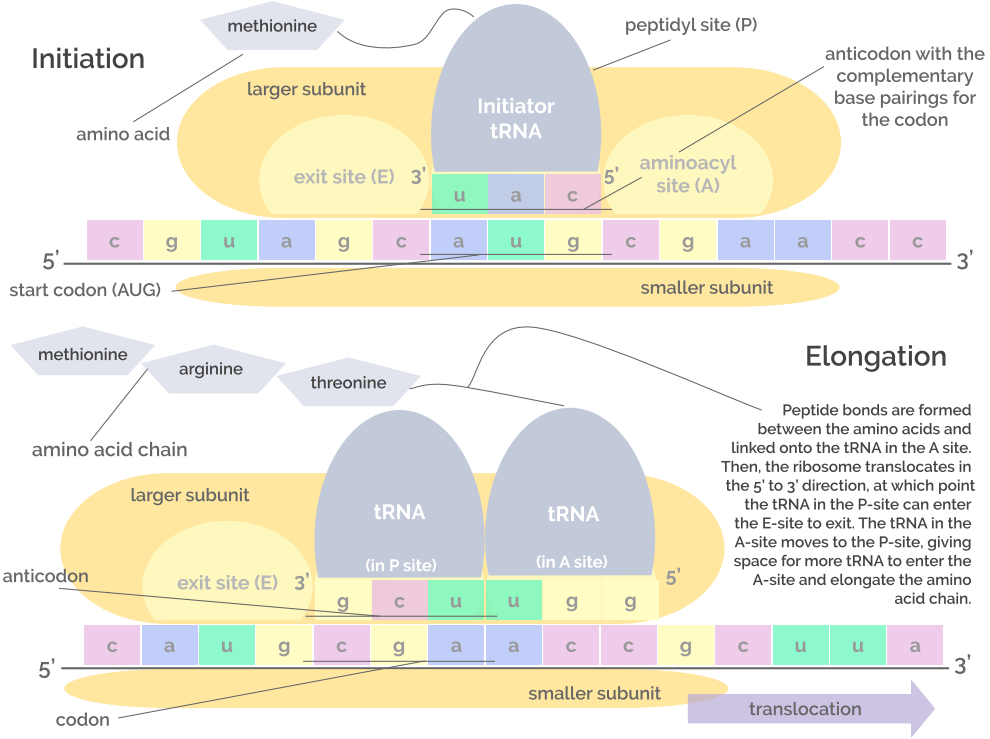


Figure **10.4.6**: At the initiation phase, the initiator tRNA carrying methionine with its anticodon encounters the AUG start codon at the P-site of the ribosome. During elongation, the ribosome translocates in the 5' to 3' direction of the mRNA, at which point the amino acids of tRNA in P-site and amino acid of tRNA in the A-site of the large subunit bond to each other via a peptide bond. This repeated movement of the ribosome creates a long amino acid chain based on the codons in the mRNA. As the ribosome translocates, the tRNA leaves the ribosome through the E-site, while new tRNA enters the A-site in order to continue elongating the amino acid chain.

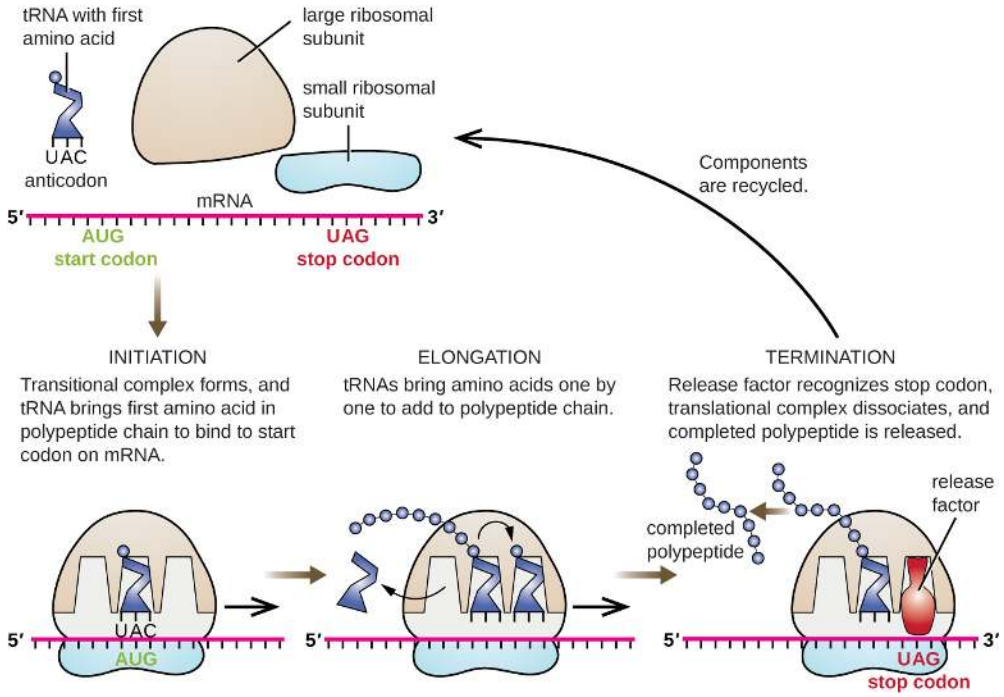


Figure **10.4.7**. Summary of protein translation. During initiation, both ribosomal subunits, mRNA, and initiator tRNA come together. The initiator anticodon of initiator tRNA hydrogen bond with the start codon. During elongation, tRNA brings amino acids one by one to add to the polypeptide chain. During termination, the release factor recognizes stop codon, all components dissociate, and the completed polypeptide is released.

WHAT HAPPENS NEXT?

After a polypeptide chain is synthesized, it may undergo additional processes. For example, it may assume a folded tertiary shape due to interactions among its amino acids. It may also bind with other polypeptides or with different types of molecules, such as lipids or carbohydrates. Many proteins travel to the Golgi apparatus within the cytoplasm to be modified for the specific job they will do.

SUMMARY OF CENTRAL DOGMA

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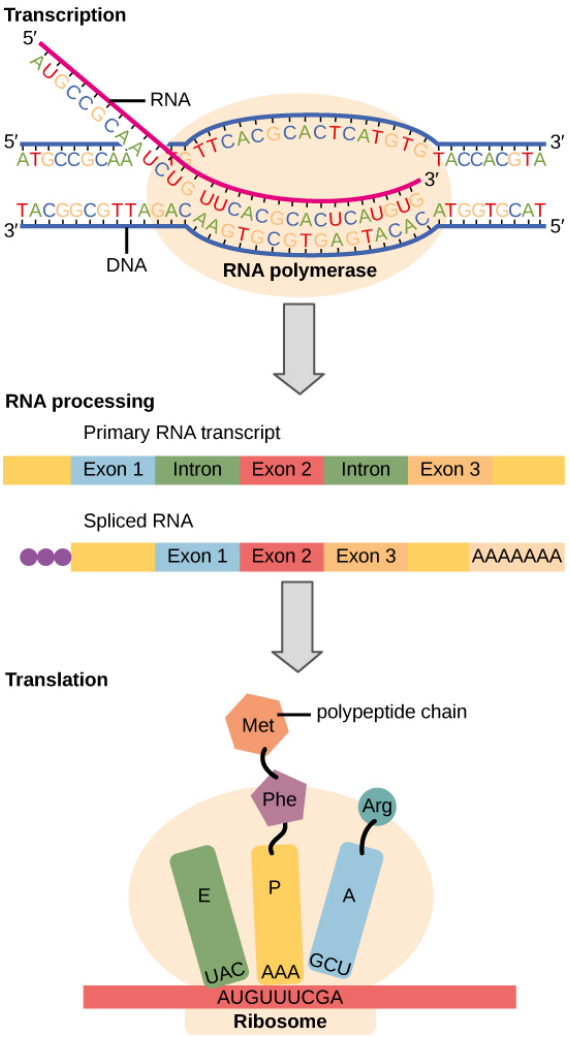


Figure **10.4.8**: The central dogma: Instructions on DNA are transcribed onto messenger RNA. Ribosomes are able to read the genetic information inscribed on a strand of messenger RNA and use this information to string amino acids together into a protein.

REVIEW

1. Relate protein synthesis and its two major phases to the central dogma of molecular biology.
2. Identify the steps of transcription, and summarize what happens during each step.
3. Explain how mRNA is processed before it leaves the nucleus.
4. Describe what happens during the translation phase of protein synthesis.
5. What additional processes may a polypeptide chain undergo after it is synthesized?
6. Where does transcription take place in eukaryotes?
7. Where does translation take place?
8. Which type of RNA (mRNA, rRNA, or tRNA) best fits each of the statements below? Choose only one type for each.
   A. Contains the codons
   B. Contains the anticodons
   C. Makes up the ribosome, along with proteins
9. If the DNA has a triplet code of CAG in one strand (the strand used as a template for transcription),
   A. What is the complementary sequence on the other DNA strand?
   B. What is the complementary sequence in the mRNA? What is this sequence called?
   C. @hat is the resulting sequence in the tRNA? What is this sequence called? What do you notice about this sequence compared to the original DNA triplet on the template strand?
10. The promoter is a region located in the:
    A. DNA
    B. mRNA
    C. tRNA
    D. Both A and B
11. *True or False.* Introns in mRNA bind to tRNA at the ribosome.
12. *True or False.* tRNAs can be thought of as the link between amino acids and codons in the mRNA.

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10.5: GENETIC CODE

CAN YOU CODE?

If someone asks you whether you can code, you probably assume they are referring to computer code. The image in Figure **10.5.1** represents an important code that you use all the time but not with a computer. It's the genetic code, and it is used by your cells to store information and make proteins.



Figure **10.5.1**: FACIL genetic code logo

WHAT IS THE GENETIC CODE?

The **genetic code** consists of the sequence of nitrogen bases in a polynucleotide chain of DNA or RNA. The bases are adenine (A), cytosine (C), guanine (G), and thymine (T) (or uracil, U, in RNA). The four bases make up the "letters" of the genetic code. The letters are combined in groups of three to form code "words," called **codons**. Each codon stands for (encodes) one amino acid unless it codes for a start or stop signal. There are 20 common amino acids in proteins. With four bases forming three-base codons, there are 64 possible codons. 61 codons are more than enough to code for the 20 amino acids, thus more than one codon codes for a single amino acid. Please find genetic codes in Table **10.5.1** or in appendix 1.

Table **10.5.1**: Codon Chart. To find the amino acid for a particular codon, find the cell in the table for the first, second, and third bases of the codon. Once you have found the codon, you can find the corresponding amino acid in the adjacent cell on the right side of the codon cell. For example CUG codes for leucine (Leu), AAG codes for lysine (Lys), and GGG codes for glycine (Gly). Text only version of the codon chart.

	Second base U	Amino acid	Second base C	Amino acid	Second base A	Amino acid	Second base G	Amino acid	
First base U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	Third base U
First base U	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	Third base C
First base U	UUA	Leu	UCA	Ser	UAA	(stop) no amino acid	UGA	(stop) no amino acid	Third base A
First base U	UUA	Leu	UCG	Ser	UAG	(stop) no amino acid	UGG	Trp	Third base G
First base C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	Third base U
First base C	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg	Third base C
First base C	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	Third base A
First base C	CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	Third base G
First base A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	Third base U
First base A	AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser	Third base C
First base A	AUA	Ile	ACA	Thr	AAA	Lys	AGA	Arg	Third base A
First base A	AUG	Met (start)	ACG	Thr	AAG	Lys	AGG	Arg	Third base G
First base G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	Third base U
First base G	GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly	Third base C
First base G	GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly	Third base A
First base G	GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly	Third base G

READING THE GENETIC CODE

If you find the codon AUG in Table **10.5.1**, you will see that it codes for the amino acid methionine. This codon is also the start codon that establishes the **reading frame** of the code. The reading frame is the way the bases are divided into codons. It is illustrated in Figure **10.5.2**. After the AUG start codon (not shown in the image), the next three bases are read as the second codon. The next three bases after that are read as the third codon, and so on. The sequence of bases is read, codon by codon, until a stop codon is reached. UAG, UGA, and UAA are all the stop codons. They do not code for any amino acids.

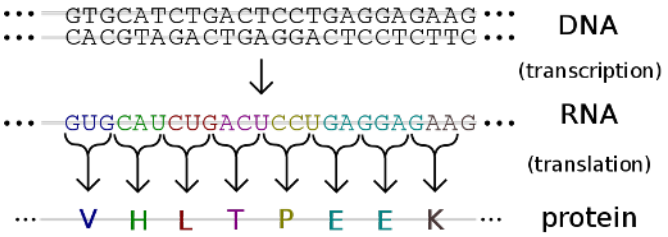


Figure **10.5.2**: Reading the Genetic Code. The genetic code is read three bases at a time. Codons are the code words of the genetic code.

CHARACTERISTICS OF THE GENETIC CODE

The genetic code has a number of important characteristics:

- The genetic code is universal. All known living things have the same genetic code. This shows that all organisms share a common evolutionary history.

- The genetic code is unambiguous. This means that each codon codes for just one amino acid (or start or stop). This is necessary so there is no question about which amino acid is the correct one.
- The genetic code is redundant. This means that each amino acid is encoded by more than one codon. For example, in the table above, four codons code for the amino acid threonine. Redundancy in the code helps prevent errors in protein synthesis. If a base in codon changes by accident, there is a good chance that it will still code for the same amino acid.

REVIEW

1. Describe the genetic code.
2. Explain how the genetic code is read.
3. Identify three important characteristics of the genetic code.
4. Summarize how the genetic code was deciphered.
5. Use the table entitled *The Genetic Code*, shown above, to answer the following questions.
   A. Is the code depicted in the table from DNA or RNA? Explain your reasoning.
   B. Which amino acid does the codon CAA code for?
   C. Does UGA code for an amino acid? Why or why not? If so, which one?
   D. Look at the codons that code for the amino acid glycine. How many of them are there? What are their similarities and differences from each other?
   E. Imagine that you are doing an experiment similar to the one performed by Nirenberg and Matthaei with 20 test tubes, each containing bacterial cell contents and all 20 amino acids, with one type of amino acid labeled in each tube. If you added synthetic RNA containing only the base cytosine, a polypeptide chain consisting of which amino acid would be produced? Explain your answer.
6. *True or False.* One codon can encode for more than one amino acid.
7. *True or False.* The codons for tyrosine in plants are the same as ones that encode for tyrosine humans.
8. *True or False.* The start codon encodes for an amino acid, in addition to its function establishing where the reading frame starts.
9. How many possible codons are there?
   A. 64
   B. 20
   C. 3
   D. It depends on the species
10. How many common amino acids are there in proteins?
    A. 64
    B. 20
    C. 3
    D. 4

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10.6: MUTATIONS

SUPERHERO

Can a mutation really turn a person into a superhero? Of course not, but mutations can sometimes result in drastic changes in living things.



Figure **10.6.1**: Superhero

WHAT ARE MUTATIONS?

Mutations are random changes in the sequence of bases in DNA. The word *mutation* may make you think of Ninja Turtles, but that's a misrepresentation of how most mutations work. First of all, everyone has mutations. In fact, most people have dozens or even hundreds of mutations in their DNA. Secondly, from an evolutionary perspective, mutations are essential. They are needed for evolution to occur because they are the ultimate source of all new genetic variation in any species.

CAUSES OF MUTATIONS

Is it possible for mutations to occur spontaneously, or does there have to be a cause of the mutation? Well, the answer is that both are possible. Mutagenesis is a process by which the genetic information of an organism is changed in a stable manner, resulting in a mutation. In nature, mutagenesis can lead to changes that are beneficial or harmful or have no effect. Harmful mutations can lead to cancer and various heritable diseases, but beneficial mutations are the driving force of evolution. In 1927, Hermann Muller first demonstrated the effects of mutations with observable changes in chromosomes. He induced mutagenesis by irradiating fruit flies with X-rays,

Mutagenesis may occur spontaneously or be induced. A spontaneous mutation can just happen. These mutations are not caused by an environmental factor but occur during normal cellular processes. A spontaneous mutation may be due to a mistake during DNA replication. Mutations may also occur during mitosis and meiosis. A mutation caused by an environmental factor, or mutagen, is known as an induced mutation. Typical mutagens include chemicals, like those inhaled while smoking, and radiation, such as X-rays, ultraviolet light, and nuclear radiation. Different mutagens have different modes of damaging DNA. For example, UV radiation may cause bonding between the adjacent nucleotides on one strand of DNA molecule (Figure **10.6.2**). This prohibits normal bonding between complementary nucleotides of the opposing strand. This causes a bulge in the DNA double helix. If this damage is not repaired, it leads to mutation. Thus, DNA does not replicate, transcribe, and translate properly.

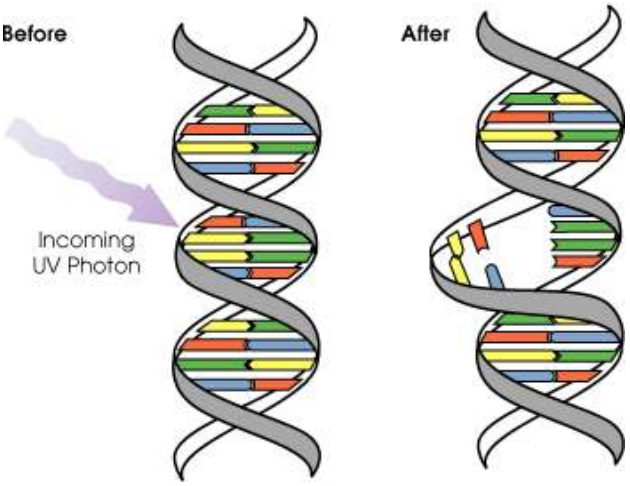


Figure **10.6.2**: Ultraviolet (UV) photons harm the DNA molecules of living organisms in different ways. In one common damage event, adjacent bases bond with each other, instead of across the “ladder.” This makes a bulge, and the distorted DNA molecule does not function properly.

TYPES OF MUTATIONS

There are a variety of types of mutations. Two major categories of mutations are germline mutations and somatic mutations.

- **Germline mutations** occur in gametes, the sex cells, such as eggs and sperm. These mutations are especially significant because they can be transmitted to offspring and every cell in the offspring will have the mutations.
- **Somatic mutations** occur in other cells of the body. These mutations may have little effect on the organism because they are confined to just one cell and its daughter cells. Somatic mutations also cannot be passed on to offspring.

Mutations also differ in the way that the genetic material is changed. Mutations may change an entire chromosome or just one or a few nucleotides.

CHROMOSOMAL ALTERATIONS

Chromosomal alterations are mutations that change chromosome structure or number. They occur when a section of a chromosome breaks off and rejoins incorrectly or does not rejoin at all. Possible ways these mutations can occur are illustrated in Figure **10.6.3**. Chromosomal alterations are very serious. They often result in the death of the organism in which they occur. If the organism survives, it may be affected in multiple ways. An example of a human chromosomal alteration is the mutation that causes Down Syndrome. It is a duplication mutation that leads to developmental delays and other abnormalities. It occurs when the individual inherits an extra copy of chromosome 21. It is also called trisomy ("three-chromosome") 21.

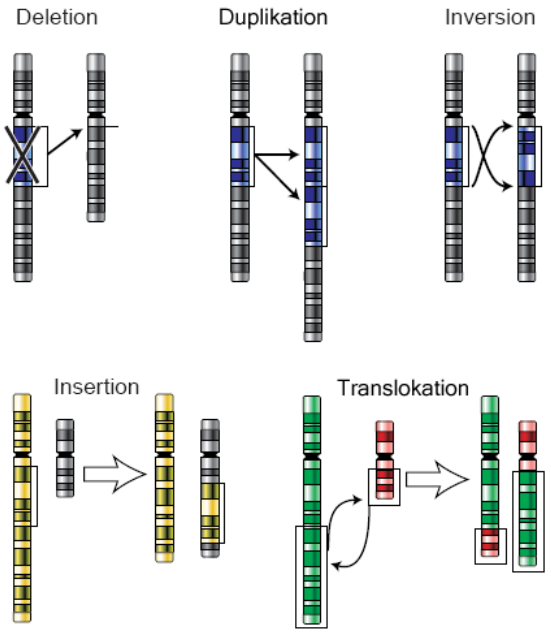


Figure **10.6.3**: Chromosomal Alterations. The chromosomal alterations may occur due to deletion or duplication of genes in a chromosome, inversion of a section of a chromosome, insertion of genes from one chromosome to another, or exchanges of genes between two chromosomes.

A **point mutation** is a change in a single nucleotide in DNA. This type of mutation is usually less serious than a chromosomal alteration. An example of a point mutation is a mutation that changes the codon UUU to the codon UCU. Point mutations can be silent, missense, or nonsense mutations, as shown in Table **10.6.1**. The effects of point mutations depend on how they change the genetic code.

Table **10.6.1**: Point Mutation Types

Type	Description	Example	Effect
Silent	mutated codon codes for the same amino acid	CAA (glutamine) → CAG (glutamine)	none
Missense	mutated codon codes for a different amino acid	CAA (glutamine) → CCA (proline)	variable
Nonsense	a mutated codon is a premature stop codon	CAA (glutamine) → UAA (stop) usually	serious

FRAMESHIFT MUTATIONS

A **frameshift mutation** is a deletion or insertion of one or more nucleotides that changes the reading frame of the base sequence. Deletions remove nucleotides, and insertions add nucleotides. Consider the following sequence of bases in RNA:

AUG-AAU-ACG-GCU = methionine-asparagine-threonine-alanine

Now assume that an insertion occurs in this sequence. Let's say an **A** nucleotide is inserted after the start codon **AUG.** Then the sequence of bases becomes:

AUG-AAA-UAC-GGC-U = methionine-lysine-tyrosine-glycine

Even though the rest of the sequence is unchanged, this insertion changes the reading frame and thus all of the codons that follow it.

As this example shows, a frameshift mutation can dramatically change how the codons in mRNA are read. This can have a drastic effect on the protein product. Another example of the frameshift mutation due to the deletion of a nucleotide is illustrated in Figure **10.6.4**. In this example, a premature stop codon is created by the mutation.

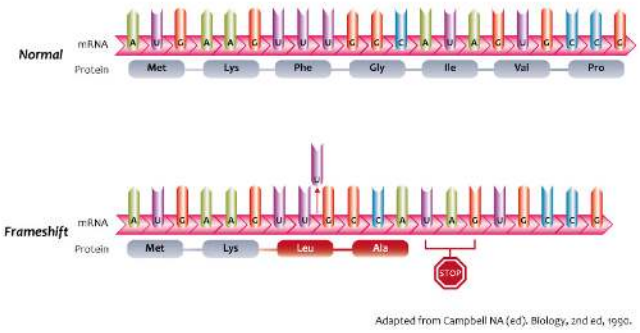


Figure **10.6.4**: The image shows how the frame of the coding sequence of a gene changes when a nucleotide gets deleted due to mutation. Normal gene codes for a polypeptide met-lys-phe-gly-ile-val-pro. When a U from the third position of the third codon gets deleted, the polypeptide reduced to met-lys-leu-ala because the third and fourth codons code for different amino acids and the fifth codon converts to a stop codon.

EFFECTS OF MUTATIONS

The majority of mutations have neither negative nor positive effects on the organism in which they occur. These mutations are called neutral mutations. Examples include silent point mutations, which are neutral because they do not change the amino acids in the proteins they encode.

Many other DNA damages or errors have no effects on the organism because they are repaired before protein synthesis occurs. Cells have multiple repair mechanisms to fix errors in DNA.

BENEFICIAL MUTATIONS

Some mutations have a positive effect on the organism in which they occur. They are referred to as beneficial mutations. They generally code for new versions of proteins that help organisms adapt to their environment. If they increase an organism's chances of surviving or reproducing, the mutations are likely to become more common over time. There are several well-known examples of beneficial mutations. Here are just two:

1. Mutations have occurred in bacteria that allow the bacteria to survive in the presence of antibiotic drugs. The mutations have led to the evolution of antibiotic-resistant strains of bacteria.
2. A unique mutation is found in people in a small town in Italy. The mutation protects them from developing atherosclerosis, which is the dangerous buildup of fatty materials in blood vessels. The individual in which the mutation first appeared has even been identified.

HARMFUL MUTATIONS

Imagine making a random change in a complicated machine such as a car engine. The chance that the random change would improve the functioning of the car is very small. The change is far more likely to result in a car that does not run well or perhaps does not run at all. By the same token, any random change in a gene's DNA is likely to result in the production of a protein that does not function normally or may not function at all. Such mutations are likely to be harmful. Harmful mutations may cause genetic disorders or cancer.

- A genetic disorder is a disease, syndrome, or other abnormal condition caused by a mutation in one or more genes or by a chromosomal alteration. An example of a genetic disorder is cystic fibrosis. A mutation in a single gene causes the body to produce thick, sticky mucus that clogs the lungs and blocks ducts in digestive organs.
- Cancer is a disease in which cells grow out of control and form abnormal masses of cells called tumors. It is generally caused by mutations in genes that regulate the cell cycle. Because of the mutations, cells with damaged DNA are allowed to divide without restrictions.

FEATURE: MY HUMAN BODY

Inherited mutations are thought to play a role in about 5 to 10 percent of all cancers. Specific mutations that cause many of the known hereditary cancers have been identified. Most of the mutations occur in genes that control the growth of cells or the repair of damaged DNA.

Genetic testing can be done to determine whether individuals have inherited specific cancer-causing mutations. Some of the most common inherited cancers for which genetic testing is available hereditary, breast, and ovarian cancer, caused by mutations in genes named BRCA1 and BRCA2. Besides breast and ovarian cancers, mutations in these genes may also cause pancreatic and prostate cancers. Genetic testing is generally done on a small sample of body fluid or tissue, such as blood, saliva, or skin cells. The sample is analyzed by a lab that specializes in genetic testing, and it usually takes at least a few weeks to get the test results.

Should you get genetic testing to find out whether you have inherited a cancer-causing mutation? Such testing is not done routinely just to screen patients for risk of cancer. Instead, the tests are generally done only when the following three criteria are met:

1. The test can determine definitively whether a specific gene is mutation is present. This is the case with the BRCA1 and BRCA2 gene mutations, for example.
2. The test results would be useful to help guide future medical care. For example, if you found out you had a mutation in the BRCA1 or BRCA2 gene, you might get more frequent breast and ovarian cancer screenings than are generally recommended.
3. You have a personal or family history that suggests you are at risk of inherited cancer.

Criterion number 3 is based, in turn, on such factors as:

- diagnosis of cancer at an unusually young age.
- several different cancers occurring independently in the same individual.
- several close genetic relatives having the same type of cancer (such as a maternal grandmother, mother, and sister all having breast cancer).
- cancer occurring in both organs in a set of paired organs (such as both kidneys or both breasts).

If you meet the criteria for genetic testing and are advised to undergo it, genetic counseling is highly recommended. A genetic counselor can help you understand what the results mean and how to make use of them to reduce your risk of developing cancer. For example, a positive test result that shows the presence of a mutation may not necessarily mean that you will develop cancer. It may depend on whether the gene is located on an autosome or sex chromosome and whether the mutation is dominant or recessive. Lifestyle factors may also play a role in cancer risk even for hereditary cancers, and early detection can often be life-saving if cancer does develop. Genetic counseling can also help you assess the chances that any children you may have will inherit the mutation.

REVIEW

1. Define mutation.
2. Identify the causes of mutation.
3. Compare and contrast germline and somatic mutations.
4. Describe chromosomal alterations, point mutations, and frameshift mutations. Identify the potential effects of each type of mutation.
5. Why are many mutations neutral in their effects?
6. Give an example of a beneficial mutation and an example of a harmful mutation.
7. Why do you think that exposure to mutagens, such as cigarette smoke, can cause cancer?
8. *True or False.* Mutations are always caused by exposure to toxic substances.
9. *True or False.* Some mutations can make chromosomes longer or shorter.
10. Explain why the insertion or deletion of a single nucleotide can cause a frameshift mutation.
11. Compare and contrast missense and nonsense mutations.
12. A mutation that substitutes one nucleotide for another is called a _____ mutation.
13. Which type of mutation is trisomy 21, or Down Syndrome?
14. Explain why mutations are important for evolution.

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10.7: REGULATION OF GENE EXPRESSION

EXPRESS YOURSELF

This sketch in Figure **10.7.1** illustrates some of the variability in human cells. The shape and other traits that make each type of cell unique depend mainly on the particular proteins that the cell type makes. For example, an ovum is a cell with a large cytoplasm because it nourishes the embryo after fertilization. Sperm is a small cell with essentially just genetic material. The job of the sperm is to transfer genetic material to the ovum. The sketch shows various other cell types. Proteins are encoded in genes. All the cells in an organism have the same genes, so they all have the genetic instructions for the same proteins. Obviously, different types of cells must use, or express, different genes to make different proteins.

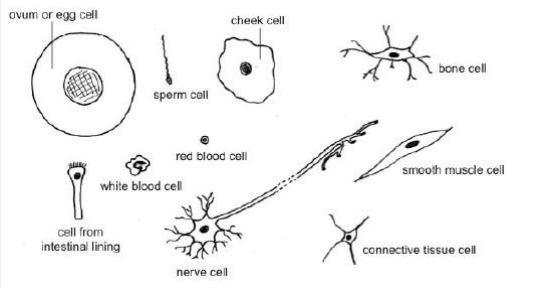


Figure **10.7.1**: Different cells have different shapes to perform their particular jobs.

WHAT IS GENE EXPRESSION?

Using a gene to make a protein is called **gene expression**. It includes the synthesis of the protein by the processes of transcription of DNA and translation of mRNA. It may also include further processing of the protein after synthesis.

Gene expression is regulated to ensure that the correct proteins are made when and where they are needed. Regulation may occur at any point in the expression of a gene, from the start of the transcription phase of protein synthesis to the processing of a protein after synthesis occurs. The regulation of transcription is one of the most complicated parts of gene regulation in eukaryotic cells and is the focus of this concept.

REGULATION OF TRANSCRIPTION

As shown in Figure **10.7.2**, transcription is controlled by **regulatory proteins** or **transcription factors**. These proteins bind to regions of DNA, called **regulatory elements** which are located near promoters. The **promoter** is the region of a gene where RNA polymerase binds to initiate transcription of the DNA to mRNA. After regulatory proteins bind to regulatory elements, the proteins can interact with RNA polymerase. Regulatory proteins are typically either activators or repressors. Activators are regulatory proteins that promote transcription by enhancing the interaction of RNA polymerase with the promoter. Repressors are regulatory proteins that prevent transcription by impeding the progress of RNA polymerase along the DNA strand so the DNA cannot be transcribed to mRNA.

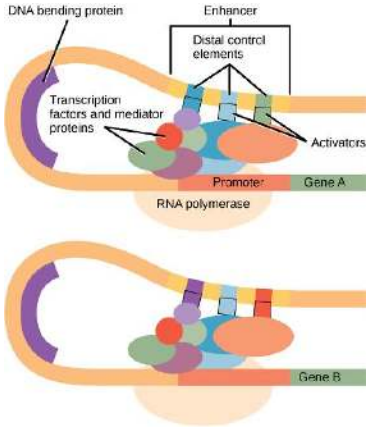


Figure **10.7.2**: An enhancer is a DNA sequence that promotes transcription. Each enhancer is made up of short DNA sequences called distal control elements. Activators bound to the distal control elements interact with mediator proteins and transcription factors. Two different genes may have the same promoter but different distal control elements, enabling differential gene expression.

ENHANCERS

Although regulatory proteins and elements are typically the key players in the regulation of transcription, other factors may also be involved. For example, regulation of transcription may also involve enhancers. Enhancers are distant regions of DNA that can loop back to interact with a gene's promoter and enhance transcription.

REGULATION DURING DEVELOPMENT

The regulation of gene expression is extremely important during the early development of an organism. Regulatory proteins must turn on certain genes in particular cells at just the right time so the individual develops normal organs and organ systems. **Homeobox genes** are a large group of genes that regulate development during the embryonic stage. In humans, there are an estimated 235 functional homeobox genes. They are present on every chromosome and generally grouped in clusters. Homeobox genes contain instructions for making chains of 60 amino acids called homeodomains. Proteins containing homeodomains are transcription factors that bind to and control the activities of other genes. The homeodomain is the part of the protein that binds to the target gene and controls its expression.

REVIEW

1. Define gene expression.
2. Why must gene expression be regulated?
3. Explain how regulatory proteins may activate or repress transcription.
4. Describe homeobox genes and their role in the development of an organism.
5. Discuss the role of regulatory gene mutations in cancer.

6. Explain the relationship between proto-oncogenes and oncogenes.
7. If a newly fertilized egg contained a mutation in a homeobox gene, what effect do you think this might have on the developing embryo? Explain your answer.
8. Which of the following are proteins?
   A. Repressors
   B. Promoters
   C. Regulatory elements
   D. All of the above
9. Which of the following is a region of DNA?
   A. Homeodomain
   B. Activator
   C. TATA box
   D. Both A and C
10. Compare and contrast enhancers and activators.
11. *True or False*. Mutations in genes that normally either promote or suppress cell division can both cause cancer.
12. *True or False*. Gene expression is only regulated at the transcriptional stage.
13. *True or False*. If RNA polymerase cannot bind to the promoter of a gene, it cannot transcribe that gene into mRNA.

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10.8: BIOTECHNOLOGY

PLEASE PASS THE POTATOES

You might want to pass on the potato plants pictured on the right in Figure **10.8.1**. They are infected with a virus, which is quickly killing them. The potato plants on the left are healthy and productive. Why aren't they infected with the same virus? The plants on the left have been engineered genetically, using methods of biotechnology, to make them resistant to the virus.



Figure **10.8.1**: Transgenic potatoes

WHAT IS BIOTECHNOLOGY?

Biotechnology is the use of technology to change the genetic makeup of living things for human purposes. Generally, the goal of biotechnology is to modify organisms so they are more useful to humans. For example, biotechnology may be used to create crops that yield more food or resist insect pests or viruses, such as the virus-resistant potatoes pictured above. Research is also underway to use biotechnology to cure human genetic disorders with gene therapy.

BIOTECHNOLOGY METHODS

Biotechnology uses a variety of techniques to achieve its aims. Two commonly used techniques are gene cloning and the polymerase chain reaction.

GENE CLONING

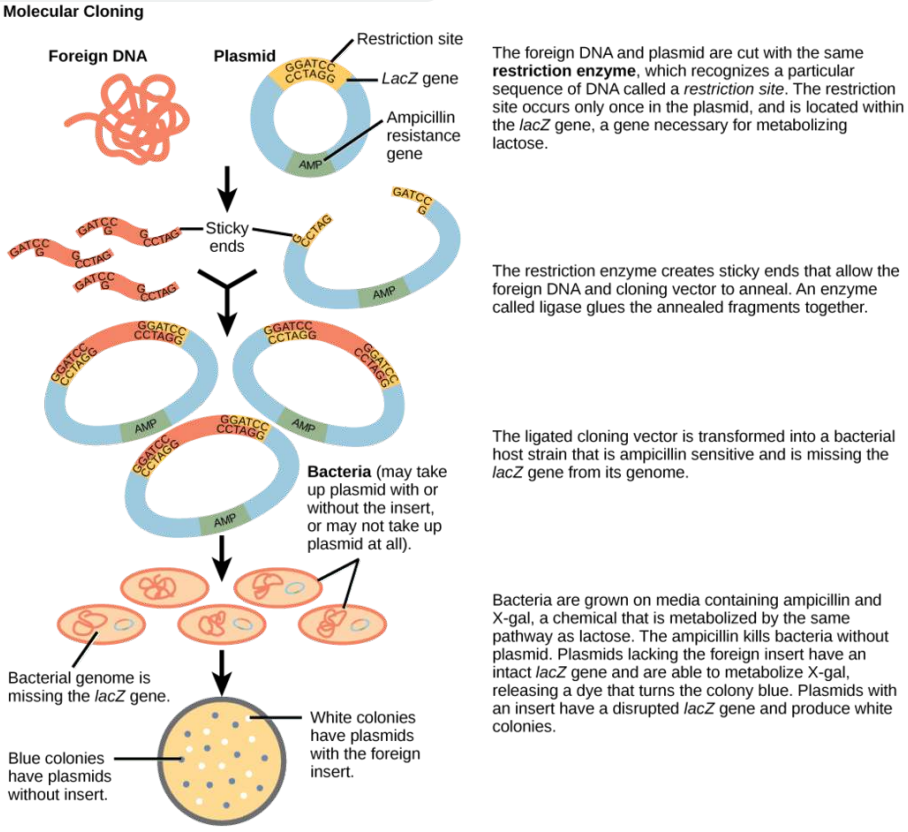


Figure **10.8.2**: The image illustrates the steps of gene cloning. First, DNA of interest is inserted into a plasmid and then the recombinant plasmid is inserted into bacteria. The successfully transformed bacteria are selected and grown to produce the protein of interest.

Gene cloning is the process of isolating and making copies of a gene. This is useful for many purposes. For example, gene cloning might be used to isolate and make copies of a normal gene for gene therapy. This is done by putting the gene in a bacterial plasmid. Plasmid DNA is circular DNA that is not part of a chromosome and can replicate independently. Gene cloning involves four steps: isolation, ligation, transformation, and selection. Refer to Figure **10.8.2** as you read below:

1. In the isolation step, a **restriction enzyme** is used to break DNA at a specific base sequence. This is done to isolate a gene in the foreign DNA. Restriction enzymes are mostly isolated from bacteria and they only cut DNA at a specific sequence in the DNA. That particular site is called the restriction site of that particular enzyme. The foreign DNA and plasmid are cut with the same restriction enzyme. The restriction enzyme creates "stick ends" which are short stretches of single stranded DNA at the cut site.
2. During ligation, the sticky end of the DNA plasmid binds to the sticky end of the isolated gene. The enzyme DNA Ligase glues the annealed fragments together. The DNA that results is called **recombinant DNA**.
3. In transformation, the recombinant DNA is inserted into a living cell, usually a bacterial cell. Changing an organism in this way is called **genetic engineering**.
4. Selection involves growing transformed bacteria to make sure they have the recombinant DNA. This is a necessary step because transformation is not always successful. Only bacteria that contain the recombinant DNA are selected for further use. Many different methods are used for selection, such are *lacZ* and antibiotic resistance genes.

POLYMERASE CHAIN REACTION

The **polymerase chain reaction (PCR)** makes many copies of a gene or other DNA segment. This might be done in order to make large quantities of a gene for genetic testing. PCR involves three steps: denaturing, annealing, and extension. The three steps are illustrated in Figure 10.8.3. They are repeated many times in a cycle to make large quantities of the gene.

1. Denaturing involves heating DNA to break the bonds holding together the two DNA strands. This yields two single strands of DNA.
2. Annealing involves cooling the single strands of DNA and mixing them with short DNA segments called primers. Primers have base sequences that are complementary to segments of the single DNA strands. As a result, bonds form between the DNA strands and primers.
3. Extension occurs when an enzyme (*Taq* polymerase or *Taq* DNA polymerase) adds nucleotides to the primers. This produces new DNA molecules, each incorporating one of the original DNA strands.

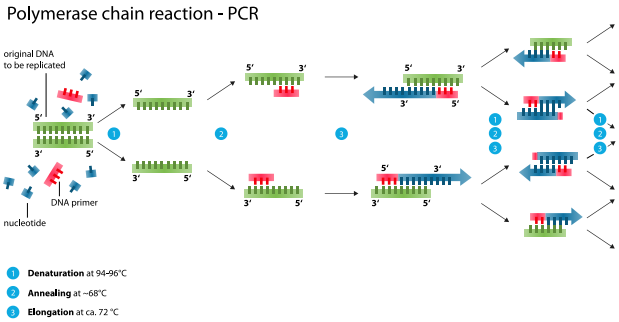


Figure **10.8.3**: The Polymerase Chain Reaction. Components of PCR, such as template DNA, primers, nucleotides, and polymerase, are assembled in a tube. The tube is inserted into a machine that controls and alters the temperature of the tube during PCR. The polymerase chain reaction involves three steps. In the first step, the temperature is increased to 94 to 96ºC to denature the template. In the second step, the temperature is lowered to about 68ºC so primers can anneal at their complement location on the single-stranded templates. Primers flank the targeted region on the template. In the third step, the temperature is increased to about 72ºC, so *Taq* polymerase can extend the strand from primer to create new DNA fragments. The enzyme *Taq* polymerase is used in PCR because it can withstand high temperatures. These three steps are repeated multiple times to created exponential copies of the targeted DNA fragment.

GEL ELECTROPHORESIS

Gel electrophoresis is an analytical technique used to separate DNA fragments by size and due to the negative charge on DNA. Notice in Figure 10.8.4 that the "gels" are rectangular in shape. The gels are made of a gelatin-like material of either agarose or polyacrylamide. An electric field, with a positive charge applied at one end of the gel, and a negative charge at the other end, forces the fragments to migrate through the gel. DNA molecules migrate from negative to positive charges due to the net negative charge of the phosphate groups in the DNA backbone. Longer molecules migrate more slowly through the gel matrix. After the separation is completed, DNA fragments of different lengths can be visualized using a fluorescent dye specific for DNA, such as ethidium bromide. The resulting stained gel shows bands correspond to DNA molecules of different lengths, which also correspond to different molecular weights. Band size is usually determined by comparison to DNA ladders containing DNA fragments of known length. Gel electrophoresis can also be used to separate RNA molecules and proteins.

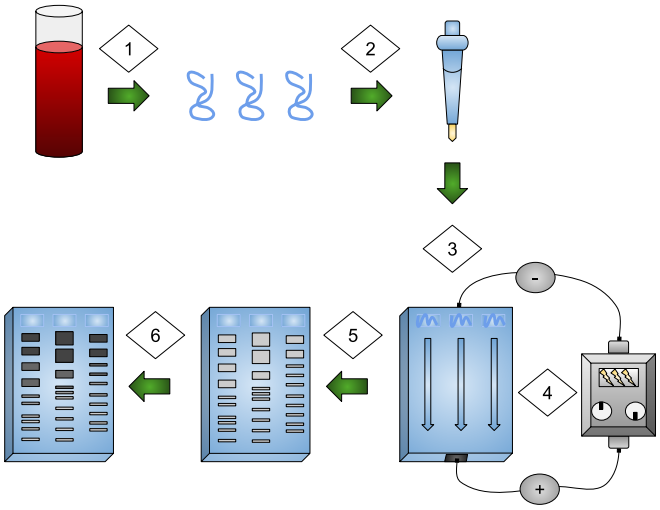


Figure **10.8.4**: This is a diagram that illustrates the process of DNA fingerprinting gel electrophoresis. DNA fingerprinting and is very useful in crime investigation since every individual has different DNA patterns in the image you see 6 steps. (1.) DNA can be extracted from any sample of body fluid(i.e. blood, semen, or saliva). DNA is mixed with restriction enzymes and amplified with PCR. (2 and 3.) The mixture of DNA fragment plus restriction enzyme is added into the wells of the agarose gel, which leads to a physical change instead of a chemical one. (4.) An electric current is applied to the gel from a power source. (5.) Negatively charged DNA moves toward the positive side. Larger fragments move slower and are located near the top whereas smaller fragments move faster and are near the bottom. (6.) Bands are stained but different shades indicate the amount of DNA each band contains

USES OF BIOTECHNOLOGY

Methods of biotechnology can be used for many practical purposes. They are used widely in both medicine and agriculture.

APPLICATIONS IN MEDICINE

In addition to gene therapy for genetic disorders, biotechnology can be used to transform bacteria so they are able to make human proteins. Proteins made by bacteria are injected into people who cannot produce them because of mutations.

Insulin was the first human protein to be produced in this way. Insulin helps cells take up glucose from the blood. People with type 1 diabetes have a mutation in the gene that normally codes for insulin. Without insulin, their blood glucose rises to harmfully high levels. At present, the only treatment for type 1 diabetes is the injection of insulin from outside sources. Until recently, there was no known way to make human insulin outside the human body. The problem was solved by gene cloning. The human insulin gene was cloned and used to transform bacterial cells, which could then produce large quantities of human insulin.

APPLICATIONS IN AGRICULTURE

Biotechnology has been used to create transgenic crops. **Transgenic crops** are genetically modified with new genes that code for traits useful to humans. Transgenic crops have been created with a variety of different traits, such as yielding more food, tasting better, surviving drought, tolerating salty soil, and resisting insect pests. Scientists have even created a transgenic purple tomato (Figure **10.8.5**) that contains high levels of cancer-fighting compounds called antioxidants.



Figure **10.8.5**: Transgenic Purple Tomatoes: Purple tomatoes are genetically modified to contain high levels of antioxidants. A gene for the compound was transferred into a normal red tomato plant.

ETHICAL, LEGAL, AND SOCIAL ISSUES

The use of biotechnology has raised a number of ethical, legal, and social issues. Here are just a few:

- Who owns genetically modified organisms such as bacteria? Can such organisms be patented like inventions?
- Are genetically modified foods safe to eat? Might they have unknown harmful effects on the people who consume them?
- Are genetically engineered crops safe for the environment? Might they harm other organisms or even entire ecosystems?
- Who controls a person's genetic information? What safeguards ensure that the information is kept private?
- How far should we go to ensure that children are free of mutations? Should a pregnancy be ended if the fetus has a mutation for a serious genetic disorder?
- Can we develop crop species that provide more nutrients and grow in harsher climates? If so, how do we ensure that farmers in impoverished areas have access to these?
- How do we educate the public so they can make well-informed decisions about new technologies?

As a society, we will need to balance the benefits and concerns of new technologies.

FEATURE: RELIABLE SOURCES

Genetically modified foods, or GM foods, are foods produced from genetically modified organisms. These are organisms that have had changes introduced into their DNA using methods of biotechnology. Commercial sale of GM foods began in 1994, with a tomato that had delayed ripening. By 2015, three major crops grown in the U.S. were raised mainly from GM seeds, including field corn, soybeans, and cotton. Many other crops were also raised from GM seeds, ranging from a variety of vegetables to sugar beets. Other sources of GM foods in our diet include meats, eggs, and dairy products from animals that have eaten GM feed, as well as a plethora of food products that contain some form of soy or corn products, such as soybean oil, soybean flour, corn oil, corn starch, and corn syrup. A quick

glance at the ingredients list of most processed foods shows that these products are added to many of the items in a typical American diet.

Most scientists think that GM foods are not any riskier to human health than conventional foods. Nonetheless, in many countries, including the U.S., GM foods are given more rigorous evaluations than conventional foods. For example, GM foods are assessed for toxicity, the ability to cause allergic reactions, and the stability of inserted genes. GM crops are also evaluated for possible environmental effects, such as **outcrossing**, which is the migration of genes from GM plants to conventional crops or wild plant species.

Despite the extra measures used to evaluate GM foods, there is a lot of public concern about them, including whether they are safe to human health, how they are labeled, and their environmental impacts. These concerns are based on a number of factors, such as the worrying belief that scientists are creating entirely new species and a perceived lack of benefits to the consumer of GM foods. People may also doubt the validity of risk assessments, especially with regard to long-term effects. Also, since all the research on safety and usefulness is presented in scientific journals, it can be difficult for the public to be fully informed about the work being done.

Over the past 50 years, there have been many hundreds of studies looking at how these crops affect the environment, the economy, and the health of humans and animals. The results of most of these studies are fairly clear. But, most people don't read the original findings because there are too many and because they can be difficult to understand. The National Academy of Sciences has written a report summarizing the research findings as well as public comments.

They explain the reason for writing the report: "Consumers in the United States and abroad get conflicting information about GM crops. Proponents tout the benefits while opponents emphasize the risks. There was a need for an independent, objective study to examine what had been learned about GM crops, assesses whether initial concerns and promises were realized since their introduction, and investigates new concerns and recent claims."

REVIEW

1. Define biotechnology.
2. What is recombinant DNA?
3. Identify the steps of gene cloning.
4. What is the purpose of the polymerase chain reaction?
5. Make a flow chart outlining the steps involved in creating a transgenic crop.
6. Explain how bacteria can be genetically engineered to produce a human protein.
7. Identify an ethical, legal, or social issue raised by biotechnology. State your view on the issue, and develop a logical argument to support your view.
8. Explain what primers are and what they do in PCR.
9. What is gel electrophoresis?
10. *True or False.* Transgenic crops can be created using recombinant DNA.
11. *True or False.* Gene cloning is defined as the creation of an identical copy of an entire organism.
12. The enzyme Taq polymerase was originally identified from bacteria that live in very hot environments, such as hot springs. Why does this fact make Taq polymerase particularly useful in PCR reactions?
13. A circular piece of DNA from bacteria that is often used to create recombinant DNA is called a _____ _.
14. In what ways are crops modified genetically? What traits are introduced, and what methods are used to introduce them?
15. What are the main human safety questions about GM foods? How is the human safety of GM foods assessed?
16. What are the main environmental concerns about GM crops? How is a risk assessment for the environment performed?
17. What are the major pros and cons of GM crops and foods? Who is most affected by these pros and cons? For example, for pros, do growers and marketers receive most of the benefits, or do consumers also reap rewards?
18. Which of the following is a possible use of biotechnology, now or in the future?

    A. Curing genetic disorders
    B. Creating transgenic crops that are resistant to pests
    C. Producing human proteins in non-human cells
    D. All of the above

19. Bacteria that contain a recombinant plasmid are said to be:

    A. Transformed
    B. Translated
    C. Transcripted
    D. A transgenic crop

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10.9: THE HUMAN GENOME

VITRUVIAN MAN

The drawing in Figure **10.9.2**, named *Vitruvian Man*, was created by Leonardo da Vinci in 1490. It was meant to show normal human body proportions. *Vitruvian Man* is used today to represent a different approach to the human body. It symbolizes a scientific research project that began in 1990, exactly 500 years after da Vinci created the drawing. That project, named the Human Genome Project, is the largest collaborative biological research project ever undertaken.

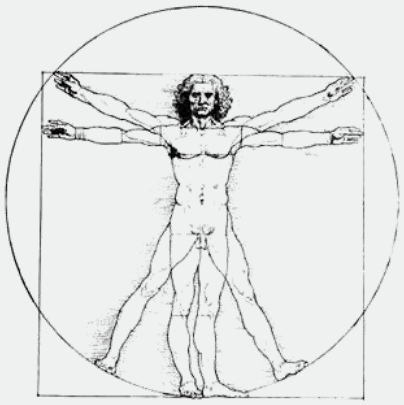


Figure **10.9.1**: Vitruvian man

WHAT IS THE HUMAN GENOME?

The **human genome** refers to all the DNA of the human species. Human DNA consists of 3.3 billion base pairs and is divided into more than 20,000 genes onto 23 pairs of chromosomes. The human genome also includes noncoding sequences (e.g. intergenic region) of DNA, as shown in Figure **10.9.2**.

DISCOVERING THE HUMAN GENOME

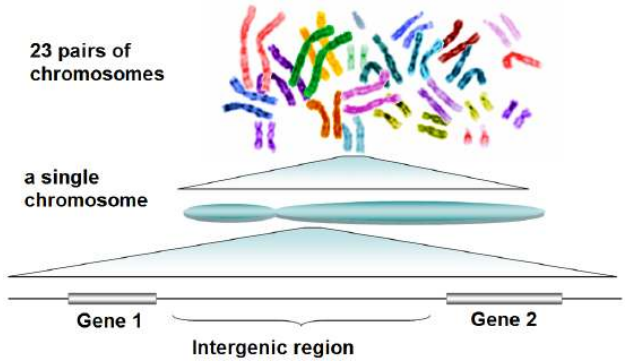


Figure **10.9.2**: Human Genome, Chromosomes, and Genes. Each chromosome of the human genome contains many genes as well as noncoding intergenic (between genes) regions. Each pair of chromosomes is shown here in a different color.

Scientists now know the sequence of all the DNA base pairs in the entire human genome. This knowledge was attained by the **Human Genome Project (HGP),** a $3 billion, international scientific research project that was formally launched in 1990. The project was completed in 2003, two years ahead of its 15-year projected deadline.

Determining the sequence of the billions of base pairs that make up human DNA was the main goal of the HGP. Another goal was mapping the location and determining the function of all the genes in the human genome. There are only about 20,500 genes in human beings.

A COLLABORATIVE EFFORT

Funding for the HGP came from the U.S. Department of Energy and the National Institutes of Health as well as from foreign institutions. The actual research was undertaken by scientists in 20 universities in the U.S., United Kingdom, Australia, France, Germany, Japan, and China. A private U.S. company named Celera also contributed to the effort. Although Celera had hoped to patent some of the genes it discovered, this was later denied.

REFERENCE GENOME OF THE HUMAN GENOME PROJECT

In 2003, the HGP published the results of its sequencing of DNA as a human reference genome. Figure **10.9.4** illustrates the process of DNA sequencing. The details of this image are out of the scope of this concept and book. The sequence of the human DNA is stored in databases available to anyone on the Internet. The U.S. National Center for Biotechnology Information (NCBI), part of the NIH, as well as comparable organizations in Europe and Japan, maintain the genomic sequences in a database known as Genbank. Protein sequences are also maintained in this database. The sequences in these databases are the combined sequences of anonymous donors, and as such do not yet address the individual differences that make us unique. However, the known sequence does lay the foundation to identify the unique differences among all of us. Most of the currently identified variations among individuals will be single nucleotide polymorphisms or SNPs. An SNP (pronounced "snip") is a DNA sequence variation occurring at a single nucleotide in the genome. For example, two sequenced DNA fragments from different individuals, GGATCTA to GGATTTA, contain a difference in a single nucleotide. If this, base change occurs in a gene, the base change then results in two alleles: the C allele and the T allele. Remember an allele is an alternative form of a gene. Almost all common SNPs have only two alleles. The effect of these SNPs on protein structure and function and any effect on the resulting phenotype are an extensive field of study.

BENEFITS OF THE HUMAN GENOME PROJECT

The sequencing of the human genome holds benefits for many fields, including molecular medicine and human evolution.

- Knowing the human DNA sequence can help us understand many human diseases. For example, it is helping researchers identify mutations linked to different forms of cancer. It is also yielding insights into the genetic basis of cystic fibrosis, liver

diseases, blood-clotting disorders, and Alzheimer's disease, among others.

- The human DNA sequence can also help researchers tailor medications to individual genotypes. This is called personalized medicine, and it has led to an entirely new field called pharmacogenomics. **Pharmacogenomics**, also called pharmacogenetics, is the study of how our genes affect the way we respond to drugs. You can read more about pharmacogenomics in the Feature below.
- The analysis of similarities between DNA sequences from different organisms is opening new avenues in the study of evolution. For example, analyses are expected to shed light on many questions about the similarities and differences between humans and our closest relatives the nonhuman primates.

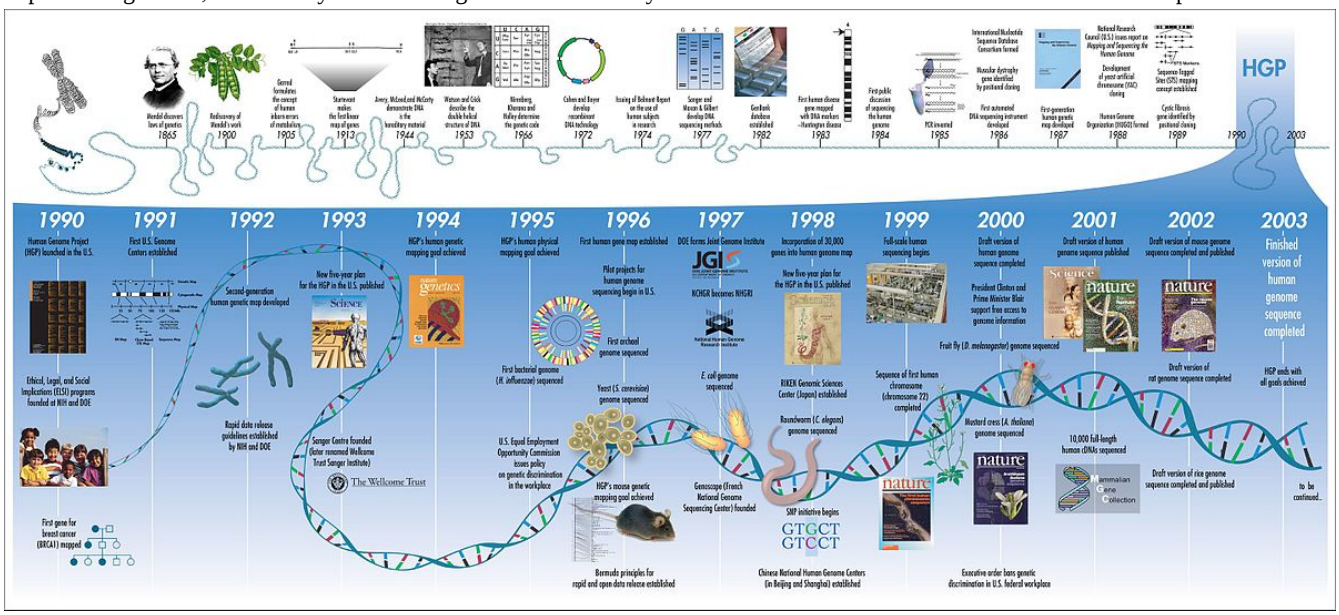


Figure **10.9.3**: Timeline of the human genome project from 1990 to 2003. The details of this timeline are more than we need here. You can see all the details at the NIH site.

ETHICAL, LEGAL, AND SOCIAL ISSUES OF THE HUMAN GENOME PROJECT

From its launch in 1990, the HGP proactively established and funded a separate committee to oversee potential ethical, legal, and social issues associated with the project. A major concern was the possible use of the knowledge generated by the project to discriminate against people. One issue was the fear that employers and health insurance companies would refuse to hire or insure people based on their genetic makeup, for instance, if they had genes that increased their risk of getting certain diseases. In response, in 1996, the U.S. passed the Health Insurance Portability and Accountability Act (HIPAA). It protects against unauthorized, nonconsensual release of individually identifiable health information to any entity not actively engaged in providing healthcare to a patient. This was followed in 2008 by the Genetic Information Nondiscrimination Act (GINA), which specifically prohibits genetic discrimination by health insurance companies and workplaces.

REVIEW

1. Describe the human genome.
2. What is the Human Genome Project?
3. Identify two main goals of the Human Genome Project.
4. What is the reference genome of the Human Genome Project? What is it based on?
5. Explain how knowing the sequence of DNA bases in the human genome is beneficial for molecular medicine.
6. What was one surprising finding of the Human Genome Project?
7. Why do you think scientists didn't just sequence the DNA from a single person for the Human Genome Project? Along those lines, why do you think it is important to include samples from different ethnic groups and genders in genome sequencing efforts?
8. *True or False.* The sequenced human genome does not include noncoding regions — it only includes actual genes.
9. *True or False.* Knowing the sequence of the human genome can give insight into human evolution.
10. What is pharmacogenomics?
    A. If a patient were to have pharmacogenomics done to optimize their medication, what do you think the first step would be?
    B. List one advantage and one disadvantage of pharmacogenomics.
11. There are approximately 20,000 human
    A. base pairs
    B. nucleotides
    C. alleles
    D. genes
12. Explain how the sequencing of the human genome relates to ethical concerns about genetic discrimination.

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10.10: CASE STUDY CONCLUSION- PARMACOGENOMICS AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: PHARMACOGENOMICS

Arya asked their doctor about Pharmacogenomics. The doctor explains to Arya that Pharmacogenomics is the tailoring of drug treatments to people's genetic makeup, a form of 'personalized medicine'.

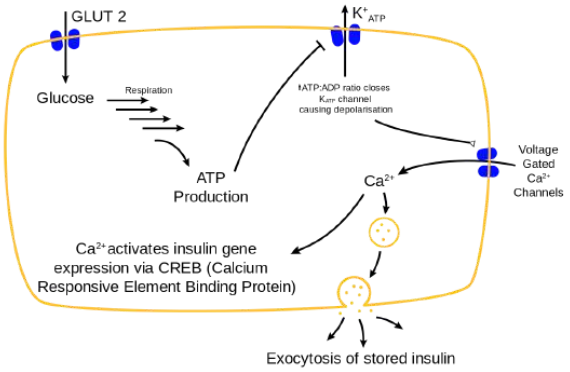


Figure **10.10.1**: Glucose insulin release.

Figure **10.10.1** shows a beta cell of the pancreas. As the blood glucose rises, it enters the cell via the GLUT 2 channel. After entering into the cell, it causes the production of ATP that closes the potassium pump. As potassium stops exiting the cell, it causes calcium channels to open and, finally, that causes insulin release from the cells. This process is even more complicated as many enzymes and proteins are skipped in this brief description of the pathway. The sulfonylurea-based drugs force the closing of a potassium pump by attaching it. This causes the release of insulin by skipping many steps. Because many enzymes and other proteins are involved in this complicated process, people respond differently to medicines. Most respond well and their health improves. Some do not gain any benefits from the treatment, and a minority suffer from side effects. After you take a drug, it is processed (metabolized) by your body. How the drug is processed and how you respond to it is determined, in part, by your genes. Understanding how different genetics affect and how a drug is processed can help doctors to more accurately determine which drug and which dose is best for individual patients. In this chapter, you learned what the genome is and how to recognize genes in the genome. In pharmacogenomics, scientists look at the genome of an individual to identify the genetic factors that influence his or her response to a drug. By finding these genes, medical researchers hope to develop genetic tests that will predict how patients will respond to a drug. This is personalized medicine.

The reason people vary in their responses to drug treatments lies in the genetic differences, or variation, between them. Following the Human Genome Project, research has focused on comparing human genomes to understand genetic variation and work out which genetic variants are important in health and in the way we respond to drugs. We also learned in this chapter that two types of variation are common in the human genome: 1) Single nucleotide polymorphisms (SNPs): changes in single nucleotide bases (A, C, G, and T). This was the case in Arya's physical response to the sulfonylurea. 2) Structural variation: changes affecting chunks of DNA that can consequently alter the structure of the entire chromosome. Structural variation can happen in a number of ways, for example, Copy number variation (CNV): when there is an increase or decrease in the amount of DNA. This can be due to: deletion, where an entire block of DNA is missing; insertion, where a block of DNA is added in duplication; or where there are additional copies of a section of DNA. Inversion: when chromosome breaks in two places and the resulting piece of DNA is reversed and reinserted back into the chromosome (the opposite way round). Translocation: when genetic material is exchanged between two different chromosomes. SNPs are like changing a single letter in the metaphorical 'recipe book of life', while structural variation is the equivalent of whole paragraphs or pages being lost or repeated. Scientists have been aware of SNPs for a long time, but the extent of structural variation was only revealed when it was possible to sequence and compare many genomes. The structural variation appears to be quite common, affecting around 12 percent of the genome. It has been found to cause a variety of genetic conditions.

FINDING DISEASE VARIANTS

Humans share around 99.5 percent of their genomes. The 0.5 percent that differs between each of us affects our susceptibility to disease and response to drugs. Although this doesn't sound like a lot, it still means that there are millions of differences between the DNA of two individuals. For example, because SNPs are common in the genome, it is difficult to work out which single letter changes cause disease and which are passengers that have just come along for the ride and have no effect on health.

SO HOW IS IT POSSIBLE TO KNOW WHICH GENETIC VARIANTS CAUSE DISEASE AND WHICH ARE PASSENGERS?

The way scientists look at disease variants is to compare the genetic makeup of a large number of people who have a specific disease with those who do not. This allows scientists to look for genetic variants that are more common in people with a disease compared to people without the disease. For example, if a particular genetic variant is present in 80 percent of patients with the disease but only 20 percent of the healthy population it suggests that this variant is increasing the risk of that disease. However, looking for a disease that is caused by variants in a single gene is the simplest example. There are many complex diseases where variants in many different genes might be involved. As well as the transcriptional and translational regulation of some enzyme production may vary due to the genetic variation in the enhancer and repressors of a gene. So,

for this type of comparison to be effective very large groups of people need to be studied, usually in the tens of thousands, to find the variants that have subtle effects on disease risk. Researchers also try to pick individuals with similar phenotypes, in both the diseased and healthy groups, so that the disease genes are easier to identify and study.

CHALLENGES OF PHARMACOGENOMICS

Although pharmacogenomics is likely to be an important part of future medical care, there are many obstacles to overcome before it becomes routine. It is relatively rare for a particular drug response to be affected by a single genetic variant. A particular genetic variant may increase the likelihood of an adverse reaction but it will not guarantee it.

As a result, some people with the variant may not experience an adverse reaction to a drug. Similarly, if an individual doesn't have the gene variant, it doesn't guarantee they won't experience an adverse reaction. Often, a large number of interacting genetic and environmental factors may influence the response to a drug.

Even when associations between a genetic variant and a drug response have been clearly demonstrated, suitable tests still have to be developed and proven to be effective in clinical trials. A test that has succeeded in a clinical trial still has to be shown to be useful and cost-effective in a healthcare setting. Regulatory agencies will have to consider how they assess and license pharmacogenetic products. Health services will have to adjust to new ways of deciding the best drug to give to an individual.

The behavior of individual doctors will need to change. A lot of side effects are due to patients not taking their drugs as prescribed or to doctors prescribing the wrong dose. Some examples of pharmacogenomics that work effectively, for example, *abacavir* for HIV, show that these challenges can be overcome. However, in most cases, implementing the findings from pharmacogenomics is likely to be a complicated process.

CHAPTER SUMMARY

- Determining that DNA is the genetic material was an important milestone in biology.
  - In the 1920s, Griffith showed that something in virulent bacteria could be transferred to nonvirulent bacteria and make them virulent as well.
  - In the 1940s, Avery and colleagues showed that the "something" Griffith found was DNA and not protein. This result was confirmed by Hershey and Chase, who demonstrated that viruses insert DNA into bacterial cells.
- In the 1950s, Chargaff showed that in DNA, the concentration of adenine is always the same as the concentration of thymine, and the concentration of guanine is always the same as the concentration of cytosine. These observations came to be known as Chargaff's rules.
- In the 1950s, James Watson and Francis Crick, building on the prior X-ray research of Rosalind Franklin and others, discovered the double-helix structure of the DNA molecule.
- Knowledge of DNA's structure helped scientists understand how DNA replicates, which must occur before cell division. DNA replication is semi-conservative because each daughter molecule contains one strand from the parent molecule and one new strand that is complementary to it.
- Genes that are located on the same chromosome are called linked genes. Linkage explains why certain characteristics are frequently inherited together.
- The central dogma of molecular biology can be summed up as DNA → RNA → Protein. This means that the genetic instructions encoded in DNA are transcribed to RNA, and then from RNA, they are translated into a protein.
- RNA is a nucleic acid. Unlike DNA, RNA consists of just one polynucleotide chain instead of two, contains the base uracil instead of thymine, and contains the sugar ribose instead of deoxyribose.
- The main function of RNA is to help make proteins. There are three main types of RNA: messenger RNA (mRNA), ribosomal RNA (rRNA), and transfer RNA (tRNA).
- According to the RNA world hypothesis, RNA was the first type of biochemical molecule to evolve, predating both DNA and proteins.
- The genetic code was cracked in the 1960s by Marshall Nirenberg. It consists of the sequence of nitrogen bases in a polynucleotide chain of DNA or RNA. The four bases make up the "letters" of the code. The letters are combined in groups of three to form code "words," or codons, each of which encodes for one amino acid or a start or stop signal.
  - AUG is the start codon, and it establishes the reading frame of the code. After the start codon, the next three bases are read as the second codon, and so on until a stop codon is reached.
  - The genetic code is universal, unambiguous, and redundant.
- Protein synthesis is the process in which cells make proteins. It occurs in two stages: transcription and translation
  - Transcription is the transfer of genetic instructions in DNA to mRNA in the nucleus. It includes the steps of initiation, elongation, and termination. After the mRNA is processed, it carries the instructions to a ribosome in the cytoplasm.
  - Translation occurs at the ribosome, which consists of rRNA and proteins. In translation, the instructions in mRNA are read, and tRNA brings the correct sequence of amino acids to the ribosome. Then rRNA helps bonds form between the amino acids, producing a polypeptide chain.
  - After a polypeptide chain is synthesized, it may undergo additional processing to form the finished protein.
- Mutations are random changes in the sequence of bases in DNA. They are the ultimate source of all new genetic variation in any species
  - Mutations may happen spontaneously during DNA replication or transcription. Other mutations are caused by

environmental factors called mutagens.
    - Germline mutations occur in gametes and may be passed on to offspring. Somatic mutations occur in other cells than gametes and cannot be passed on to offspring.
    - Chromosomal alterations are mutations that change chromosome structure or number and usually affect the organism in multiple ways. Down syndrome (trisomy 21) is an example of a chromosomal alteration.
    - Point mutations are changes in a single nucleotide. The effects of point mutations depend on how they change the genetic code and may range from no effects to very serious effects.
    - Frameshift mutations change the reading frame of the genetic code and are likely to have a drastic effect on the encoded protein.
    - Many mutations are neutral and have no effects on the organism in which they occur. Some mutations are beneficial and improve fitness, while others are harmful and decrease fitness.
- Using a gene to make a protein is called gene expression. Gene expression is regulated to ensure that the correct proteins are made when and where they are needed. Regulation may occur at any stage of protein synthesis or processing.
- The regulation of transcription is controlled by regulatory proteins that bind to regions of DNA called regulatory elements, which are usually located near promoters. Most regulatory proteins are either activators that promote transcription or repressors that impede transcription.
- The regulation of gene expression is extremely important during the early development of an organism. Homeobox genes, which encode for chains of amino acids called homeodomains, are important genes that regulate development.
- Some types of cancer occur because of mutations in genes that control the cell cycle. Cancer-causing mutations most often occur in two types of regulatory genes, called tumor-suppressor genes and proto-oncogenes.
- Biotechnology is the use of technology to change the genetic makeup of living things for human purposes.
    - Biotechnology methods include gene cloning and the polymerase chain reaction. Gene cloning is the process of isolating and making copies of a DNA segment such as a gene. The polymerase chain reaction makes many copies of a gene or other DNA segment.
    - Biotechnology can be used to transform bacteria so they are able to make human proteins, such as insulin. It can also be used to create transgenic crops, such as crops that yield more food or resist insect pests.
    - Biotechnology has raised a number of ethical, legal, and social issues including health, environmental, and privacy concerns.
- The human genome refers to all of the DNA of the human species. It consists of more than 3.3 billion base pairs divided into 20,500 genes on 23 pairs of chromosomes.
- The Human Genome Project (HGP) was a multi-billion dollar international research project that began in 1990. By 2003, it had sequenced and mapped the location of all of the DNA base pairs in the human genome. It published the results as a human reference genome that is available to anyone on the Internet.
- The sequencing of the human genome is helping researchers better understand cancer and genetic diseases. It is also helping them tailor medications to individual patients, which is the focus of the new field of pharmacogenomics. In addition, it is helping researchers better understand human evolution.

REVIEW:

1. Put the following units in order from the smallest to the largest:
    A. chromosome
    B. gene
    C. nitrogen base
    D. nucleotide
    E. codon
2. Put the following processes in the correct order of how a protein is produced, from earliest to latest:
    A. tRNA binding to mRNA
    B. transcription
    C. traveling of mRNA out of the nucleus
    D. folding of the polypeptide
3. What are the differences between a sequence of DNA and the sequence of mature mRNA that it produces?
4. Scientists sometimes sequence DNA that they “reverse transcribe” from the mRNA in an organism’s cells, which is called complementary DNA (cDNA). Why do you think this technique might be particularly useful for understanding an organism’s proteins versus sequencing the whole genome (i.e. nuclear DNA) of the organism?
5. What are proteins are made in the cytoplasm on small organelles called?
6. What might happen if codons encoded for more than one amino acid?
7. Explain why a human gene can be inserted into bacteria and can still produce the correct human protein, despite being in a very different organism.
8. *True or False*. All of your genes are expressed by all the cells of your body.
9. What does The central dogma of molecular biology describe?

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CHAPTER OVERVIEW

11: CELL REPRODUCTION

This chapter introduces two types of cell divisions. First, it explains mitosis and then meiosis. This chapter also explains why cells divide and how the divisions are regulated. The errors in the division may lead to diseases, such as leukemia.

11.1: Case Study- Genetic Similarities and Differences
11.2: Cell Cycle and Cell Division
11.3: Mitotic Phase - Mitosis and Cytokinesis
11.4: Mutations and Cancer
11.5: Sexual Reproduction- Meiosis and gametogenesis
11.6: Genetic Variation
11.7: Mitosis vs. Meiosis and Disorders
11.8: Case Study Conclusion- Genes and Chapter Summary

Thumbnail: Image of the mitotic spindle in a human cell showing microtubules in green, chromosomes (DNA) in blue, and kinetochores in red. (Public Domain; Afunguy).

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11.1: CASE STUDY- GENETIC SIMILARITIES AND DIFFERENCES

CASE STUDY: ABNORMAL CELL DIVISION

Like the little children in Figure **11.1.1**, seven-year-old Kim is battling leukemia, a type of cancer that affects blood cells. Leukemia usually starts in the bone marrow, where blood cells are produced. It causes the production of abnormal blood cells, most commonly white blood cells, but it can affect other types of blood cells depending on the type of leukemia. The abnormal blood cells replace the patient's normal blood cells over time. This can lead to symptoms such as fatigue, frequent infections, and easy bruising or bleeding. Leukemia can be fatal, but fortunately, there are some treatment options available that can prolong life and even may cure the disease.



Figure **11.1.1**: Pediatric patients receiving chemotherapy

Kim has undergone chemotherapy to kill the cancerous cells, but his doctors have told his parents that it is not enough. Kim needs a bone marrow transplant in order to replace his abnormal bone marrow with healthy bone marrow. His family members are eager to donate bone marrow to him, but first, they must be tested to see if they are a compatible match.

Unlike blood transfusions where it is relatively easy to find a compatible blood donor, bone marrow transplants require much more specific matching between donor and recipient. They must share several of the same types of proteins, called human leukocyte antigens (HLAs), on the surface of their cells. One type of HLA protein is illustrated in Figure **11.1.2**. Different people have different types of HLA proteins, or markers, depending on their specific genes. Typically, eight to ten HLA markers are tested and compared in the potential bone marrow donor and recipient. At least six or seven of these HLA markers need to be identical between them in order for a match to be made.

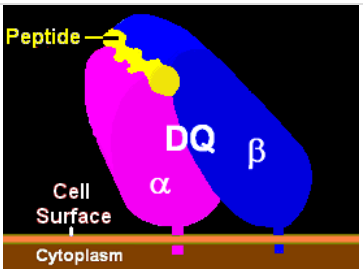


Figure **11.1.2**: An illustration of a human leukocyte antigen protein, HLA-DQ, attached to the surface of a cell, showing its α (pink) and β (blue) chains.

If the match is not good, the patient's body could reject the bone marrow transplant, or, conversely, the transplanted bone marrow could produce immune cells that attack the patient's body. A good match between donor and recipient is critical for bone marrow donation to be safe and effective.

A full sibling frequently provides the best match for bone marrow donation because they share many of the same genes from their parents. Kim's sister is tested, but unfortunately, she is not a match for him. This is not all that surprising since there is only about a 25% chance that a sibling will be an identical HLA match. His parents and other family members are also tested, but none of them is a match either. Kim must join the 70% of patients that need to look outside of their families for a bone marrow donor.

Read the rest of this chapter to learn more about how cells originate from cells. Why one damaged cell gives rise to more damaged cells which can lead to diseases like cancer. You will also learn why not every cell becomes cancerous and why cancerous cells divide uncontrollably. You will also learn why two siblings are not exact copies of each other.

CHAPTER OVERVIEW: CELL REPRODUCTION

In this chapter, you will learn about:

- The phases of the cell cycle and how cells divide through mitosis.
- How cancer can result from an unregulated cell division due to a mutation.
- Sexual reproduction.
- Differences and similarities between sexual and asexual reproduction.

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

- How cancer originates?
- Why every person doesn't have cancer?
- How chemotherapy kills cancerous cells?
- Why Kim's sister and other family members do not have exactly the same HLA markers?

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11.2: CELL CYCLE AND CELL DIVISION

SO MANY CELLS!

The baby in Figure **11.2.1** has a lot of growing to do before they are as big as their mom. Most of their growth will be the result of cell division. By the time the baby is an adult, their body will consist of trillions of cells. Cell division is just one of the stages that all cells go through during their life. This includes cells that are harmful, such as cancer cells. Cancer cells divide more often than normal cells and grow out of control. In fact, this is how cancer cells cause illness. In this concept, you will read about how cells divide, what other stages cells go through, and what causes cancer cells to divide out of control and harm the body.



Figure **11.2.1**: Baby and mother

THE CELL CYCLE

Cell division is the process in which one cell, called the parent cell, divides to form two new cells, referred to as daughter cells. How this happens depends on whether the cell is prokaryotic or eukaryotic. Cell division is simpler in prokaryotes than eukaryotes because prokaryotic cells themselves are simpler. Prokaryotic cells have a single circular chromosome, no nucleus, and few other organelles. Eukaryotic cells, in contrast, have multiple chromosomes contained within a nucleus and many other organelles. All of these cell parts must be duplicated and then separated when the cell divides. Cell division is just one of several stages that a cell goes through during its lifetime. The **cell cycle** is a repeating series of events that include growth, DNA synthesis, and cell division. The cell cycle in prokaryotes is quite simple: the cell grows, its DNA replicates, and the cell divides. This form of division in prokaryotes is called asexual reproduction. In eukaryotes, the cell cycle is more complicated.

EUKARYOTIC CELL CYCLE

Figure **11.2.2** represents the cell cycle of a eukaryotic cell. As you can see, the eukaryotic cell cycle has several phases. The mitotic phase (M) includes both mitosis and cytokinesis. This is when the nucleus and then the cytoplasm divide. The other three phases (G_1, S, and G_2) are generally grouped together as **interphase**. During interphase, the cell grows, performs routine life processes, and prepares to divide. These phases are discussed below.

INTERPHASE

The Interphase of the eukaryotic cell cycle can be subdivided into the following phases (Figure **11.2.2**).

- **Growth Phase 1 (G_1):** The cell spends most of its life in the first gap (sometimes referred to as growth) phase, G_1. During this phase, a cell undergoes rapid growth and performs its routine functions. During this phase, the biosynthetic and metabolic activities of the cell occur at a high rate. The synthesis of amino acids and hundreds of thousands or millions of proteins that are required by the cell occurs during this phase. Proteins produced include those needed for DNA replication. If a cell is not dividing, the cell enters the G_0 phase from this phase.
- **G_0 phase:** The G_0 phase is a resting phase where the cell has left the cycle and has stopped dividing. Non-dividing cells in multicellular eukaryotic organisms enter G_0 from G_1. These cells may remain in G_0 for long periods of time, even indefinitely, such as with neurons. Cells that are completely differentiated may also enter G_0. Some cells stop dividing when issues of sustainability or viability of their daughter cells arise, such as with DNA damage or degradation, a process called **cellular senescence**. Cellular senescence occurs when normal diploid cells lose the ability to divide, normally after about 50 cell divisions.
- **Synthesis Phase (S):** Dividing cells enter the Synthesis (S) phase from G_1. For two genetically identical daughter cells to be formed, the cell's DNA must be copied through DNA replication. When the DNA is replicated, both strands of the double helix are used as templates to produce two new complementary strands. These new strands then hydrogen bond to the template strands and two double helices form. During this phase, the amount of DNA in the cell has effectively doubled, though the cell remains in a diploid state.
- **Growth Phase 2 (G_2):** The second gap (growth) (G_2) phase is a shortened growth period in which many organelles are reproduced or manufactured. Parts necessary for mitosis and cell division are made during G_2, including **microtubules** used in the mitotic spindle.

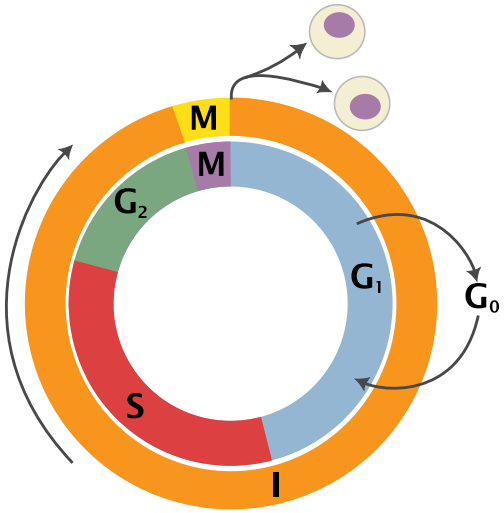


Figure 11.2.2: Eukaryotic Cell Cycle. The First Gap (G1), Synthesis (S), and Second Gap (G2) phases make up interphase (I). The mitotic phase (yellow M) includes mitosis (purple M) and cytokinesis. During cytokinesis two cells result. Some cells do not divide and they enter into G_0 phage.

MITOTIC PHASE

Before a eukaryotic cell divides, all the DNA in the cell's multiple chromosomes is replicated. Its organelles are also duplicated. This happens in the interphase. Then, when the cell divides (mitotic phase), it occurs in two major steps, called **mitosis** and **cytokinesis**, both of which are described in greater detail in the concept *Mitotic Phase: Mitosis and Cytokinesis*.

- The first step in the mitotic phase of a eukaryotic cell is mitosis, a multi-phase process in which the nucleus of the cell divides. During mitosis, the nuclear envelope (membrane) breaks down and later reforms. The chromosomes are also sorted and separated to ensure that each daughter cell receives a complete set of chromosomes.
- The second major step is cytokinesis. This step, which occurs in prokaryotic cells as well, is when the cytoplasm divides and two daughter cells form.

Table 11.2.2: Cell Cycle Summary

State	Name	Description
Quiescent Senescent	Resting phase (G0)	A resting phase where the cell has left the cycle and has stopped dividing.
Interphase	1st growth phase (G_1) Synthesis phase (S) 2ndgrowth phase (G_2)	Cells increase in size in G1. Cells perform their normal activities. DNA replication occurs during this phase. The cell will continue to grow and many organelles will divide during their phase.
Cell division	Mitosis (M)	Cell growth stops at this stage. Mitosis divides the nucleus into two nuclei, followed by cytokinesis which divides the cytoplasm. Two genetically identical daughter cells result.

CONTROL OF THE CELL CYCLE

If the cell cycle occurred without regulation, cells might go from one phase to the next before they were ready. What controls the cell cycle? How does the cell know when to grow, synthesize DNA, and divide? The cell cycle is controlled mainly by regulatory proteins. These proteins control the cycle by signaling the cell to either start or delay the next phase of the cycle. They ensure that the cell completes the previous phase before moving on. Regulatory proteins control the cell cycle at key checkpoints, which are shown in Figure 11.2.3. There are a number of main checkpoints:

1. The G1 checkpoint: just before entry into the S phase, makes the key decision of whether the cell big enough to divide. If the cell is not big enough, it goes into the resting period (G_0)
2. DNA synthesis Checkpoint: The S checkpoint determines if the DNA has been replicated properly.
3. The mitosis checkpoint: This checkpoint ensures that all the chromosomes are properly aligned before the cell is allowed to divide.

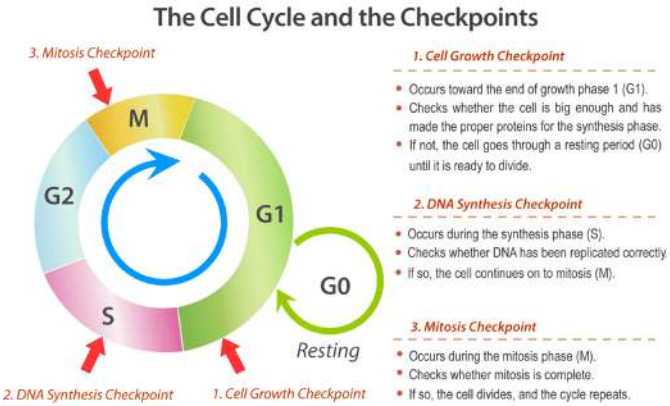


Figure 11.2.3: Checkpoints in the eukaryotic cell cycle ensure that the cell is ready to proceed before it moves on to the next phase of the cycle.

CANCER AND THE CELL CYCLE

Cancer is a disease that occurs when the cell cycle is no longer regulated. This happens because a cell's DNA becomes damaged. This results in mutations in the genes that regulate the cell cycle. Damage can occur due to exposure to hazards such as radiation or toxic chemicals. Cancerous cells generally divide much faster than normal cells. They may form a mass of abnormal cells called a **tumor** (see Figure 11.2.4). The rapidly dividing cells take up nutrients and space that normal cells need. This can damage tissues and organs and eventually lead to death. When uncontrolled cell division happens in the bone marrow, abnormal and nonfunctional blood cells are produced because the division is happening before the cell is ready for division. In these types of cancer, there is not any evident tumor.

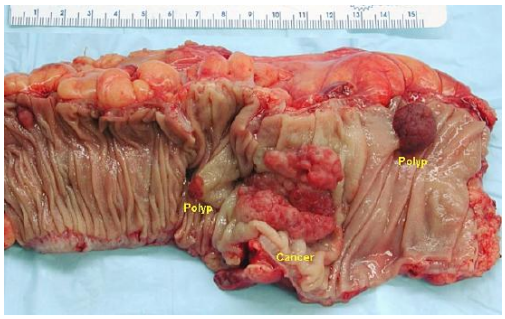


Figure **11.2.4**: Gross appearance of an opened large intestine specimen containing an invasive **colorectal carcinoma** and two **adenomatous polyps**. The cancer cells have grown out of control and forming a tumor.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Henrietta Lacks sought treatment for her cancer at Johns Hopkins University Hospital at a time when researchers were trying to grow human cells in the lab for medical testing. Despite many attempts, the cells always died before they had undergone many cell divisions. Mrs. Lacks's doctor took a small sample of cells from her tumor without her knowledge and gave them to a Johns Hopkins researcher, who tried to grow them on a culture plate. For the first time in history, human cells grown on a culture plate kept dividing...and dividing and dividing and dividing. Copies of Henrietta's Lacks cells — called HeLa cells for her name — are still alive today. In fact, there are currently many billions of HeLa cells in laboratories around the world!

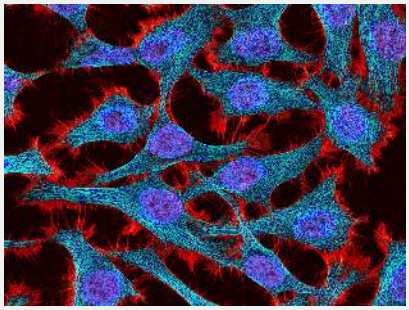


Figure **11.2.5**: Fluorescently dyed HeLa Cells. The woman named Henrietta Lacks died in 1951 of an unusual form of cervical cancer, she was just 31 years old. A poor, African-American tobacco farmer and mother of five, she (or at least her cells) would eventually be called immortal.

Why Henrietta Lacks' cells lived on when other human cells did not is still something of a mystery, but they are clearly extremely hardy and resilient cells. By 1953, when researchers learned of their ability to keep dividing indefinitely, factories were set up to start producing the cells commercially on a large scale for medical research. Since then, HeLa cells have been used in thousands of studies and have made possible hundreds of medical advances. For example, Jonas Salk used the cells in the early 1950s to test his polio vaccine. Over the decades since then, HeLa cells have been used to make important discoveries in the study of cancer, AIDS, and many other diseases. The cells were even sent to space on early space missions to learn how human cells respond to zero gravity. HeLa cells were also the first human cells ever cloned, and their genes were some of the first ever mapped. It is almost impossible to overestimate the profound importance of HeLa cells to human biology and medicine.

You would think that Henrietta Lacks' name would be well known in medical history for her unparalleled contributions to biomedical research. However, until 2010, her story was virtually unknown. That year, a science writer named Rebecca Skloot published a nonfiction book about Henrietta Lacks, named *The Immortal Life of Henrietta Lacks*. Based on a decade of research, the book is riveting, and it became an almost instantaneous best seller. As of 2016, Oprah Winfrey and collaborators planned to make a movie based on the book, and in recent years, numerous articles about Henrietta Lacks have appeared in the press.

Ironically, Henrietta herself never knew her cells had been taken, and neither did her family. While her cells were making a lot of money and building scientific careers, her children were living in poverty, too poor to afford medical insurance. The story of Henrietta Lacks and her immortal cells raises ethical issues about human tissues and who controls them in biomedical research. However, there is no question that Henrietta Lacks deserves far more recognition for her contribution to the advancement of science and medicine.

REVIEW

1. What are the two main phases of the cell cycle in a eukaryotic cell?
2. Describe the three phases of interphase in a eukaryotic cell.
3. Explain how the cell cycle is controlled.
4. How is cancer-related to the cell cycle?
5. What are the two major steps of cell division in a eukaryotic cell?
6. In which phase of the eukaryotic cell cycle do cells typically spend most of their lives?
7. Which phases of the cell cycle will have cells with twice the amount of DNA? Explain your answer.
8. If there is damage to a gene that encodes for a cell cycle regulatory protein, what do you think might happen? Explain your answer.
9. *True or False*. Cells go into G_0 if they do not pass the G_1 checkpoint.
10. In which phase within interphase does the cell make final preparations to divide?
    A. Mitosis
    B. Cytokinesis
    C. G_2
    D. S
11. What were scientists trying to do when they took tumor cells from Henrietta Lacks? Why did they specifically use tumor cells to try to achieve their goal?

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11.3: MITOTIC PHASE - MITOSIS AND CYTOKINESIS

DIVIDE AND SPLIT

Can you guess what this colorful image represents? It shows a eukaryotic cell during the process of cell division. In particular, the image shows the nucleus of the cell dividing. In eukaryotic cells, the nucleus divides before the cell itself splits in two; and before the nucleus divides, the cell's DNA is replicated, or copied. There must be two copies of the DNA so that each daughter cell will have a complete copy of the genetic material from the parent cell. How is the replicated DNA sorted and separated so that each daughter cell gets a complete set of genetic material? To answer that question, you first need to know more about DNA and the forms it takes.

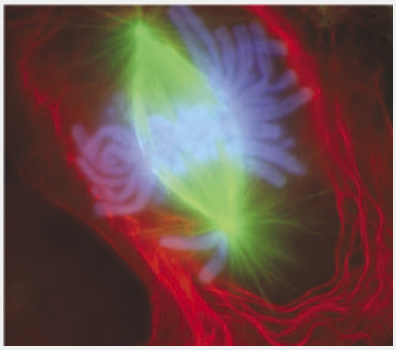


Figure 11.3.1: Dividing cell stained with fluorescent dyes. You can see chromosomes in blue and spindles in green.

THE FORMS OF DNA

Except when a eukaryotic cell divides, its nuclear DNA exists as a grainy material called **chromatin.** Only when a cell is about to divide and its DNA has replicated does DNA condense and coil into the familiar X-shaped form of a **chromosome,** like the one shown in Figure 11.3.2. Because DNA has already replicated, each chromosome actually consists of two identical copies. The two copies of a chromosome are called sister **chromatids.** Sister chromatids are joined together at a region called a centromere.

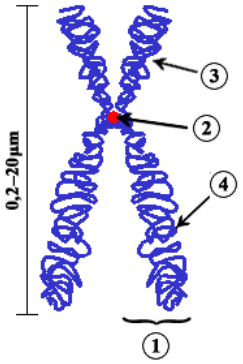


Figure 11.3.2: Chromosome. After DNA replicates, it forms X-shaped chromosomes like the one shown here. 1. Chromatid, 2. Centromere, 3. short arm, 4. long arm. Centromere contains proteins called kinetochores (not shown) where spindles attach during mitosis.

The process in which the nucleus of a eukaryotic cell divides is called **mitosis.** During mitosis, the two sister chromatids that make up each chromosome separate from each other and move to opposite poles of the cell. Mitosis occurs in four phases. The phases are called prophase, metaphase, anaphase, and telophase. They are shown in Figure 11.3.3 and described in detail below.

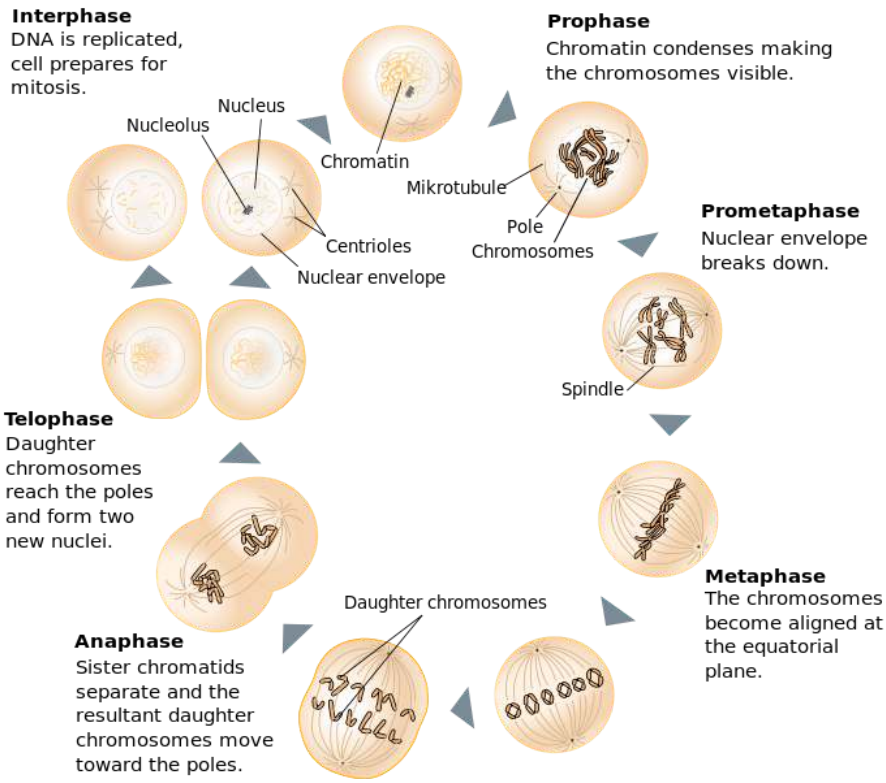


Figure **11.3.3**: Mitosis is the phase of the eukaryotic cell cycle that occurs between DNA replication and the formation of two daughter cells. Mitosis has four substages, prophase, metaphase, anaphase, and telophase.

PROPHASE

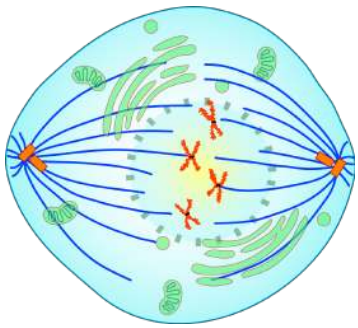


Figure **11.3.4**: Prophase in later stage is called prometaphase. The spindle starts to form during the prophase of mitosis. The spindles start to attach to the Kinetochores of centromeres of sister chromatids during Prometaphase.

The first and longest phase of mitosis is prophase. During prophase, chromatin condenses into chromosomes, and the nuclear envelope (the membrane surrounding the nucleus) breaks down. In animal cells, the centrioles near the nucleus begin to separate and move to opposite poles of the cell. Centrioles are small organelles found only in eukaryotic cells that help ensure the new cells that form after cell division each contain a complete set of chromosomes. As the centrioles move apart, a spindle starts to form between them. The blue spindle, shown in Figure **11.3.4**, consists of fibers made of microtubules.

METAPHASE

During **metaphase**, spindle fibers fully attach to the centromere of each pair of sister chromatids. As you can see in Figure **11.3.5**, the sister chromatids line up at the equator, or center, of the cell. The spindle fibers ensure that sister chromatids will separate and go to different daughter cells when the cell divides. Some spindles do not attach to the kinetochore protein of the centromeres. These spindles are called non-kinetochore spindles that help in the elongation of the cell. This is visible in Figure **11.3.5**.

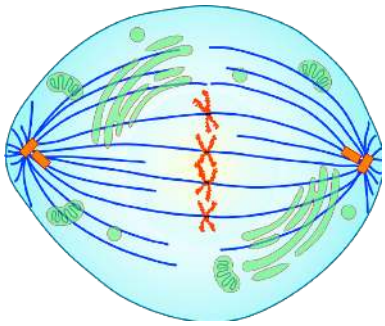


Figure **11.3.5**: Chromosomes, consisting of sister chromatids, line up at the equator or middle of the cell during metaphase. The blue lines are spindles, and the orange rectangles at the cell poles are centrioles. Some spindles from the opposing centrioles attach with each other, and some spindles attach to the kinetochores of the sister chromosomes from their respective sides. Each chromosome is attached to two spindles.

ANAPHASE

During **anaphase**, sister chromatids separate and the centromeres divide. The sister chromatids are pulled apart by the shortening of the spindle fibers. This is a little like reeling in a fish by shortening the fishing line. One sister chromatid moves to one pole of the cell, and the other sister chromatid moves to the opposite pole (see Figure

11.3.6). At the end of anaphase, each pole of the cell has a complete set of chromosomes

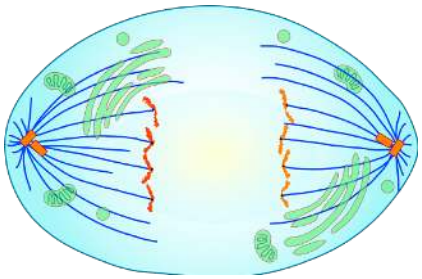


Figure 11.3.6: Anaphase: Sister chromatids break apart and move to the opposite pole with the help of spindles. The newly separated sister chromatids are called chromosomes now.

TELOPHASE

The chromosomes reach the opposite poles and begin to *decondense* (unravel), relaxing once again into a stretched-out chromatin configuration. The mitotic spindles are depolymerized into tubulin monomers that will be used to assemble cytoskeletal components for each daughter cell. Nuclear envelopes form around the chromosomes, and nucleosomes appear within the nuclear area (see Figure 11.3.7.

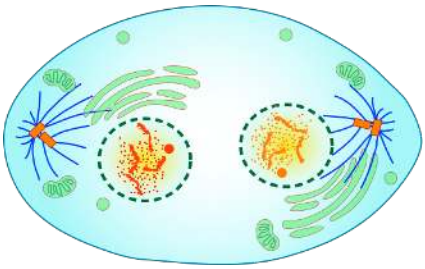


Figure 11.3.7: Telophase: The chromosomes decondense, spindles start to disappear, two nuclei form in a cell.

CYTOKINESIS

Cytokinesis is the final stage of cell division in eukaryotes as well as prokaryotes. During cytokinesis, the cytoplasm splits in two and the cell divides. The process is different in plant and animal cells, as you can see in Figure 11.3.8. In animal cells, the plasma membrane of the parent cell pinches inward along the cell's equator until two daughter cells form. In the plant cells, a cell plate forms along the equator of the parent cell. Then, a new plasma membrane and cell wall form along each side of the cell plate.

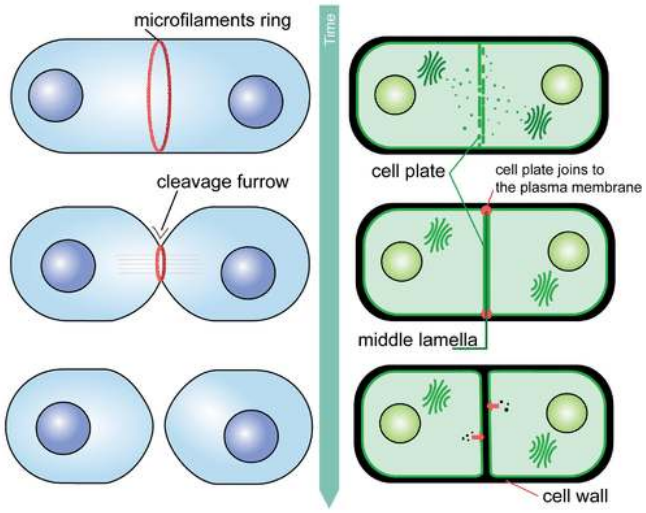


Figure 11.3.8: Cytokinesis is the final stage of eukaryotic cell division. It occurs differently in animal (left) and plant (right) cells. You can see a microfilament ring forming at the center of the elongated animal cell. This creates a depression called cleavage furrow. This invagination ultimately separates the cell cytoplasm into two cells. A cell plate forms at the center of the elongated plant cell. Then a new plasma membrane and cell wall form along each side of the cell plate.

REVIEW

1. Describe the different forms that DNA takes before and during cell division in a eukaryotic cell.
2. Identify the four phases of mitosis in an animal cell, and summarize what happens during each phase.
3. Explain what happens during cytokinesis in an animal cell.
4. What are the main differences between mitosis and cytokinesis?
5. The familiar X-shaped chromosome represents:
   A. How DNA always looks in eukaryotic cells
   B. How DNA in eukaryotic cells looks once it is replicated and the cell is about to divide
   C. Female sex chromosomes only
   D. How DNA appears immediately after cytokinesis
6. Which of the following is not part of a chromosome in eukaryotic cells?
   A. Centriole
   B. Centromere
   C. Chromatid
   D. DNA
7. What do you think would happen if the sister chromatids of one of the chromosomes did not separate during mitosis?
8. Put the following processes in order of when they occur during cell division, from first to last:
   A. separation of sister chromatids
   B. DNA replication
   C. cytokinesis
   D. lining up of chromosomes in the center of the cell
   E. condensation and coiling of DNA into a chromosome

9. Why do you think the nuclear envelope breaks down at the start of mitosis?
10. What are the fibers made of microtubules that attach to the centromeres during mitosis are called?
11. *True or False.* Chromosomes begin to uncoil during anaphase.
12. *True or False.* During cytokinesis in animal cells, sister chromatids line up along the equator of the cell.
13. *True or False.* After mitosis, the result is typically two daughter cells with identical DNA to each other.

EXPLORE MORE

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11.4: MUTATIONS AND CANCER

WHAT WOULD HAPPEN IF THIS CYCLE PROCEEDS AT WILL?

Your cells may grow and divide without performing their necessary functions, or without fully replicating their DNA, or without copying their organelles. Probably not much good could come of that. So the cell cycle needs to be highly regulated and tightly controlled. And it is.

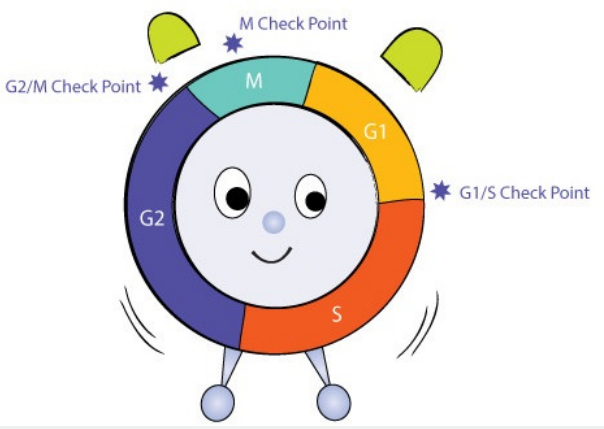


Figure **11.4.1**: Cell Cycle

CONTROL OF THE CELL CYCLE

How does the cell know when to divide? How does the cell know when to replicate its DNA? How does the cell know when to proceed into mitosis or cytokinesis? The answers to these questions have to do with the control of the cell cycle. But how is the cell cycle controlled or regulated? Regulation of the cell cycle involves processes crucial to the survival of a cell. These include the detection and repair of damage to DNA, as well as the prevention of uncontrolled cell division. Uncontrolled cell division can be deadly to an organism; its prevention is critical for survival.

CYCLINS AND KINASES

The cell cycle is controlled by a number of protein-controlled feedback processes. Two types of proteins involved in the control of the cell cycle are **kinases** and **cyclins**. Cyclins activate kinases by binding to them, specifically they activate **cyclin-dependent kinases (CDK)**. **Kinases** are enzymes that catalyze the transfer of a phosphate group from ATP to another molecule in a cell. They function as a control switch in many cellular functions, turning a function on or off, and regulating other cellular processes. Many times they are involved in activating a cascade of reactions. Cyclins comprise a group of proteins that are rapidly produced at key stages in the cell cycle. Once activated by a cyclin, CDK enzymes activate or inactivate other target molecules through phosphorylation. It is this precise regulation of proteins that triggers advancement through the cell cycle. Leland H. Hartwell, R. Timothy Hunt, and Paul M. Nurse won the 2001 Nobel Prize in Physiology or Medicine for their discovery of these critical proteins.

WHAT MAKES A CELL CANCEROUS?

Cancer is a disease characterized by a population of cells that grow and divide without respect to normal limits. These cancerous cells invade and destroy adjacent tissues, and they may spread throughout the body. The process by which normal cells are transformed into cancer cells is known as **carcinogenesis**. This process is also known as oncogenesis or tumorigenesis.

Nearly all cancers are caused by mutations in the DNA of abnormal cells. These mutations may be due to the effects of **carcinogens**, cancer-causing agents such as tobacco smoke, radiation, chemicals, or infectious agents. These carcinogens may act as an environmental "trigger," stimulating the onset of cancer in certain individuals and not others. Do all people who smoke get cancer? No. Can secondhand smoke increase a nonsmoking person's chance of developing lung cancer? Yes. It also increases a nonsmoking person's chance of developing heart disease.

Complex interactions between carcinogens and an individual's genome may explain why only some people develop cancer after exposure to an environmental trigger and others do not. Do all cancers need an environmental trigger to develop? No. Cancer-causing mutations may also result from errors incorporated into the DNA during replication, or they may be inherited. Inherited mutations are present in all cells of the organism.

ONCOGENES AND TUMOR SUPPRESSOR GENES

Some types of cancer occur because of mutations in genes that control the cell cycle. Cancer-causing mutations most often occur in two types of regulatory genes, called proto-oncogenes and tumor-suppressor genes.

- Proto-oncogenes are genes that normally help cells divide. When a proto-oncogene mutates to become an oncogene, it is continuously active, even when it is not supposed to be. This is like a car's accelerator pedal being stuck at full throttle. The car keeps racing at top speed. In the case of a cell, the cell keeps dividing out of control, which can lead to cancer.
- Tumor suppressor genes are genes that normally slow down or stop cell division. When a mutation occurs in a tumor suppressor gene, it can no longer control cell division. This is like a car without brakes. The car can't be slowed or stopped. In the case of a cell, the cell keeps dividing out of control, which can lead to cancer.

Several Mutations to Cause Cancer

Oncogenes may be growth factors, protein kinases, GTPases or transcription factors. **Growth factors** are naturally occurring substances, usually a protein or steroid hormone, capable of stimulating cellular growth, proliferation, and differentiation. They are important for regulating a variety of cellular processes. Usually, they must bind to an extracellular or intracellular receptor to initiate a cellular reaction.

Typically, a series of several mutations that constitutively activate oncogenes and inactivate tumor suppressor genes is required to transform a normal cell into a cancer cell (Figure **11.4.2**). Cells have developed a number of control mechanisms to overcome mutations in proto-oncogenes. Therefore, a cell needs multiple mutations to transform into a cancerous cell. A mutation in one proto-oncogene would not cause cancer, as the effects of the mutation would be masked by the normal control of the cell cycle and the actions of tumor suppressor genes. Similarly, a mutation in one tumor suppressor gene would not cause cancer either, due to the presence of many "backup" genes that duplicate its functions. It is only when enough proto-oncogenes have mutated into oncogenes and enough tumor suppressor genes have been deactivated that the cancerous transformation can begin. Signals for cell growth overwhelm the signals for growth regulation, and the cell quickly spirals out of control. Often, because many of these genes regulate the processes that prevent most damage to the genes themselves, DNA damage accumulates as one ages.

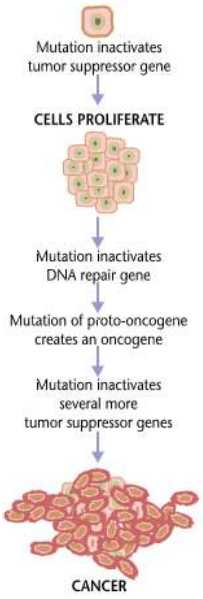


Figure **11.4.2**: How Cancer Develops. Mutations in a tumor suppressor gene allow the proliferation of cells. As many times the cells divide, they acquire more mutation. Some mutations may lead to the inactivation of the DNA repair genes. Also, proto-oncogenes may convert into oncogenes due to mutations. Several other mutations inactivate many tumor suppressor genes. Eventually, a series of mutations in tumor-suppressor genes and proto-oncogenes leads to cancer

Usually, oncogenes are dominant alleles, as they contain gain-of-function mutations. The actions of the mutant allele gene product, many times resulting in a constitutively activated protein, are dominant to the gene product produced by the "normal" allele. Meanwhile, mutated tumor suppressors are generally recessive alleles, as they contain loss-of-function mutations. A proto-oncogene needs only a mutation in one copy of the gene to generate an oncogene; a tumor suppressor gene needs a mutation in both copies of the gene to render both products defective. There are instances when, however, one mutated allele of a tumor suppressor gene can render the other copy non-functional. These instances result in what is known as a dominant negative effect.

REVIEW

1. Define cancer.
2. What are cyclin-dependent kinases? What is their role?
3. Discuss the role of oncogenes and tumor suppressor genes in carcinogenesis.
4. Why are multiple mutations required for transformation into a cancerous cell?
5. Identify all the categories of oncogenes and describe two categories.

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11.5: SEXUAL REPRODUCTION- MEIOSIS AND GAMETOGENESIS

ALL IN THE FAMILY

The family photo in Figure **11.5.1** illustrates an important point. Children in a family resemble their parents and each other, but the children are never exactly the same unless they are identical twins. Each of the children in the photo inherited a unique combination of traits from the parents. In this concept, you will learn how this happens. It all begins with sex — sexual reproduction, that is.



Figure **11.5.1**: Family photo

SEXUAL REPRODUCTION

Why do you look similar to your parents, but not identical? First, it is because you have two parents. Second, it is because of sexual reproduction. Whereas asexual reproduction produces genetically identical clones, sexual reproduction produces genetically diverse individuals. **Sexual reproduction** is the creation of a new organism by combining the genetic material of two organisms. As both parents contribute half of the new organism's genetic material, the offspring will have traits of both parents, but will not be exactly like either parent.

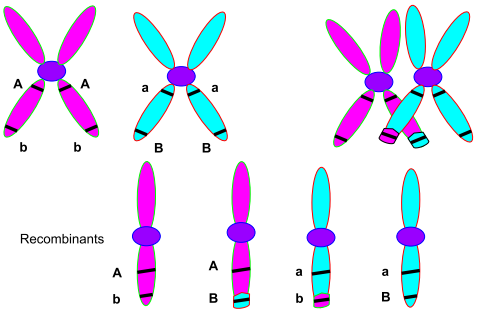


Figure **11.5.2**: Crossing over occurs during meiosis I, and is the process where homologous chromosomes pair up with each other and exchange different segments of their genetic material to form recombinant chromosomes. In some species crossing over is essential for the normal segregation of chromosomes during meiosis. Crossing over also increases genetic variation, because due to the swapping of genetic material during crossing over, the chromatids held together by the centromere are no longer identical. So, when the chromosomes go on to meiosis II and separate, some of the daughter cells receive daughter chromosomes with recombined alleles. Due to this genetic recombination, the offspring have a different set of alleles and genes than their parents do. In the diagram, genes B and b are crossed over with each other, making the resulting recombinants after meiosis Ab, AB, ab, and aB.l.

Organisms that reproduce sexually by joining **gametes**, a process known as **fertilization**, must have a mechanism to produce **haploid** gametes. This mechanism is **meiosis**, a type of cell division that halves the number of chromosomes. During meiosis, the pairs of chromosomes separate and segregate randomly to produce gametes with one chromosome from each pair. Meiosis involves two nuclear and cell divisions without interphase in between, starting with one diploid cell and generating four haploid cells. Each division, named meiosis I and meiosis II, has four stages: prophase, metaphase, anaphase, and telophase. These stages are similar to those of mitosis, but there are distinct and important differences.

Prior to meiosis, the cell's DNA is replicated, generating chromosomes with two sister chromatids. A human cell prior to meiosis will have 46 chromosomes, 22 pairs of homologous autosomes, and 1 pair of sex chromosomes. **Homologous chromosomes** (Figure **11.5.2**), or homologs, are similar in size, shape, and genetic content; they contain the same genes, though they may have different alleles of those genes. The genes/alleles are at the same **loci** on homologous chromosomes. You inherit one chromosome of each pair of homologs from your mother and the other one from your father. Sexual reproduction is the primary method of reproduction for the vast majority of multicellular organisms, including almost all animals and plants. Fertilization joins two haploid gametes into a **diploid** zygote, the first cell of a new organism. The zygote enters G1 of the first cell cycle, and the organism begins to grow and develop through mitosis and cell division.

MEIOSIS

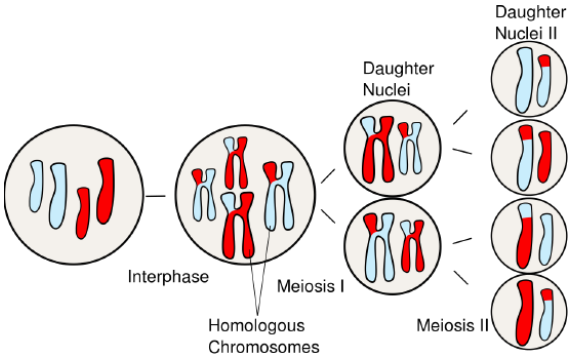


Figure **11.5.3**: Overview of Meiosis. During meiosis, homologous chromosomes separate and go to different daughter cells. This diagram shows just the nuclei of the cells. Notice the exchange of genetic material that occurs prior to the first cell division.

The process that produces haploid gametes is called meiosis. **Meiosis** is a type of cell division in which the number of chromosomes is reduced by half. It occurs only in certain special cells of an organism. In mammals, Meiosis occurs only in gamete producing cells within the gonads. During meiosis, homologous (paired) chromosomes separate, and haploid cells form that have only one chromosome from each pair. Figure **11.5.3** gives an overview of meiosis.

As you can see from the meiosis diagram, two cell divisions occur during the overall process, so a total of four haploid cells are produced. The two cell divisions are called meiosis I and meiosis II.

Meiosis I begins after DNA replicates during interphase. Meiosis II follows meiosis I without DNA replicating again. Both meiosis I and meiosis II occur in four phases, called prophase, metaphase, anaphase, and telophase. You may recognize these four phases from mitosis, the division of the nucleus that takes place during routine cell division of eukaryotic cells.

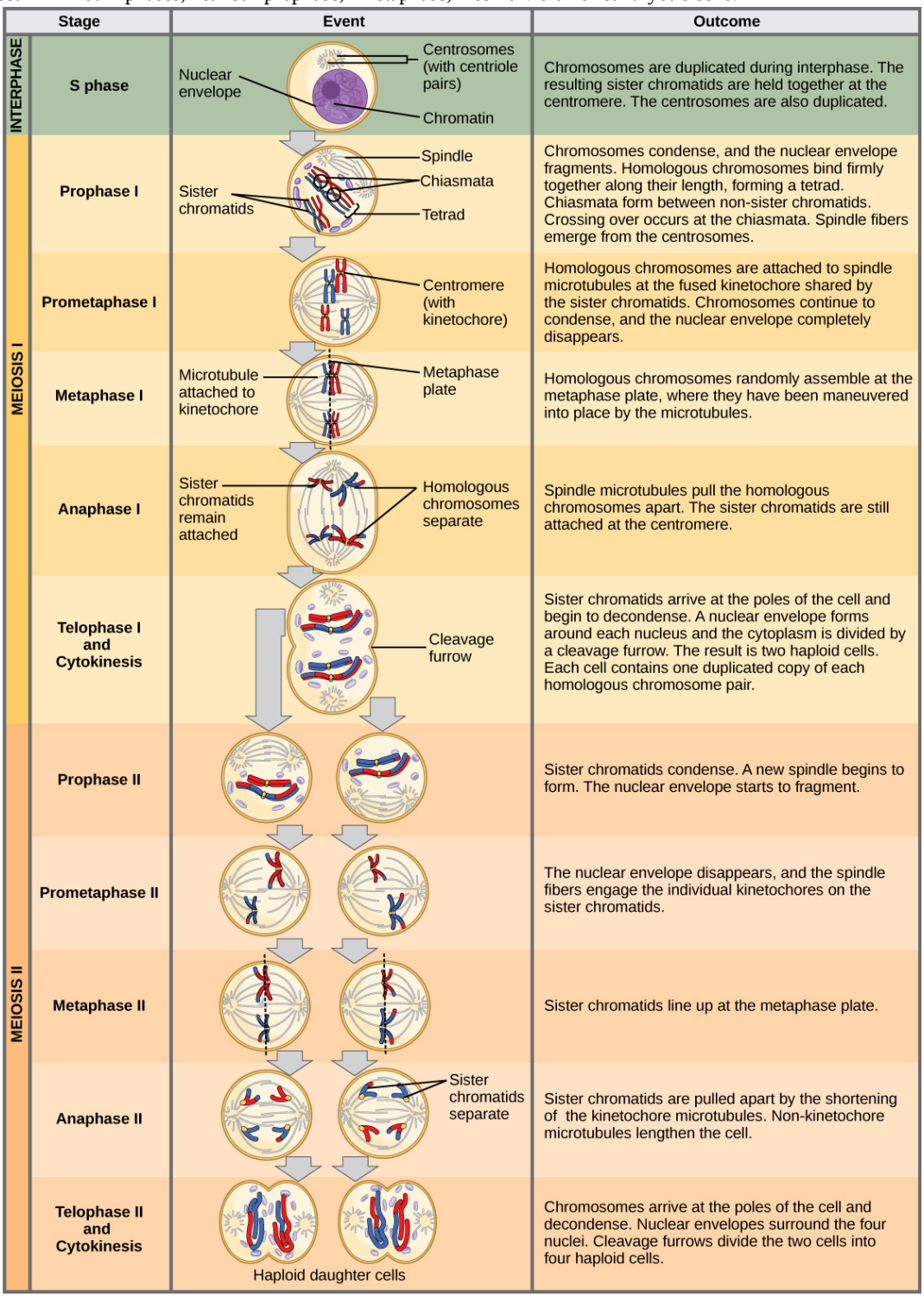


Figure **11.5.4**: Complete Stages of Meiosis: An animal cell with a diploid number of four (2n = 4) proceeds through the stages of meiosis to form four haploid daughter cells.

MEIOSIS I

1. **Prophase I**: The nuclear envelope begins to break down, and the chromosomes condense. Centrioles start moving to opposite poles of the cell, and a spindle begins to form. Importantly, homologous chromosomes pair up, which is unique to prophase I. In prophase of mitosis and meiosis II, homologous chromosomes do not form pairs in this way. During prophase I,

crossing-over occurs. The significance of crossing-over is discussed in the next section called variations.

2. **Metaphase I**: Spindle fibers attach to the paired homologous chromosomes. The paired chromosomes line up along the equator of the cell. This occurs only in metaphase I. In metaphase of mitosis and meiosis II, it is sister chromatids that line up along the equator of the cell.
3. **Anaphase I**: Spindle fibers shorten, and the chromosomes of each homologous pair start to separate from each other. One chromosome of each pair moves toward one pole of the cell, and the other chromosome moves toward the opposite pole.
4. **Telophase I** and Cytokinesis: The spindle breaks down, and new nuclear membranes form. The cytoplasm of the cell divides, and two haploid daughter cells result. The daughter cells each have a random assortment of chromosomes, with one from each homologous pair. Both daughter cells go on to meiosis II.

MEIOSIS II

1. **Prophase II**: The nuclear envelope breaks down and the spindle begins to form in each haploid daughter cell from meiosis I. The centrioles also start to separate.
2. **Metaphase II**: Spindle fibers line up the sister chromatids of each chromosome along the equator of the cell.
3. **Anaphase II**: Sister chromatids separate and move to opposite poles.
4. **Telophase II** and **Cytokinesis**: The spindle breaks down, and new nuclear membranes form. The cytoplasm of each cell divides, and four haploid cells result. Each cell has a unique combination of chromosomes.

GAMETOGENESIS

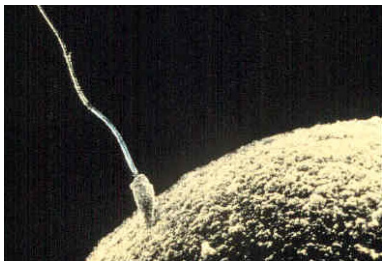


Figure **11.5.5**: A human sperm is a tiny cell with a tail. A human egg is much larger. Both cells are mature haploid gametes that are capable of fertilization. What process is shown in this photograph?

At the end of meiosis, four haploid cells have been produced, but the cells are not yet gametes. The cells need to develop before they become mature gametes capable of fertilization. The development of diploid cells into gametes is called **gametogenesis**. It differs between males and females.

- A gamete produced by a male is called a **sperm,** and the process that produces a mature sperm is called **spermatogenesis**. During this process, a sperm cell grows a tail and gains the ability to “swim,” like the human sperm cell shown in the figure below.
- A gamete produced by a female is called an **egg,** and the process that produces a mature egg is called **oogenesis**. Just one egg is produced from the four haploid cells that result from meiosis. The single egg is a very large cell, as you can see from the human egg also shown in Figure **11.5.5**.

SPERMATOGENESIS

Spermatogenesis occurs in the wall of the **seminiferous tubules**, with **stem cells** at the periphery of the tube and the spermatozoa at the **lumen** of the tube. Immediately under the capsule of the tubule are diploid, undifferentiated cells. These stem cells, called spermatogonia (singular: spermatagonium), go through mitosis with one offspring going on to differentiate into a sperm cell, while the other gives rise to the next generation of sperm.

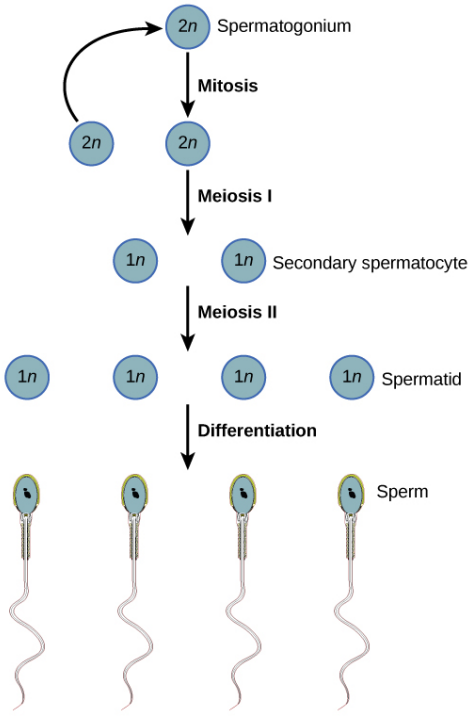


Figure **11.5.6**: Spermatogenesis During spermatogenesis, four sperm result from each primary spermatocyte, which divides into two haploid secondary spermatocytes; these cells will go through a second meiotic division to produce four spermatids.

Meiosis begins with a cell called a primary spermatocyte. At the end of the first meiotic division, a haploid cell is produced called a secondary spermatocyte. This haploid cell must go through another meiotic cell division. The cell produced at the end of meiosis is called a spermatid. When it reaches the lumen of the tubule and grows a flagellum (or "tail"), it is called a sperm cell. Four sperm result from each primary spermatocyte that goes through meiosis.

Stem cells are deposited during gestation and are present at birth through the beginning of adolescence but in an inactive state. During adolescence, gonadotropic hormones from the anterior pituitary cause the activation of these cells and the production of viable sperm. This continues into old age.

OOGENESIS

Oogenesis occurs in the outermost layers of the ovaries. As with sperm production, oogenesis starts with a germ cell, called an oogonium (plural: oogonia), but this cell undergoes mitosis to

increase in number, eventually resulting in up to one to two million cells in the embryo.

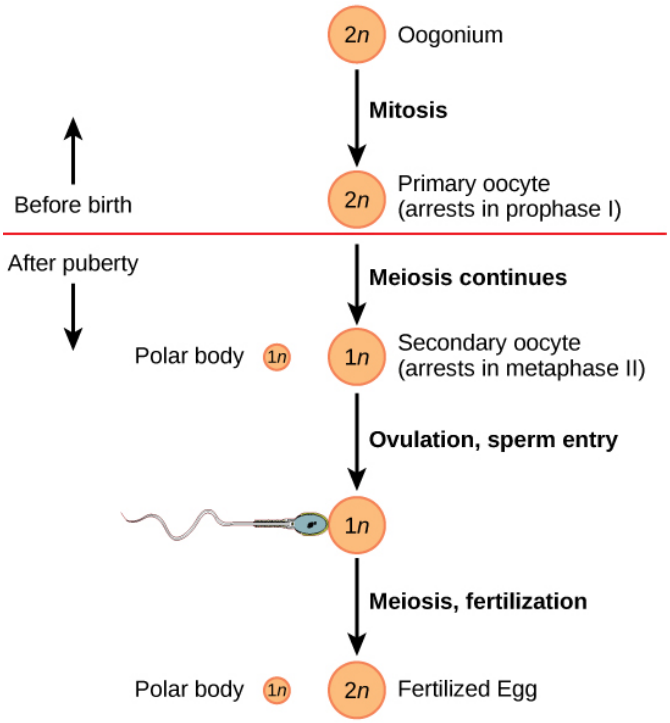


Figure **11.5.7**: Oogenesis The process of oogenesis occurs in the ovary's outermost layer. A primary oocyte begins the first meiotic division but then arrests until later in life when it will finish this division in a developing follicle. This results in a secondary oocyte, which will complete meiosis if it is fertilized.

The cell starting meiosis is called a primary oocyte. This cell will begin the first meiotic division, but be arrested in its progress in the first prophase stage. At the time of birth, all future eggs are in the prophase stage. At adolescence, anterior pituitary hormones cause the development of a number of follicles in an ovary. This results in the primary oocyte finishing the first meiotic division. The cell divides unequally, with most of the cellular material 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. A secondary meiotic arrest occurs, this time at the metaphase II stage. At ovulation, this secondary oocyte will be released and travel toward the uterus through the oviduct. If the secondary oocyte is fertilized, the cell continues through the meiosis II, completing meiosis, producing a second polar body and a fertilized egg containing all 46 chromosomes of a human being, half of them coming from the sperm.

REVIEW

1. Explain how sexual reproduction occurs at the cellular level.
2. Summarize what happens during meiosis.
3. Compare and contrast gametogenesis in males and females.
4. Explain mechanisms that increase genetic variation in offspring produced by sexual reproduction.
5. Why do gametes need to be haploid? What would happen to the chromosome number after fertilization if they were diploid?
6. Describe one difference between prophase I of meiosis and prophase of mitosis.
7. Do all of the chromosomes that you got from your mother go into one of your gametes? Why or why not?
8. *True or False*. Crossing-over is the exchange of genetic material between sister chromatids.
9. *True or False*. Human sperms are haploid.
10. *True or False*. Sister chromatids separate from each other during meiosis I.
11. How many cells are produced after a single cell goes through meiosis?
12. Which stage of meiosis (prophase I or II; metaphase I or II; anaphase I or II; telophase I or II) best fits the descriptions below? Choose only one for each description.

    A. Pairs of homologous chromosomes line up along the equator of the cell
    B. Sister chromatids separate
    C. Homologous chromosomes separate from each other

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11.6: GENETIC VARIATION

WHAT HELPS ENSURE THE SURVIVAL OF A SPECIES?

Genetic variation. It is this variation that is the essence of evolution. Without genetic differences among individuals, "survival of the fittest" would not be likely. Either all survive, or all perish.



Figure **11.6.1**: Profile photos

GENETIC VARIATION

Sexual reproduction results in infinite possibilities of genetic variation. In other words, sexual reproduction results in offspring that are genetically unique. They differ from both parents and also from each other. This occurs for a number of reasons.

- When homologous chromosomes form pairs during prophase I of meiosis I, crossing-over can occur. **Crossing-over** is the exchange of genetic material between homologous chromosomes. It results in new combinations of genes on each chromosome.
- When cells divide during meiosis, homologous chromosomes are randomly distributed to daughter cells, and different chromosomes segregate independently of each other. This called is called **independent assortment**. It results in gametes that have unique combinations of chromosomes.
- In sexual reproduction, two gametes unite to produce an offspring. But which two of the millions of possible gametes will it be? This is likely to be a matter of chance. It is obviously another source of genetic variation in offspring. This is known as **random fertilization.**

All of these mechanisms working together result in an amazing amount of potential variation. Each human couple, for example, has the potential to produce more than 64 trillion genetically unique children. No wonder we are all different!

CROSSING-OVER

Crossing-over occurs during prophase I, and it is the exchange of genetic material between non-sister chromatids of homologous chromosomes. Recall during prophase I, homologous chromosomes line up in pairs, gene-for-gene down their entire length, forming a configuration with four chromatids, known as a **tetrad**. At this point, the chromatids are very close to each other and some material from two chromatids switch chromosomes, that is, the material breaks off and reattaches at the same position on the homologous chromosome (Figure 11.6.2). This exchange of genetic material can happen many times within the same pair of homologous chromosomes, creating unique combinations of genes. This process is also known as **recombination**.

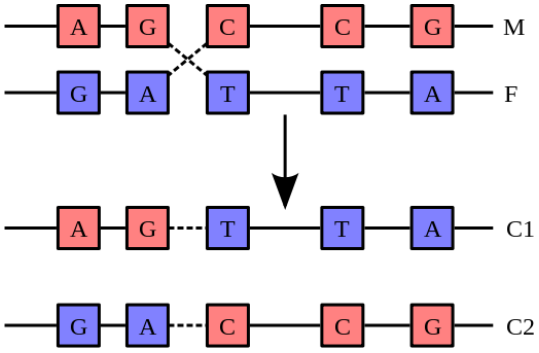


Figure **11.6.2**: Crossing-over. A maternal strand of DNA is shown in red. A paternal strand of DNA is shown in blue. Crossing over produces two chromosomes that have not previously existed. The process of recombination involves the breakage and rejoining of parental chromosomes (M, F). This results in the generation of novel chromosomes (C1, C2) that share DNA from both parents.

During prophase I, chromosomes condense and become visible inside the nucleus. As the nuclear envelope begins to break down, homologous chromosomes move closer together. The synaptonemal complex, a lattice of proteins between the homologous chromosomes, forms at specific locations, spreading to cover the entire length of the chromosomes. The tight pairing of the homologous chromosomes is called synapsis. In synapsis, the genes on the chromatids of the homologous chromosomes are aligned with each other. The synaptonemal complex also supports the exchange of chromosomal segments between non-sister homologous chromatids in a process called crossing over. The crossover events are the first source of genetic variation produced by meiosis. A single crossover event between homologous non-sister chromatids leads to an exchange of DNA between chromosomes. Following crossover, the synaptonemal complex breaks down and the cohesin connection between homologous pairs is also removed. At the end of prophase I, the pairs are held together only at the chiasmata; they are called tetrads because the four sister chromatids of each pair of homologous chromosomes are now visible.

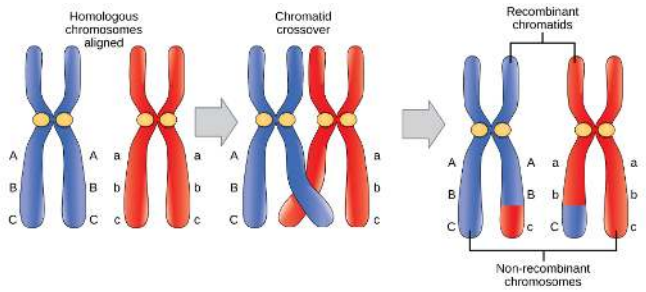


Figure 11.6.3: Crossover between homologous chromosomes Crossover occurs between non-sister chromatids of homologous chromosomes. The result is an exchange of genetic material between homologous chromosomes. This occurs when homologous chromosomes align. Chromatids from each chromosome can cross over and recombine (swap sections). This results in two recombinant chromosomes and two non-recombinant chromosomes.

INDEPENDENT ASSORTMENT AND RANDOM FERTILIZATION

During metaphase I, the tetrads move to the metaphase plate with kinetochores facing opposite poles. The homologous pairs orient themselves randomly at the equator. This event is the second mechanism that introduces variation into the gametes or spores. In each cell that undergoes meiosis, the arrangement of the tetrads is different. The number of variations is dependent on the number of chromosomes making up a set. There are two possibilities for orientation at the metaphase plate. The possible number of alignments, therefore, equals 2^n, where n is the number of chromosomes per set. Given these two mechanisms, it is highly unlikely that any two haploid cells resulting from meiosis will have the same genetic composition.

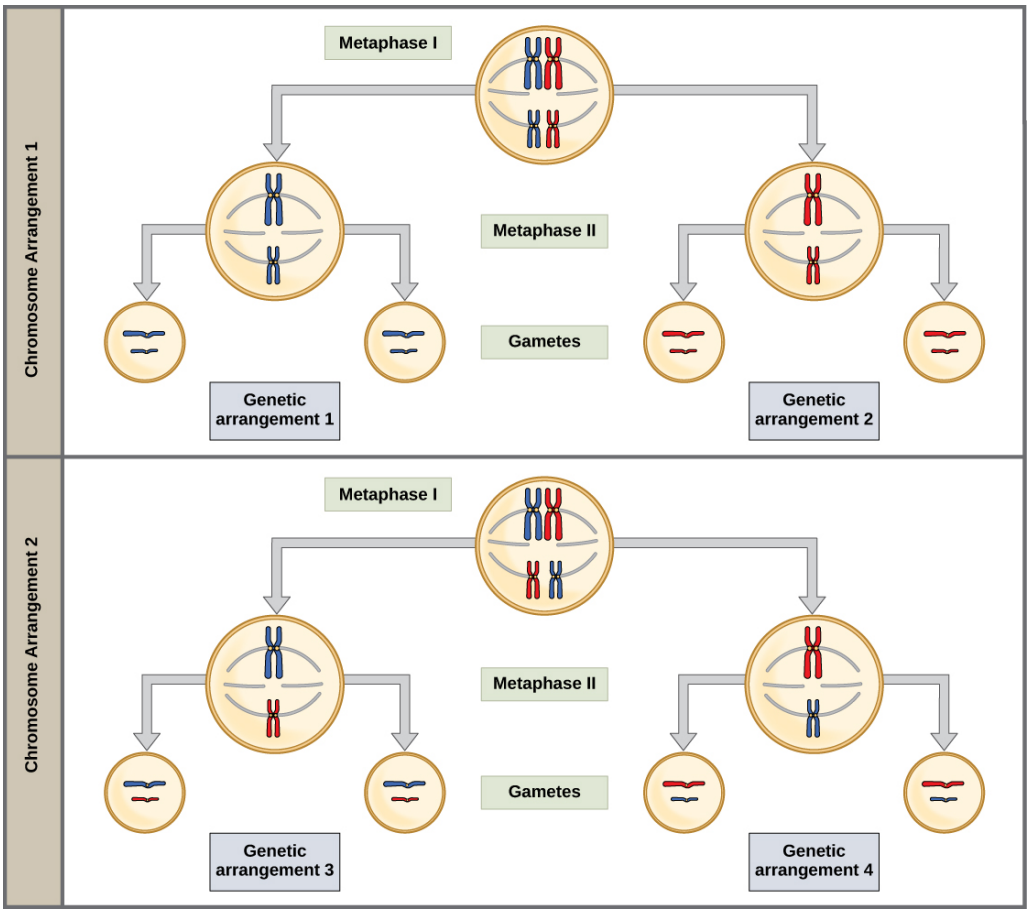


Figure 11.6.4: Meiosis I ensures unique gametes Random, independent assortment during metaphase I can be demonstrated by considering a cell with a set of two chromosomes (n = 2). In this case, there are two possible arrangements at the equatorial plane in metaphase I. The total possible number of different gametes is 2n, where n equals the number of chromosomes in a set. In this example, there are four possible genetic combinations for the gametes. With n = 23 in human cells, there are over 8 million possible combinations of paternal and maternal chromosomes.

In humans, there are over 8 million configurations in which the chromosomes can line up during metaphase I of meiosis. It is the specific process of meiosis, resulting in four unique haploid cells, that results in these many combinations. This independent assortment, in which the chromosome inherited from either the father or mother can sort into any gamete, produces the potential for tremendous genetic variation. Together with random fertilization, more possibilities for genetic variation exist between any two people than the number of individuals alive today. Sexual reproduction is the random fertilization of a gamete from the female using a gamete from the male. A sperm cell, with over 8 million chromosome combinations, fertilizes an egg cell, which also has over 8 million chromosome combinations. That is over 64 trillion unique combinations, not counting the unique combinations produced by crossing-over.

REVIEW

1. What is crossing-over and when does it occur?
2. Describe how crossing-over, independent assortment, and random fertilization lead to genetic variation.
3. How many combinations of chromosomes are possible from sexual reproduction in humans?
4. Create a diagram to show how crossing-over occurs and how it creates new gene combinations on each chromosome.

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11.7: MITOSIS VS. MEIOSIS AND DISORDERS

MITOSIS OR MEIOSIS?

Figure **11.7.1** shows a tiny embryo just beginning to form. Once an egg is fertilized, the resulting single cell must divide many times to develop a fetus. Both mitosis and meiosis involve cell division; is this type of cell division an example of mitosis or meiosis? The answer is mitosis. With each division, you are making a genetically exact copy of the parent cell, which only happens through mitosis.



Figure **11.7.1**: 4-celled embryo

MITOSIS VS. MEIOSIS

Both **mitosis** and **meiosis** result in eukaryotic cell division. The primary difference between these divisions is the differing goals of each process. The goal of mitosis is to produce two **daughter cells** that are genetically identical to the parent cell. Mitosis happens when you grow. You want all your new cells to have the same DNA as the previous cells. The goal of meiosis is to produce sperm or eggs, also known as **gametes**. The resulting gametes are not genetically identical to the parent cell. Gametes are **haploid** cells, with only half the DNA present in the **diploid** parent cell. This is necessary so that when a sperm and an egg combine at **fertilization**, the resulting **zygote** has the correct amount of DNA—not twice as much as the parents. The zygote then begins to divide through mitosis.

Table **11.7.1**: comparison of mitosis and meiosis

	Mitosis	Meiosis
Purpose	To produce new cells	To produce gametes
Number of Cells Produced	2	4
Rounds of Cell Division	1	2
Haploid or Diploid	Diploid	Haploid
Are daughter cells identical to parent cells?	Yes	No
Are daughter cells identical to each other?	Yes	No

Figure **11.7.2** shows a comparison of mitosis, meiosis, and binary fission.

- Binary fission occurs in bacterial. Note that bacterial cells have a single loop of DNA. The DNA of the cell is replicated. Each loop of DNA moves to the opposite side of the cell and the cell splits in half.
- Mitosis and Meiosis both occur in eukaryotic cells. In the example below the cell has 4 total chromosomes. These are replicated during the S phase.
  - In mitosis, the chromosomes line up in the center of the cell. Then, sister chromatids separate and move to the opposite poles of the cell. The cell divides, producing two cells with 4 total chromosomes
  - In meiosis, the homologous chromosomes line up in the center of the cell. Then each chromosome moves to opposite poles and the cell divides.
    - Next, the chromosomes line up in the center of the cell. Then, sister chromatids separate and move to the opposite poles of the cell. This produces four cells with 2 chromosomes each. These are the gametes.
    - Two gametes combine to form a zygote with 4 total chromosomes.

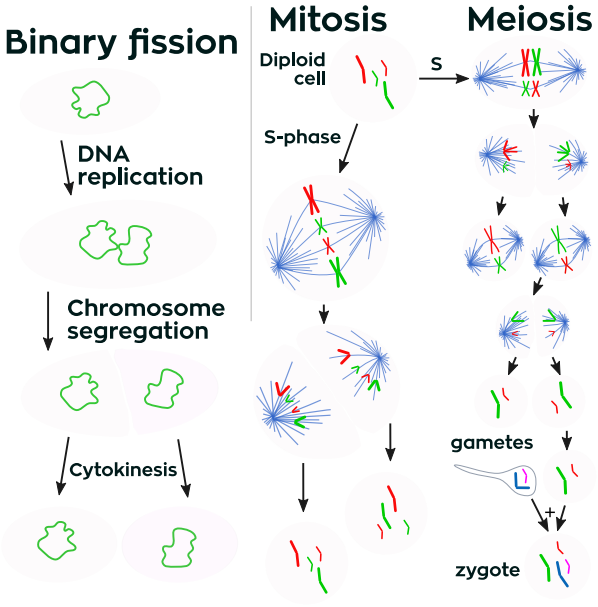


Figure **11.7.2**: A comparison between binary fission, mitosis, and meiosis.

CHROMOSOME DISORDERS

Changes in Chromosome Number

What would happen if an entire chromosome were missing or duplicated? What if a human had only 45 chromosomes? Or 47? This real possibility is usually due to mistakes during meiosis; the chromosomes do not fully separate from each other during sperm or egg formation. Specifically, **nondisjunction** occurs when

homologous chromosomes or sister chromatids fail to separate during meiosis, resulting in an abnormal chromosome number. Nondisjunction may occur during meiosis I or meiosis II Most human atypical chromosome numbers result in the death of the developing embryo, often before a woman even realizes she is pregnant. Occasionally, a zygote with an extra chromosome can become a viable embryo and develop.

Trisomy is a state where humans have an extra autosome. That is, they have three of a particular chromosome instead of two. For example, trisomy 18 results from an extra chromosome 18, resulting in 47 total chromosomes. To identify the chromosome number (including an abnormal number), a sample of cells is removed from an individual or developing fetus. Metaphase chromosomes are photographed and a karyotype is produced. A **karyotype** will display any abnormalities in chromosome number or large chromosomal rearrangements. Trisomy 8, 9, 12, 13, 16, 18, and 21 have been identified in humans. Trisomy 16 is the most common trisomy in humans, occurring in more than 1% of pregnancies. This condition, however, usually results in spontaneous miscarriage in the first trimester. The most common trisomy in viable births is **Trisomy 21**.

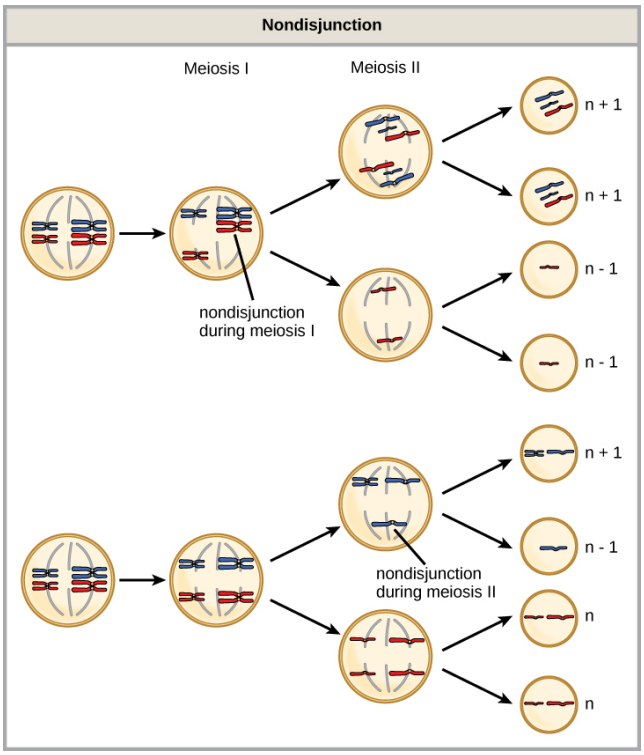


Figure **11.7.3**: Nondisjunction in Meiosis: Nondisjunction occurs when homologous chromosomes or sister chromatids fail to separate during meiosis, resulting in an abnormal chromosome number. Nondisjunction may occur during meiosis I or meiosis II. If nondisjunction occurs in meiosis I, the homologous pair of chromosomes remain bound. This results in an extra chromosome (n + 1) in two of the gametes and a missing chromosome (n - 1) in two of the gametes. If nondisjunction occurs in meiosis II, two cells enter meiosis II with the correct number of chromosomes. Nondisjunction occurs in one of these cells when one of the sister chromatids does not separate. This results in a cell with an extra chromosome (n +1), a cell missing a chromosome (n - 1), and two cells with the expected number of chromosomes (n).

TRISOMY 21: DOWN SYNDROME



Figure **11.7.4**: A child with Down syndrome, exhibiting characteristic facial appearance.

One of the most common chromosome abnormalities is **Down syndrome**, due to nondisjunction of chromosome 21 resulting in an extra complete chromosome 21, or part of chromosome 21 (Figure **11.7.5**). Down syndrome is the only autosomal trisomy where an affected individual may survive to adulthood. Individuals with Down syndrome often have some degree of mental and physical impairments and a specific facial appearance. With proper assistance, individuals with Down

syndrome can become successful, contributing members of society. The risk of having a child with Down syndrome is significantly higher among women age 35 and older.

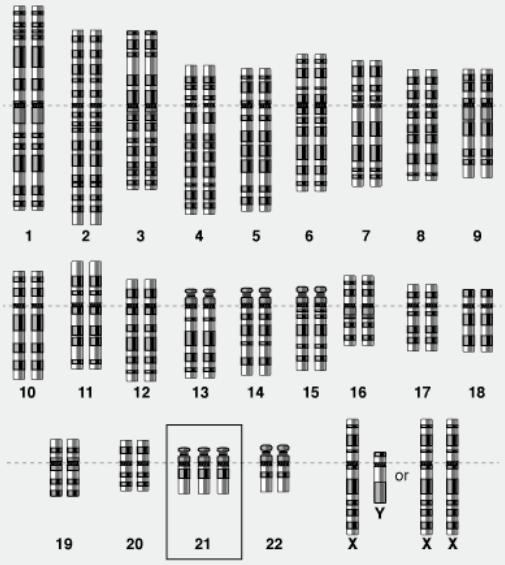


Figure **11.7.5**: Trisomy 21 (Down Syndrome) Karyotype. A karyotype is a picture of a cell's chromosomes. Note that there are two of each chromosome but three copies of chromosome 21.

REVIEW

1. Define genetic disorder.
2. What is nondisjunction? Why may it cause genetic disorders?
3. Explain why genetic disorders caused by abnormal numbers of chromosomes most often involve the X chromosome.
4. How is Down syndrome detected *in utero*?
5. Compare and contrast genetic disorders and congenital disorders.
6. Explain why parents that do not have Down syndrome can have a child with Down syndrome.
7. What is the goal of mitosis? Or meiosis?
8. How many cells are created from cytokinesis following mitosis? Following meiosis?
9. Which process, mitosis or meiosis, creates genetically identical cells?
10. "Gametes are haploid cells." What does this sentence mean?

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11.8: CASE STUDY CONCLUSION- GENES AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: GENETIC SIMILARITIES AND DIFFERENCES

Humans are much more genetically similar to each other than they are different. Any two people on Earth are 99.9% genetically identical to each other. But the mere 0.1% that is different can be very important, as in the case of bone marrow donation to treat diseases such as leukemia. These variations are passed on in a family with sexual reproduction. A good match must exist between a bone marrow donor and recipient in genes that encode for human leukocyte antigen (HLA) proteins. If a patient receives a bone marrow transplant from a donor that has different types of HLAs than the patient does, antibodies in their immune system will identify the antigens as “nonself” and will launch an attack on the transplanted cells. Also, since bone marrow produces immune cells, antibodies in the transplanted tissue can actually attack the patient’s own cells through the same mechanism.

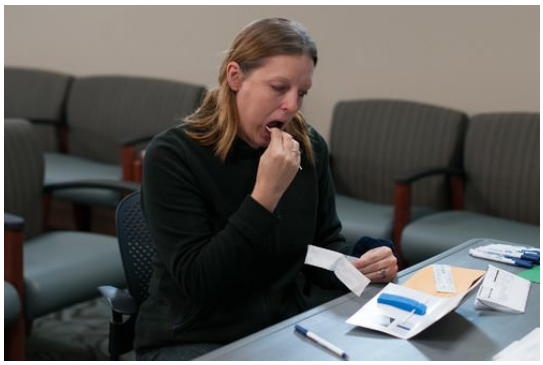


Figure **11.8.1**: Swabbing for DNA match

As you have also learned, a good HLA match is often difficult to find, even between full siblings. This is due to the genetic variations within gametes of a single person due to crossing over and random assortment. The variations are multiplied when two unique gametes fertilize. Kim has to find his match outside of his family. Every year, about 14,000 people in the United States must try to find a compatible donor from a bone marrow registry. These registries store information on HLA type from potential donors, like the woman shown above. She is swabbing her cheeks for a DNA match. It can take months to years to find a compatible match — if one is found at all.

In the meantime, Kim has to stop the production of abnormal WBCs with chemotherapy. Chemotherapy is the treatment of cancer with drugs ("anticancer drugs") that can destroy cancer cells. In current usage, the term "chemotherapy" usually refers to cytotoxic drugs which affect rapidly dividing cells in general, in contrast with targeted therapy (see below). Chemotherapy drugs interfere with cell division in various possible ways, e.g. with the duplication of DNA or the separation of newly formed chromosomes. Chemotherapy has the potential to harm healthy tissue, especially those tissues that have a high replacement rate (e.g. intestinal lining). Due to these side effects, patients may lose their hair follicles, Digestive system lining, and taste buds. These cells usually repair themselves after chemotherapy. Because some drugs work better together than alone, two or more drugs are often given at the same time. This is called "combination chemotherapy"; most chemotherapy regimens are given in a combination.

CHAPTER SUMMARY

In this chapter, you learned about human sexual and asexual reproduction.

- The cell cycle is a repeating series of events that include growth, DNA synthesis, and cell division. It is more complicated in eukaryotic than prokaryotic cells.
- In a eukaryotic cell, the cell cycle has two major phases: interphase and mitotic phase. During interphase, the cell grows, performs routine life processes, and prepares to divide. During the mitotic phase, first, the nucleus divides (mitosis) and then the cytoplasm divides (cytokinesis), which produces two daughter cells.
    - Except when a eukaryotic cell divides, its nuclear DNA exists as a grainy material called chromatin. After DNA replicates and the cell is about to divide, the DNA condenses and coils into the X-shaped form of a chromosome. Each replicated chromosome consists of two sister chromatids, which are joined together at a centromere.
    - During mitosis, sister chromatids separate from each other and move to opposite poles of the cell. This happens in four phases, called prophase, metaphase, anaphase, and telophase.
- The cell cycle is controlled mainly by regulatory proteins that signal the cell to either start or delay the next phase of the cycle at key checkpoints.
- Cancer is a disease that occurs when the cell cycle is no longer regulated, for example, because the cell's DNA has become damaged. Cancerous cells grow out of control and may form a mass of abnormal cells called a tumor.
- In sexual reproduction, two parents produce gametes that unite in the process of fertilization to form a single-celled zygote. Gametes are haploid cells with only one of each pair of homologous chromosomes, and the zygote is a diploid cell with two of each pair of chromosomes.
- Meiosis is the type of cell division that produces four haploid daughter cells that may become gametes. Meiosis occurs in two stages, called meiosis I and meiosis II, each of which occurs in four phases (prophase, metaphase, anaphase, and telophase).
- Meiosis is followed by gametogenesis, the process in which the haploid daughter cells change into mature gametes. Males produce gametes called sperm in a process known as spermatogenesis, and females produce gametes called eggs in the process known as oogenesis.
- Sexual reproduction produces offspring that are genetically unique. Crossing-over, independent assortment, and the random

union of gametes work together to result in an amazing amount of potential genetic variation.

- Sexual reproduction has the potential to produce tremendous genetic variation in offspring.
- During prophase I, the homologous chromosomes condense and become visible as the x shape we know, pair up to form a tetrad, and exchange genetic material by crossing over.
- In metaphase I, the tetrads line themselves up at the metaphase plate and homologous pairs orient themselves randomly.
- This variation is due to independent assortment and crossing-over during meiosis, and random union of gametes during fertilization.
- The goal of mitosis is to produce a new cell that is identical to the parent cell.
- The goal of meiosis is to produce gametes that have half the DNA of the parent cell.
- When chromosomes do not divide equally among gametes, the damaged gametes produce. This process is called nondisjunction.
- Trisomy is a state where humans have an extra autosome; they have three of a particular chromosome instead of two.
- The most common trisomy in viable births is Trisomy 21 (Down Syndrome) due to nondisjunction.

CHAPTER SUMMARY REVIEW

1. What are cyclin-dependent kinases? What is their role?
2. What are cell cycle checkpoints?
3. What is interphase?
4. Summarize each phase of the cell cycle.
5. Describe the structure of a chromosome in the prophase of mitosis.
6. What is cytokinesis and when does it occur?
7. What is centromere?
8. Describe the main steps of mitosis.
9. Cells go through a series of events that include growth, DNA synthesis, and cell division. Why are these events best represented by a cycle diagram?
10. Explain how the cell cycle is regulated.
11. Define and explain random assortment and random fertilization.
12. Why is DNA replication essential to the cell cycle?
13. *True or False*. When a eukaryotic cell divides, the nucleus divides first in the process of mitosis.
14. What happens during mitosis?
15. What is meiosis?
16. What is diploid? How many chromosomes are in a diploid human cell?
17. What is a zygote? How does the zygote form the organism?
18. What is the result of crossing-over?
19. How many cell divisions occur during meiosis?
20. Why are you genetically distinct?
21. Describe the steps of Meiosis I and Meiosis II.
22. Describe nondisjunction. List and explain some of the chromosome disorders.
23. Compare and contrast mitosis and meiosis.

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CHAPTER OVERVIEW

12: INHERITANCE

This chapter provides the molecular background for understanding heredity; explains Mendelian and non-Mendelian inheritance in humans; some genetic disorders and their treatment, and explores recent advances in genetics.

12.1: Case Study- Genes and Inheritance
12.2: Laws of Inheritance
12.3: Genetics of Inheritance
12.4: Simple Inheritance
12.5: Complex Inheritance
12.6: Genetic Disorders
12.7: Case Study Conclusion- Cancer and Chapter Summary

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12.1: CASE STUDY- GENES AND INHERITANCE

CASE STUDY: CANCER IN THE FAMILY

People tend to look similar to their biological parents, as illustrated by the family tree in Figure **12.1.1**. But, you can also inherit traits from your parents that you can't see. Rebecca becomes very aware of this fact when she visits her new doctor for a physical exam. Her doctor asks several questions about her family's medical history, including whether Rebecca has or had relatives with cancer. Rebecca tells her that her grandmother, aunt, and uncle, who have all passed away, all had cancer. They all had breast cancer, including her uncle, and her aunt additionally had ovarian cancer. Her doctor asks how old they were when they were diagnosed with cancer. Rebecca is not sure exactly, but she knows that her grandmother was fairly young at the time, probably in her forties.

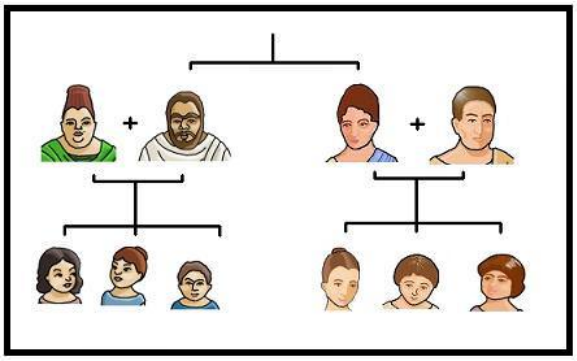


Figure **12.1.1**: Two family trees. Each shows children that have features similar to their parents.

Rebecca's doctor explains that while the vast majority of cancers are not due to inherited factors, a cluster of cancers within a family may indicate that there are mutations in certain genes that increase the risk of getting certain types of cancer, particularly breast and ovarian cancer. Some signs that cancers may be due to these genetic factors are present in Rebecca's family, such as cancer with an early age of onset (e.g. breast cancer before age 50), breast cancer in men, and breast cancer and ovarian cancer within the same person or family.

Based on her family medical history, Rebecca's doctor recommends that she see a genetic counselor because these professionals can help determine whether the high incidence of cancers in her family could be due to inherited mutations in their genes. If so, they can test Rebecca to find out whether she has the particular variations of these genes that would increase her risk of getting cancer.

When Rebecca sees the genetic counselor, he asks how her grandmother, aunt, and uncle with cancer are related to her. She says that these relatives are all on her mother's side — they are her mother's mother and siblings. The genetic counselor records this information in the form of a specific type of family tree, called a pedigree, indicating which relatives had which type of cancer and how they are related to each other and to Rebecca. He also asks her ethnicity. Rebecca says that her family, on both sides, are Ashkenazi Jews, meaning Jews whose ancestors came from central and eastern Europe. "But what does that have to do with anything?" she asks. The counselor tells Rebecca that mutations in two tumor-suppressor genes called BRCA1 and BRCA2, located on chromosome 17 and 13, respectively, are particularly prevalent in people of Ashkenazi Jewish descent and greatly increase the risk of getting cancer. About 1 in 40 Ashkenazi Jewish people have one of these mutations, compared to about 1 in 800 in the general population. Her ethnicity, along with the types of cancer, age of onset, and the specific relationships between her family members who had cancer indicate to the counselor that she is a good candidate for genetic testing for the presence of these mutations.

Rebecca says that her 72-year-old mother never had cancer, and nor had many other relatives on that side of the family, so how could the cancers be genetic? The genetic counselor explains that the mutations in the BRCA1 and BRCA2 genes, although dominant, are not inherited by everyone in a family. Also, even people with mutations in these genes do not necessarily get cancer — the mutations simply increase their risk of getting cancer. For instance, 55 to 65% of women with a harmful mutation in the BRCA1 gene will get breast cancer before age 70, compared to 12% of women in the general population who will get breast cancer sometime over the course of their lives.

Rebecca is not sure she wants to know whether she has a higher risk of cancer. The genetic counselor understands her apprehension but explains that if she knows that she has harmful mutations in either of these genes, her doctor will screen her for cancer more often and at earlier ages. Therefore, any cancers she may develop are likely to be caught earlier when they are often much more treatable. Rebecca decides to go through with the testing, which involves taking a blood sample, and nervously waits for her results.

CHAPTER OVERVIEW: GENETICS

At the end of this chapter, you will find out Rebecca 's test results. By then, you will have learned how mutations in genes such as BRCA1 and BRCA2 can be passed down and cause disease. Especially, you will learn about:

- How Gregor Mendel discovered the laws of inheritance for certain types of traits.
- The science of heredity, known as genetics, and the relationship between genes and traits.
- Simple and more complex inheritance of some human traits.
- Genetic Disorders.

As you read this chapter, keep Rebecca's situation in mind and think about the following questions:

1. What do the BRCA1 and BRCA2 genes normally do? How can they cause cancer?
2. Are BRCA1 and BRCA2 considered linked genes? And are they on autosomes or sex chromosomes?
3. After learning more about pedigrees, draw the pedigree for cancer in Rebecca's family. Use the pedigree to help you think about why it is possible that her mother does not have one of the

BRCA gene mutations, even if her grandmother, aunt, and uncle did have it.

4. Why do you think certain gene mutations are prevalent in certain ethnic groups?

ATTRIBUTIONS

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12.2: LAWS OF INHERITANCE

OF PEAS AND PEOPLE

These purplish-flowered plants are not just pretty to look at. Plants like these led to a huge leap forward in biology. The plants are common garden peas, and they were studied in the mid-1800s by an Austrian monk named Gregor Mendel. With his careful experiments, Mendel uncovered the secrets of heredity, or how parents pass characteristics to their offspring. You may not care much about heredity in pea plants, but you probably care about your own heredity. Mendel's discoveries apply to people as well as to peas — and to all other living things that reproduce sexually. In this concept, you will read about Mendel's experiments and the secrets of heredity that he discovered.



Figure **12.2.1**: Sweet Pea flower

MENDEL AND HIS PEA PLANTS

Gregor Mendel, shown below, was born in 1822 and grew up on his parents' farm in Austria. He did well in school and became a monk. He also went to the University of Vienna, where he studied science and math. His professors encouraged him to learn science through experimentation and to use math to make sense of his results. Mendel is best known for his experiments with pea plants like the one pictured above.



Figure **12.2.2**: Gregor Mendel. The Austrian monk Gregor Mendel experimented with pea plants. He did all of his research in the garden of the monastery where he lived.

BLENDING THEORY OF INHERITANCE

During Mendel's time, the blending theory of inheritance was popular. This is the theory that offspring have a blend, or mix, of the characteristics of their parents. Mendel noticed plants in his own garden that weren't a blend of the parents. For example, a tall plant and a short plant had offspring that were either tall or short but not medium in height. Observations such as these led Mendel to question the blending theory. He wondered if there was a different underlying principle that could explain how characteristics are inherited. He decided to experiment with pea plants to find out. In fact, Mendel experimented with almost 30,000 pea plants over the next several years!

WHY STUDY PEA PLANTS?

Why did Mendel choose common, garden-variety pea plants for his experiments? Pea plants are a good choice because they are fast growing and easy to raise. They also have several visible **characteristics** that vary. These characteristics, some of which are illustrated in Figure **12.2.3**. Each of these characteristics has two common **traits** (values).

1. Seeds can be round or wrinkled
2. Seeds can have yellow or green cotyledons. Cotyledons refer to the tiny leaves inside the seeds.
3. Flowers can be white or violet
4. The seed pod can be full or constricted
5. The seed pod can be yellow or green
6. The flowers can occur along the stem (in axial pods) or at the end of a stem (in terminal pods)
7. Stems can be long (6-7 feet) or short (less than 1 foot).

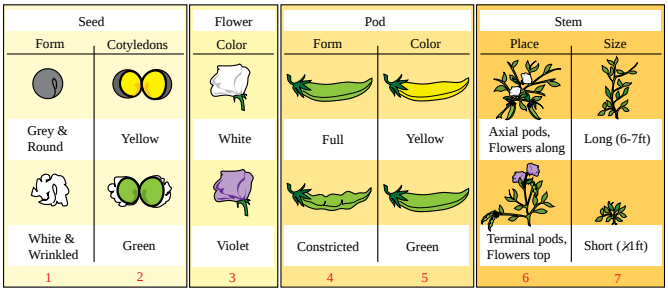


Figure **12.2.3**: Mendel investigated seven different characteristics in pea plants.

CONTROLLING POLLINATION

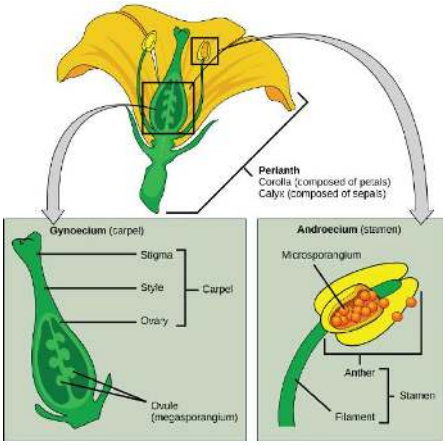


Figure **12.2.4**: Flowers are the reproductive organs of plants. Each pea plant flower has both male and female parts. The anther is part of the stamen, the male structure that produces male gametes (pollen). The stigma is part of the pistil, the female structure that produces female gametes and guides the pollen grains to them. The stigma receives the pollen grains and passes them to the ovary, which contains female gametes.

To research how characteristics are passed from parents to offspring, Mendel needed to control pollination. Pollination is the fertilization step in the sexual reproduction of plants. Pollen consists of tiny grains that are the male sex cells, or gametes, of plants. They are produced by a male flower part called the anther (Figure **12.2.4**). Pollination occurs when pollen is transferred from the anther to the stigma of the same or another flower. The stigma is a female part of a flower. It passes the pollen grains to female gametes in the ovary.

Pea plants are naturally self-pollinating. In self-pollination, pollen grains from anthers on one plant are transferred to stigmas of flowers on the same plant. Mendel was interested in the offspring of two different parent plants, so he had to prevent self-pollination. He removed the anthers from the flowers of some of the plants in his experiments. Then he pollinated them by hand with pollen from other parent plants of his choice. When pollen from one plant fertilizes another plant of the same species, it is called cross-pollination. The offspring that result from such a cross are called hybrids. When the term *hybrid* is used in this context, it refers to any offspring resulting from the breeding of two genetically distinct individuals.

MENDEL'S FIRST SET OF EXPERIMENTS

At first, Mendel experimented with just one characteristic at a time. He began with flower color. As shown in Figure **12.2.5**, Mendel cross-pollinated violet-flowered and white-flowered parent plants. The parent plants in the experiments are referred to as the P (for parent) generation.

F1 AND F2 GENERATIONS

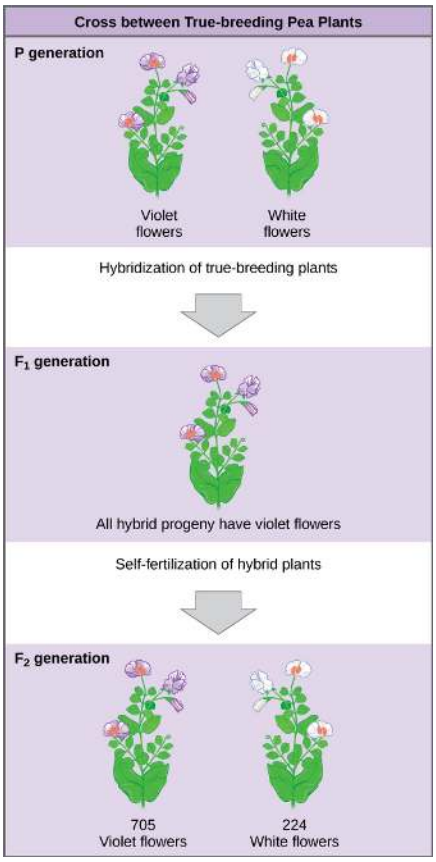


Figure **12.2.5**: In one of his experiments on inheritance patterns, Mendel crossed plants that were true-breeding for violet flower color with plants true-breeding for white flower color (the P generation). The resulting hybrids in the F1 generation all had violet flowers. In the F2 generation, approximately three-quarters of the plants had violet flowers, while one-quarter had white flowers.

The offspring of the P generation are called the F1 (for filial, or "offspring") generation. As shown in Figure **12.2.5**, all of the plants in the F1 generation had violet flowers. None of them had white flowers. Mendel wondered what had happened to the white-flower characteristic. He assumed some type of inherited factor produces white flowers and some other inherited factor produces violet flowers. Did the white-flower factor just disappear in the F1 generation? If so, then the offspring of the F1 generation — called the F2 generation — should all have violet flowers like their parents.

To test this prediction, Mendel allowed the F1 generation plants to self-pollinate. He was surprised by the results. Some of the F2 generation plants had white flowers. He studied hundreds of F2 generation plants, and for every three violet-flowered plants, there was an average of one white-flowered plant.

LAW OF SEGREGATION

Mendel did the same experiment for all seven characteristics. In each case, one value of the characteristic disappeared in the F1 plants and then showed up again in the F2 plants. And in each case, 75 percent of F2 plants had one value of the characteristic and 25 percent had the other value. Based on these observations, Mendel formulated his first law of inheritance. This law is called the **law of segregation**. It states that there are two factors controlling a given

characteristic, one of which dominates the other, and these factors separate and go to different gametes when a parent reproduces.

MENDEL'S SECOND SET OF EXPERIMENTS

Mendel wondered whether different characteristics are inherited together. For example, are purple flowers and tall stems always inherited together? Or do these two characteristics show up in different combinations in offspring? To answer these questions, Mendel next investigated two characteristics at a time. For example, he crossed plants with yellow round seeds and plants with green wrinkled seeds. The results of this cross are shown in Figure **12.2.5**.

F1 AND F2 GENERATIONS

In this set of experiments, Mendel observed that plants in the F1 generation were all alike. All of them had yellow round seeds like one of the two parents. When the F1 generation plants were self-pollinated, however, their offspring—the F2 generation—showed all possible combinations of the two characteristics. Some had green round seeds, for example, and some had yellow wrinkled seeds. These combinations of characteristics were not present in the F1 or P generations.

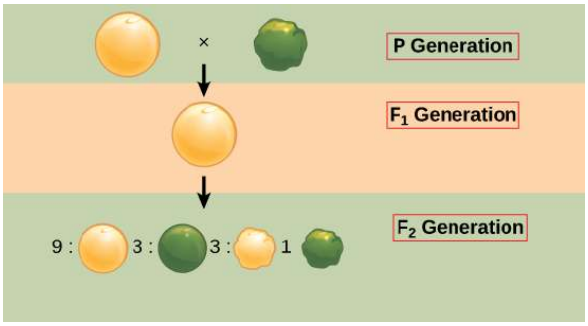


Figure **12.2.6**: The parent generation consisted of smooth yellow peas and green wrinkled peas. The first offspring generation all had smooth yellow seeds. When these F1 plants were crossed, the offspring had Smooth yellow, smooth green, wrinkled yellow and wrinkled green seeds in a ratio of 9:3:3:1.

LAW OF INDEPENDENT ASSORTMENT

Mendel repeated this experiment with other combinations of characteristics, such as flower color and stem length. Each time, the results were the same as those shown in the figure above. The results of Mendel's second set of experiments led to his second law. This is the **law of independent assortment**. It states that factors controlling different characteristics are inherited independently of each other.

MENDEL'S LEGACY

You might think that Mendel's discoveries would have made a big impact on science as soon as he made them, but you would be wrong. Why? Because Mendel's work was largely ignored. Mendel was far ahead of his time and working from a remote monastery. He had no reputation among the scientific community and limited previously published work. He also published his research in an obscure scientific journal. As a result, when Charles Darwin published his landmark book on evolution in 1869, although Mendel's work had been published just a few years earlier, Darwin was unaware of it. Consequently, Darwin knew nothing about Mendel's laws and didn't understand heredity. This made Darwin's arguments about evolution less convincing to many people.

Then, in 1900, three different European scientists — named DeVries, Correns, and Tschermak — independently arrived at Mendel's laws. All three had done experiments similar to Mendel's and come to the same conclusions that he had drawn several decades earlier. Only then was Mendel's work rediscovered and Mendel himself given the credit he was due. Although Mendel knew nothing about genes, which were discovered after his death, he is now considered the father of genetics.

REVIEW

1. What is the blending theory of inheritance? What observations led Mendel to question this theory?
2. Why were pea plants a good choice for Mendel's experiments?
3. Describe Mendel's first set of experiments, including the results.
4. State Mendel's two laws of inheritance.
5. How did the outcome of Mendel's second set of experiments lead to his second law?
6. Discuss Mendel's legacy.
7. In Mendel's first set of experiments:
   A. Why did he use pea plants with different characteristics for the parental generation?
   B. Why do you think he only tested one characteristic at a time?
   C. Why did he allow the plants in the F1 generation to self-pollinate?
   D. If he observed 200 F2 plants, approximately how many would have purple flowers? Approximately how many would have white flowers? Explain your answers.
   E. Which flower color seemed to dominate over the other? Explain your answer.
8. If Mendel's law of independent assortment was *not* correct, and characteristics were *always inherited* together, what types of offspring do you think would have been produced by crossing plants with yellow round seeds and green wrinkled seeds? Explain your answer.
9. *True or False*. In Mendel's experiments, the F1 generations are hybrids.
10. *True or False*. A single gamete of a pea plant contains factors that result in both a purple flower and a white flower.

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12.3: GENETICS OF INHERITANCE

LIKE FATHER, LIKE SON

This father-son duo is serving in the army together. The shape of their faces and their facial features look very similar. If you saw them together, you might well guess that they are father and son. People have long known that the characteristics of living things are similar in parents and their offspring. However, it wasn't until the experiments of Gregor Mendel that scientists understood how traits are inherited by offspring.



Figure **12.3.1**: Father and son

THE FATHER OF GENETICS

Mendel did experiments with pea plants to show how traits such as seed shape and flower color are inherited. Based on his research, he developed his two well-known laws of inheritance: the law of segregation and the law of independent assortment. When Mendel died in 1884, his work was still virtually unknown. In 1900, three other researchers working independently came to the same conclusions that Mendel had drawn almost half a century earlier. Only then was Mendel's work rediscovered.

Mendel knew nothing about genes. They were discovered after his death. However, he did think that some type of "factors" controlled traits and were passed from parents to offspring. We now call these "factors" genes. Mendel's laws of inheritance, now expressed in terms of genes, form the basis of **genetics**, the science of heredity. For this reason, Mendel is often called the father of genetics.

THE LANGUAGE OF GENETICS

Today, we know that the traits of organisms are controlled by genes on chromosomes. To talk about inheritance in terms of genes and chromosomes, you need to know the language of genetics. Figure **12.3.2** shows the location of genes in a eukaryotic cell. The nucleus is a membrane-enclosed organelle found in most eukaryotic cells. The nucleus is the largest organelle in the cell and contains chromosomes which make up most of the cell's genetic information. Mitochondria also contain DNA, called mitochondrial DNA, but it makes up just a small percentage of the cell's overall DNA content. The genetic information, which contains the information for the structure and function of the organism, is found encoded in DNA in the form of genes.

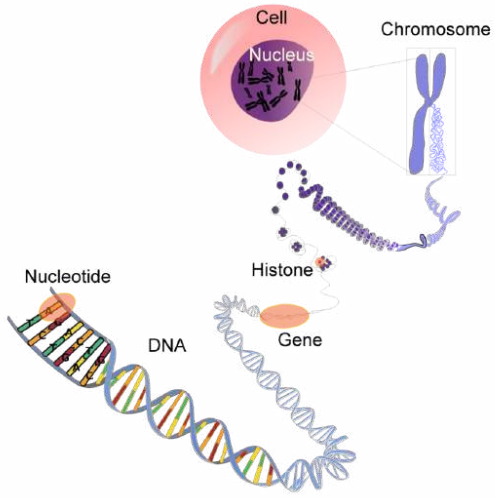


Figure **12.3.2**: The human genome has 23 pairs of chromosomes located in the nucleus of somatic cells. Chromosomes are strands of DNA wrapped around proteins called histones. Chromosomes contain small segments of DNA called genes, which code for proteins. DNA is made of nucleotides. Nucleotides are the DNA "code" and determine what proteins are made by a given gene.

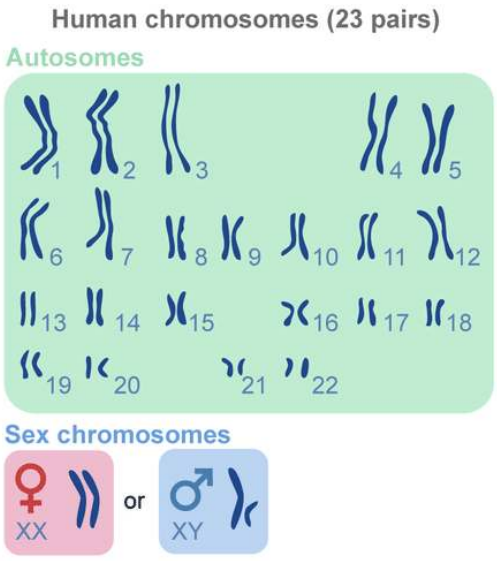


Figure **12.3.3**: Humans have 23 pairs of chromosomes. Pairs 1-22 are autosomes. Females have two X chromosomes, and males have an X and a Y chromosome.

A gene is a short segment of DNA that contains information to encode an RNA molecule or a protein strand. DNA in the nucleus is organized in long linear strands that are attached to different proteins. These proteins help the DNA coil up for better storage in the nucleus. Think about how a string gets tightly coiled up if you twist one end while holding the other end. These long strands of coiled-up DNA and proteins are called chromosomes.

Each chromosome contains many genes. The function of the nucleus is to maintain the integrity of these genes and to control the activities of the cell by regulating gene expression. Gene expression is the

process by which the information in a gene is "decoded" by various cell molecules to produce a functional gene product, such as a protein molecule or an RNA molecule. The human species is characterized by 23 pairs of chromosomes (Figure **12.3.3**).

AUTOSOMES

Of the 23 pairs of human chromosomes, 22 pairs are autosomes (the lines numbered 1–22 in Figure **12.3.3**). Autosomes are chromosomes that contain genes for characteristics that are unrelated to sex. These chromosomes are the same in males and females. The great majority of human genes are located on autosomes. The genes located on these chromosomes are called **autosomal genes**.

SEX CHROMOSOMES

The remaining pair of human chromosomes consists of the sex chromosomes, X and Y. Females have two X chromosomes, and males have one X and one Y chromosome. In females, one of the X chromosomes in each cell is inactivated and known as a **Barr body**. This ensures that females, like males, have only one functioning copy of the X chromosome in each cell.

As you can see from Figure **12.3.3**, the X chromosome is much larger than the Y chromosome. The X chromosome has about 2,000 genes, whereas the Y chromosome has fewer than 100, none of which are essential to survival. (For comparison, the smallest autosome, chromosome 22, has over 500 genes.) Virtually all of the X chromosome genes are unrelated to sex. The genes located on the X chromosomes are called **X-linked genes**. Only the Y chromosome contains genes that determine sex. A single Y chromosome gene, called SRY (which stands for sex-determining region Y gene), triggers an embryo to develop into a male. Without a Y chromosome, an individual develops into a female, so you can think of a female as the default sex of the human species. Can you think of a reason why the Y chromosome is so much smaller than the X chromosome?

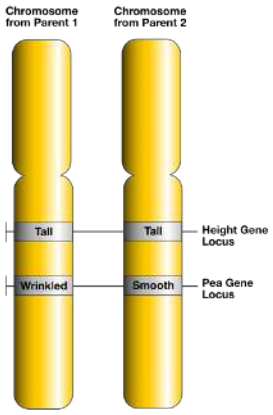


Figure **12.3.4**: Chromosome, Gene (for height and pea gene), Locus, and Allele (tall, wrinkled, or smooth). This diagram shows how the concepts of the chromosome, gene, locus, and allele are related. These terms are defined below

The following terms are a good starting point. They are illustrated in Figure **12.3.4** that follows.

- A gene is the part of a chromosome that contains the genetic code for a given protein. For example, in pea plants, a given gene might code for flower color.
- The position of a given gene on a chromosome is called its **locus** (plural, loci). For example, a gene might be located near the center or at one end or the other of a chromosome.
- A given gene may have different normal versions called **alleles.** For example, in pea plants, there is a smooth seed allele (S) and a wrinkled seed allele (s) for the seed shape gene. Different alleles account for much of the variation in the traits of organisms including people.
- In sexually reproducing organisms, each individual has two copies of each type of chromosome. Paired chromosomes of the same type are called **homologous chromosomes**. They are about the same size and shape, and they have all the same genes at the same loci.

GENOTYPE

When sexual reproduction occurs, sex cells called gametes unite during fertilization to form a single cell called a zygote. The zygote inherits two of each type of chromosome, with one chromosome of each type coming from the sperm donor and the other coming from the egg donor. Because homologous chromosomes have the same genes at the same loci, each individual also inherits two copies of each gene. The two copies may be the same allele or different alleles. The alleles an individual inherits for a given gene make up the individual's **genotype**. As shown in the table below, an organism with two of the same allele (for example, *BB* or *bb*) is called a **homozygote**. An organism with two different alleles (in this example, *Bb*) is called a **heterozygote**.

Table **12.3.1**: Alleles and genotypes

Alleles	Genotypes	Phenotypes
	BB (homozygous dominant)	purple flowers
B (purple)	*Bb* (heterozygous)	purple flowers
b (white)	*bb* (homozygous recessive)	white flowers

PHENOTYPE

The expression of an organism's genotype is referred to as its **phenotype**. The phenotype refers to the organism's traits, such as purple or white flowers in pea plants. As you can see from Table **12.3.1**, different genotypes may produce the same phenotype. In this example, both *BB* and *Bb* genotypes produce plants with the same phenotype, purple flowers. Why does this happen? In a *Bb* heterozygote, both alleles are expressed but only the *B* allele is seen in phenotype because it masks the expression of b, so the *b* allele doesn't influence the phenotype. The allele B is called **dominant,** and the allele that doesn't show in the phenotype is called **recessive.**

The terms *dominant* and *recessive* may also be used to refer to phenotypic traits. For example, purple flower color in pea plants is a dominant trait. It shows up in the phenotype whenever a plant inherits even one dominant allele for the trait. Similarly, white flower color is a recessive trait. Like other recessive traits, it shows

up in the phenotype only when a plant inherits two recessive alleles for the trait.

REVIEW

1. Define genetics.
2. Why is Gregor Mendel sometimes called the father of genetics if genes were not discovered until after his death?
3. Correctly use the terms gene, allele, locus, and chromosome in one or more sentences.
4. Compare and contrast genotype and phenotype.
5. Imagine that there are two alleles, *R* and *r*, for a given gene. *R* is dominant to *r*. Answer the following questions about this gene.
   A. What are the possible homozygous and heterozygous genotypes?
   B. Which genotype or genotypes express the dominant *R* phenotype? Explain your answer.
   C. Are *R* and *r* on different loci? Why or why not?
   D. Can *R* and *r* be on the same exact chromosome? Why or why not? If not, where are they located?
6. If a child has the genotype *Dd* and inherited the *D* from their mother, where did the *d* likely come from?
   A. Either their mother or their father
   B. Their father
   C. Their maternal grandmother
   D. Their maternal grandfather
7. *True or False*. Each phenotype has only one genotype.
8. *True or False*. Recessive genes are never expressed in a phenotype.
9. *True or False*. An observable physical trait is a phenotype.
10. A gene for flower color and a gene for seed shape could be on the same:
    A. chromosome
    B. locus
    C. allele
    D. Both A and B
11. What does a gene usually codes for?

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12.4: SIMPLE INHERITANCE

DIMPLES

This person is exhibiting a genetic trait — the dimples in their cheeks when they smiles. **Genetic traits** are characteristics that are encoded in DNA. Some genetic traits, like dimples, have a simple inheritance pattern like the traits that Gregor Mendel studied in pea plants. The way these traits are inherited by offspring from their parents is called simple inheritance.



Figure **12.4.1**: Dimples

WHAT IS SIMPLE INHERITANCE?

Simple (or Mendelian) inheritance refers to the inheritance of traits controlled by a single gene with two alleles, one of which may be completely dominant to the other. The pattern of inheritance of simple traits depends on whether the traits are controlled by genes on autosomes or by genes on sex chromosomes.

- **Autosomal traits** are controlled by genes on one of the 22 pairs of human autosomes. Autosomes are all the chromosomes except the X or Y chromosome, and they do not differ between males and females, so autosomal traits are inherited in the same way regardless of the sex of the parent or offspring.
- Traits controlled by genes on the sex chromosomes are called **sex-linked traits.** Because of the small size of the Y chromosome, most sex-linked traits are controlled by genes on the X chromosome. These traits are called **X-linked traits**. Single-gene X-linked traits have a different pattern of inheritance than single-gene autosomal traits because males have just one X chromosome. Males always inherit their X chromosome from their mother, and they pass on their X chromosome to all of their daughters but none of their sons.

STUDYING INHERITANCE PATTERNS

There are two very useful tools for studying how traits are passed from one generation to the next. One tool is a pedigree, the other is a Punnett square.

PEDIGREE

The charts below are called **pedigrees**. A pedigree shows how a trait is passed from generation to generation within a family. A pedigree can show, for example, whether a trait is an autosomal dominant, autosomal recessive, or X-linked trait. Pedigrees show relationships and identify individuals with a given trait. In the pedigrees below:

- affected individuals are shown in red, unaffected individuals are shown in blue
- males are shown as squares, females are shown as circles
- The top row of a pedigree is the original couple. Two individuals who are connected by a horizontal line are breeding pairs. The children of the couple are connected to them by vertical lines.
- The next row of the pedigree shows the couple's children, as well as the partners of the children. And, the third row of the pedigree shows the next generation (the grandchildren of the couple at the top of the pedigree). Larger pedigrees can have more rows showing additional generations.

Figure **12.4.2** is an example of a pedigree of an autosomal dominant trait. This pedigree begins with an affected male and an unaffected female. The couple's first child (on the left) is an affected male whose partner is an unaffected female. They produce two children: an affected female and an unaffected male. The next child is an unaffected male partnered with an unaffected female. Their children are two unaffected females and an unaffected male. The next child is an unpartnered affected female. The fourth child is an unpartnered unaffected female. The youngest child is an affected female partnered with an unaffected male. Their children are an affected male, followed by an unaffected male, followed by an affected female, followed by an unaffected female.

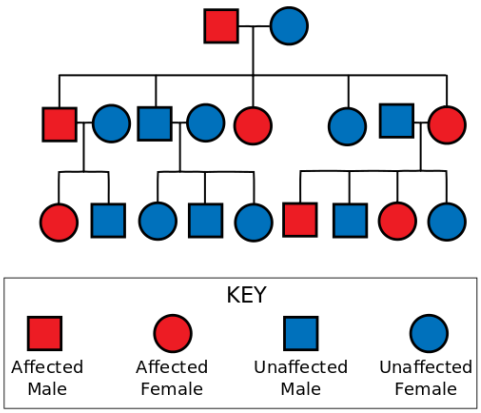


Figure **12.4.2**: Pedigree of an autosomal dominant trait.

In an autosomal dominant trait, a child that has the trait will always have at least one parent with the trait. In an autosomal recessive trait, two individuals without the trait can have a child with the trait.

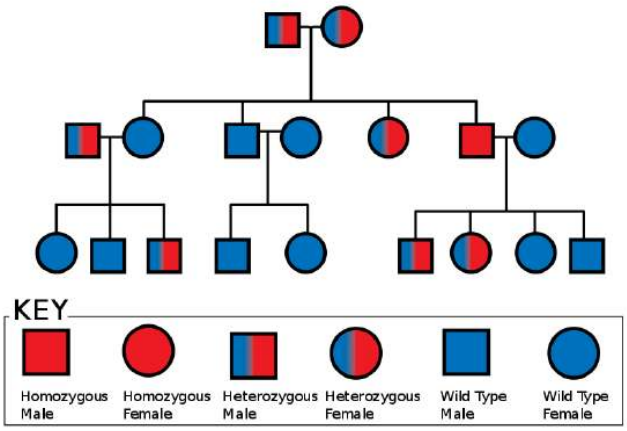


Figure **12.4.3**: Pedigree of an autosomal recessive trait.

Figure **12.4.3** is a pedigree of an autosomal recessive trait. In this pedigree, individuals that are half-shaded are heterozygous (and therefore do not show the trait). In this example, two heterozygous individuals have four children. Their youngest child is an affected male. This individual mates with an unaffected female to produce two heterozygous children and two unaffected children. The original couple's next youngest is a heterozygous female. The original couple's second child is an unaffected male, who partners with an unaffected female to produce two unaffected children. The original couple's oldest child is an unaffected female whose partner is a heterozygous male. Their children are an unaffected female, an unaffected male, and a heterozygous male.

PUNNETT SQUARE

A **Punnett square** is a chart that allows you to easily determine the expected ratios of possible genotypes in the offspring of two parents. The mating between two parents is called a cross. The Punnett square is named after its developer, British geneticist Reginald C. Punnett. You can see a hypothetical example in Figure **12.4.4**. In this case, the gene is autosomal, and both parents are heterozygotes *(Aa)* for the gene. Half the gametes produced by each parent will have the *A* allele and half will have the *a* allele. That's because the two alleles are on homologous chromosomes, which always separate and go to separate gametes during meiosis. According to Mendel's law of segregation, the alleles in the gametes from each parent are written down the side and across the top of the Punnett square. Filling in the cells of the Punnett square gives the possible genotypes of their children. It also shows the most likely ratios of the genotypes, which in this case is 25 percent *AA*, 50 percent *Aa*, and 25 percent *aa*.

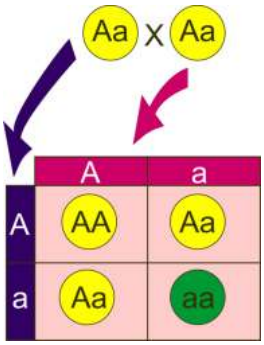


Figure **12.4.4**: A Punnett square shows the most likely proportions of offspring by genotype for a particular mating type.

Predicting Genotypes and phenotype with Punnett Squares

Mendel developed the law of segregation by following only a single characteristic, such as pod color, in his pea plants. In a monohybrid cross, such as the one in Figure **12.4.5**, the Punnett square shows every possible combination when combining one maternal (biological mother) allele with one paternal (biological father) allele. In this example, both organisms are heterozygous for flower color Bb (purple). Both plants produce gametes that contain either the B and b alleles. If the gametes from both parents contain the dominant alleles, the resulting plant will be homozygous dominant and have purple flowers. If the gametes from both parents contain the recessive alleles, the resulting plant will be homozygous recessive and have white flowers. If the gamete from one parent contains the dominant allele and the gamete from the other parent contains the recessive allele, the resulting plant will be heterozygous and have purple flowers. The probability of any single offspring showing the dominant trait is 3:1, or 75%.

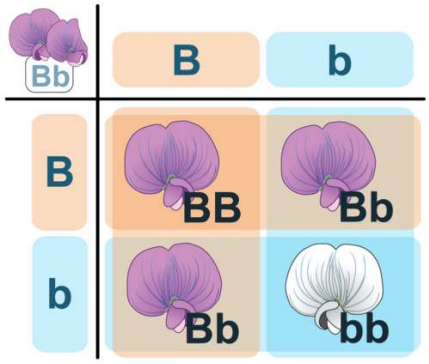


Figure **12.4.5**: This Punnett square shows a cross between two heterozygotes, Bb. To develop a Punnett square, possible combinations of alleles in a gamete are placed on the top and left side of a square.

DIHYBRID CROSS

For a monohybrid cross, we are only looking at a single gene. Therefore, the outside of the Punnett square will only have single letters (single alleles). For a dihybrid cross, pairs of alleles are used. This means the outside of the square will have pairs of letters. A Punnett square for a monohybrid cross is divided into four squares, whereas a Punnett square for a dihybrid cross is divided into 16 squares. How many boxes would a Punnett square need if three traits were examined? The squares are filled in with the possible

combinations of alleles formed when gametes combine, such as in a zygote.

These types of crosses can be challenging to set up, and the square you create will be 4x4. This simple guide will walk you through the steps of solving a typical dihybrid cross common in genetics. The method can also work for any cross that involves two traits.

CONSIDER THIS CROSS

This cross focuses on two traits in peas.

- The trait for yellow peas (Y) is dominant to the trait for green peas (y).
- The trait for round peas (R) is dominant to the trait for wrinkled peas (r).

Figure **12.4.6** outlines two generations of crosses. In the Parental (P) generation two homozygous plants are crossed: a plant that produces yellow round peas (YYRR) is crossed with a plant that produces green wrinkled peas (yyrr). The Punnett square for this cross is not shown, but all of the offspring would be heterozygous (have the YyRr genotype) and produce yellow round peas. To arrive at this:

- The parent with the YYRR genotype produces gametes that are all YR
- The parent with the yr genotype produces gametes that are all yr
- The YR and yr gametes produce YyRr offspring

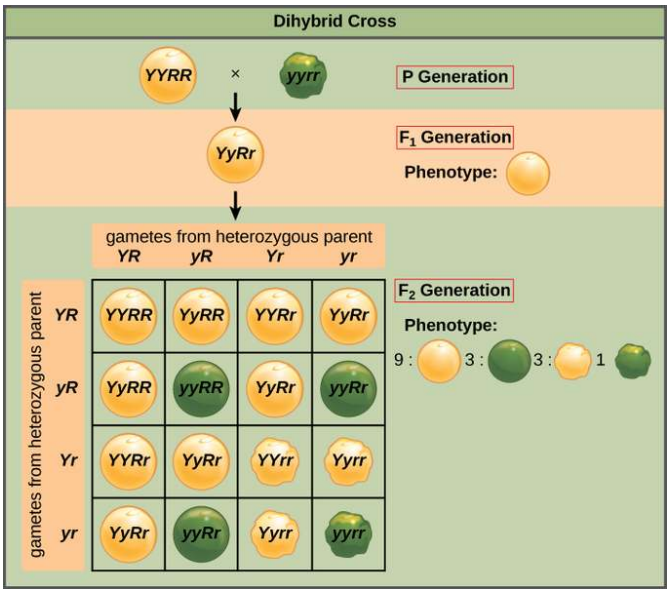


Figure **12.4.6**: A Punnett square showing genotypes and phenotypes of parents and offspring of a dihybrid cross

Two heterozygous plants (YyRr) are crossed. What gametes do each of these plants produce? When gametes are produced, they can either have the dominant R or the recessive r. And, they can either have the dominant Y or the recessive y. Combine the R's and Ys of each parent to represent sperm and egg.

- A gamete that gets the Y allele:
  - can either get the R allele and be YR
  - or it can get the r allele and be Yr
- A gamete that gets the y allele:
  - can either get the R allele and be yR
  - or it can get the r allele and be yr

A plant that is YyRr will produce 4 different gametes: YR, Yr, yR, yr. These gametes are written on the outside of the Punnett square in Figure **12.4.6**. Next the gametes are combined to form the offspring's genotypes (written in the center of the Punnet square). The resulting offspring will have the following ratios:

- 9/16 round, yellow peas; having the genotypes
  - YYRR (1)
  - YyRR (2)
  - YYRr (2)
  - YyRr (4)
- 3/16 round, green peas; having the genotypes yyRR (1) and yyRr (2)
- 3/16 wrinkled, yellow peas; having the genotypes YYrr (3)
- 1/16 wrinkled green peas; having the genotype yyrr

AUTOSOMAL SINGLE-GENE TRAITS IN HUMANS

Single-gene autosomal traits include widow's peak and freckles, both of which are illustrated below. Widow's peak refers to a point in the hairline at the center of the forehead. Assume that the dominant and recessive alleles for the widow's peak gene are represented by *W*and *w*, respectively. Because this is a dominant trait, people with the genotype *WW* and the genotype *Ww* will have a widow's peak, and only people with the genotype ww will not have the trait.



Figure **12.4.7**: Widow's peak is a dominant trait that is controlled by a gene located on an autosomal chromosome.

Assume that the dominant and recessive alleles for freckles are represented by *F* and *f*, respectively. Because it is a dominant trait, people with the genotype *FF* and the genotype *Ff* will have freckles, and only people with the genotype *ff* will not have the trait.



Figure **12.4.8**: Having freckles is a single-gene autosomal dominant trait

SEX INHERITANCE

What determines if a baby is a male or female? Recall that you have 23 pairs of chromosomes—and one of those pairs is the sex chromosomes. Everyone normally has two sex chromosomes. Later, you will learn that due to nondisjunction, males and females may have one less or one extra X chromosome. Your sex chromosomes can be X or Y. Females have two X chromosomes (XX), while males have one X chromosome and one Y chromosome (XY). If a baby inherits an X chromosome from the father and an X chromosome from the mother, what will be the child's sex? The baby will have two X chromosomes, so it will be female. If the father's sperm carries the Y chromosome, the child will be male. Notice that a mother can only pass on an X chromosome, so the sex of the baby is determined by the father. The father has a 50 percent chance of passing on the Y or X chromosome, so there is a 50 percent chance that a child will be male, and there is a 50 percent chance a child will be female. This 50:50 chance occurs for each baby. A couple's first five children could all be boys. The sixth child still has a 50:50 chance of being a girl. A Punnett square can also be used to show how the X and Y chromosomes are passed from parents to their children. This is illustrated in the Punnett square below. It may help you understand the inheritance pattern of sex-linked traits.

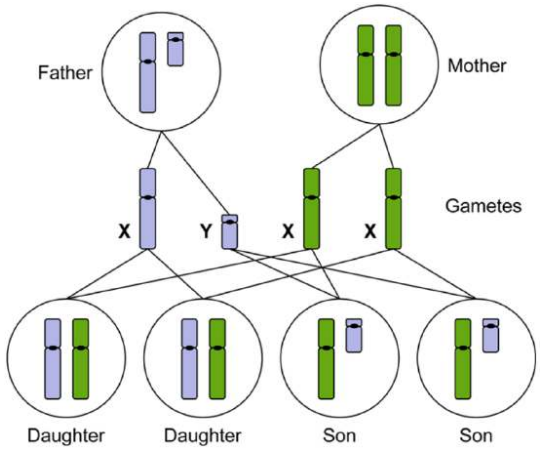


Figure **12.4.9**. The X and Y chromosomes determine male or female sexual development Males produce haploid gametes (sperm) that are either 23,X or 23,Y. Females produce haploid gametes (eggs) that are 23,X. Daughters inherit an X chromosome from their mother and an X chromosome from their father. Sons inherit an X chromosome from their mother and a Y chromosome from their father (paternal chromosomes indicated in blue, maternal chromosomes indicated in green)

X-LINKED MENDELIAN TRAITS IN HUMANS

One example of a sex-linked trait is red-green colorblindness. People with this type of colorblindness cannot tell the difference between red and green. They often see these colors as shades of brown (*Figure* **12.4.11**).

Males are much more likely to be colorblind than females because colorblindness is a sex-linked, recessive trait. Because males have just one X chromosome, they have only one allele for any X-linked trait. Therefore, a recessive X-linked allele is always expressed in males. Because females have two X chromosomes, they have two alleles for any X-linked trait. Females can have one X chromosome with the colorblind gene and one X chromosome with a normal gene for color vision. Since colorblindness is recessive, the dominant normal gene will mask the recessive colorblind gene. Females with one colorblindness allele and one normal allele are referred to as carriers. They carry the allele but do not express it. Females must inherit two copies of the recessive allele to express an X-linked recessive trait. This explains why X-linked recessive traits are less common in females than males and why they show a different pattern of inheritance than autosomal traits.

According to this Punnett square (Table **12.4.1**), the son of a woman who carries the colorblindness trait and a male with normal vision has a 50% chance of being colorblind. Figure **12.4.10** shows a simple pedigree for this trait.

Table **12.4.1**: Punnet Square for color blindness

	X^b	X^B
X^B	X^bX (**carrier** female)	X^BX^B (unaffected female)
Y	X^bY (colorblind male)	X^BY (unaffected male)

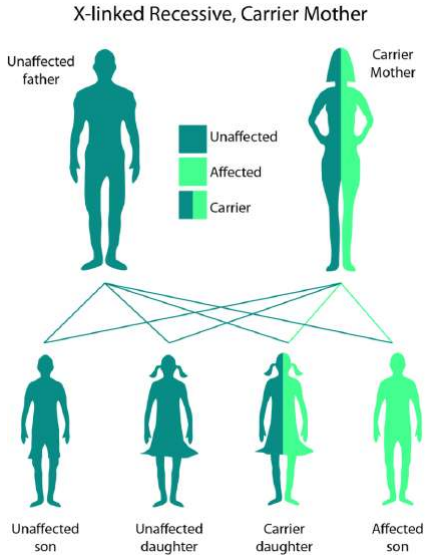


Figure **12.4.10**: Pedigree for Color Blindness. Color blindness is an X-linked recessive trait. A carrier mother and unaffected father can produce unaffected sons and daughters, carrier daughters, and colorblind sons.

Another example of a recessive X-linked Mendelian trait is hemophilia. This is a disorder characterized by the inability of blood to clot normally. England's Queen Victoria was a carrier of the disorder. Two of Queen Victoria's five daughters inherited the hemophilia allele from their mother and were carriers. When they married royalty in other European countries, they spread the allele across Europe, including the royal families of Spain, Germany, and Russia. Victoria's son Prince Leopold also inherited the hemophilia allele from his mother and actually suffered from the disease. For these reasons, hemophilia was once popularly called "the royal disease."

FEATURE: MY HUMAN BODY

Are you color blind or think you might be? If you inherited this X-linked recessive disorder, a world without clear differences between certain colors seems normal to you. It's all you have ever known. That's why some people who are color blind are not even aware of it. Simple tests have been devised to determine whether a person is color blind and the degree of this visual deficit. An example of such a test is pictured below. What do you see when you look at this circle? Can you clearly perceive the number 74? If so, you probably have normal red-green color vision. If you cannot see the number, you may have red-green color blindness.

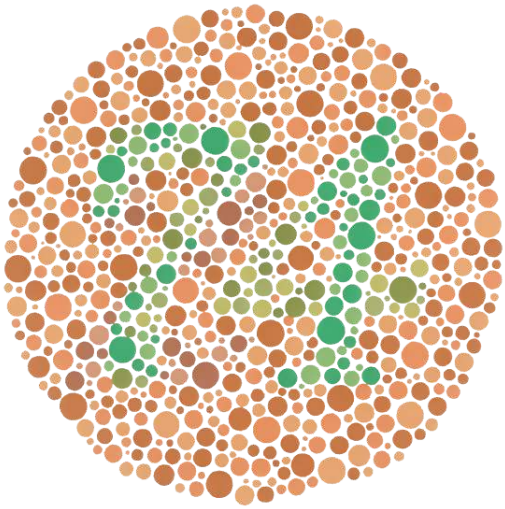


Figure **12.4.11**: This circle of colors containing the number 74 is part of the Ishihara color blindness test.

Being color blind may cause a number of problems. These may range from minor frustrations to outright dangers. For example:

- If you are color blind, it may be difficult to color-coordinate clothing and furnishings. You may end up wearing color combinations that people with normal color vision think are odd or clashing.
- Many LED indicator lights are red or green. For example, power strips and electronic devices may have indicator lights to show whether they are on (green) or off (red).
- Test strips for pH, hard water, swimming pool chemicals, and other common tests are also often color coded. Litmus paper for testing pH, for example, turns red in the presence of an acid, but if you are color blind, you may not be able to read the test result.
- Do you like your steak well done? If you are color blind, you may not be able to tell if the meat is still undercooked (red) or grilled just right. You also may not be able to distinguish ripe (red) from unripe (green) fruits and vegetables such as tomatoes. And some foods, such as dark green spinach, may look more like mud than food and be totally unappetizing.
- Weather maps often are color coded. Is that rain (green) in your forecast or a wintry mix of sleet and freezing rain (pink or red)? If you can't tell the difference, you may go out on the roads when you shouldn't and put yourself in danger.
- Being able to distinguish red from green traffic lights may be a matter of life or death. This can be very difficult for someone with red-green color blindness. That's why in some countries, people with this vision defect are not allowed to drive.

Being aware of conditions such as colorblindness is also important for anyone creating content online. Developing webpages that are legible to all users is an important skill for a variety of jobs. You can use online tools (such as the Toptal Color Blind Filter) to ensure that the content you create is usable by all of your customers.

REVIEW

1. Define genetic traits and simple inheritance.
2. Explain why autosomal and X-linked traits have different patterns of inheritance.
3. What is a pedigree, and why is it useful for studying how traits are passed from one generation to the next?
4. What is a Punnett square, and what does it show?
5. Identify examples of human autosomal and X-linked traits.
6. Imagine a hypothetical human gene that has two alleles, *Q* and *q*. *Q* is dominant to *q* and the inheritance of this gene is simple. Answer the following questions about this gene.
   A. If a woman has the genotype *Qq* and her partner has the genotype *QQ*, list each of their possible gametes and what proportion of their gametes will have each allele.
   B. What are the likely proportions of their offspring being *QQ*, *Qq*, or *qq*?
   C. Is this an autosomal trait or an X-linked trait? How do you know?
   D. What are the chances of their offspring exhibiting the dominant *Q* trait? Explain your answer.
7. Explain why fathers always pass their X chromosome down to their daughters.
8. *True or False*. Women are more likely to have X-linked diseases than men.
9. *True or False*. Most human autosomal traits are controlled by a single gene with two alleles, similar to Mendel's pea plants.
10. For each of the scenarios below, choose whether you would use a Punnett square or a pedigree. Choose only the one that best fits the scenario.
    A. A man and a woman have known genotypes and you want to predict the possible genotypes of their offspring.
    B. You want to document which members of your family had or have breast cancer.

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ATTRIBUTIONS

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12.5: COMPLEX INHERITANCE

FAMILY PORTRAIT

This photo of a South African family shows some of the variations that exist in human skin color. The color of human skin can range from very light to very dark with every possible gradation in between. As you might expect, the skin color trait has a more complex genetic basis than just one gene with two alleles, which is the type of simple trait that Mendel studied in pea plants. Like skin color, many other human traits have more complicated modes of inheritance than Mendelian traits. Such modes of inheritance are called **non-Mendelian inheritance,** and they include inheritance of multiple allele traits, traits with codominance or incomplete dominance, and polygenic traits, among others, all of which are described below.



Figure **12.5.1**: Family

MULTIPLE ALLELE TRAITS

The majority of human genes are thought to have more than two normal versions or alleles. Traits controlled by a single gene with more than two alleles are called **multiple allele traits**. An example is ABO blood type. Your blood type refers to which of certain proteins called antigens are found on your red blood cells. There are three common alleles for this trait, which are represented by the letters I^A, I^B, and i.

Table **12.5.1**: ABO Blood Group

Genotype	Phenotype (blood type)
I^AI^A	A
I^Ai	A
I^BI^B	B
I^Bi	B
ii	O
I^AI^B	AB

As shown in the table below, there are six possible ABO genotypes because the three alleles, taken two at a time, result in six possible combinations. The IA and IB alleles are dominant to the i allele. As a result, both I^AI_A and I^Ai genotypes have the same phenotype, with the A antigen in their blood (type A blood). Similarly, both I^BI^B and I^Bi genotypes have the same phenotype, with the B antigen in their blood (type B blood). No antigen is associated with the i allele, so people with the ii genotype have no antigens for ABO blood type in their blood (type O blood).

CODOMINANCE

Look at the genotype I^AI^B in the ABO blood group table. Alleles I^A and I^B for ABO blood type are neither dominant nor recessive to one another. Instead, they are codominant to each other. **Codominance** occurs when two alleles for a gene are expressed equally in the phenotype of heterozygotes. In the case of ABO blood type, I^AI^B heterozygotes have a unique phenotype, with both A and B antigens in their blood (type AB blood).

INCOMPLETE DOMINANCE

Another relationship that may occur between alleles for the same gene is **incomplete dominance.** This occurs when the dominant allele is not completely dominant, so an intermediate phenotype results in heterozygotes who inherit both alleles. Generally, this happens when the two alleles for a given gene both produce proteins but one protein is not functional. As a result, the heterozygote individual produces only half the amount of normal protein as is produced by an individual who is homozygous for the normal allele.

An example of incomplete dominance in humans is Tay Sachs disease. The normal allele for the gene, in this case, produces an enzyme that is responsible for breaking down lipids. A defective allele for the gene results in the production of a nonfunctional enzyme. Heterozygotes who have one normal and one defective allele produce half as much functional enzyme as the normal homozygote, and this is enough for normal development. However, homozygotes who have only defective alleles produce only the nonfunctional enzyme. This leads to the accumulation of lipids in the brain beginning *in utero*, which causes significant brain damage. Most individuals with Tay Sachs disease die at a young age, typically by the age of five years.

POLYGENIC TRAITS

Many human traits are controlled by more than one gene. These traits are called **polygenic traits**. The alleles of each gene have a minor additive effect on the phenotype. There are many possible combinations of alleles, especially if each gene has multiple alleles. Therefore, a whole continuum of phenotypes is possible.

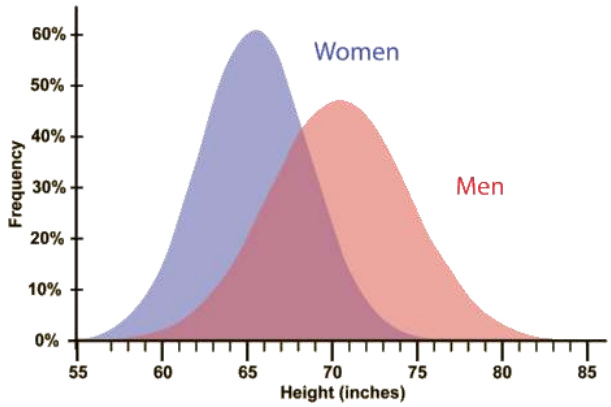


Figure **12.5.2**. Human Adult Height. Like many other polygenic traits, adult height has a bell-shaped distribution.

An example of a human polygenic trait is adult height. Several genes, each with more than one allele, contribute to this trait, so there are many possible adult heights. For example, one adult's height might be 1.655 m (5.430 feet), and another adult's height might be 1.656 m (5.433 feet). Adult height ranges from less than 5 feet to more than 6 feet, with males being somewhat taller than females on average. The majority of people fall near the middle of the range of heights for their sex, as shown in the graph in Figure **12.5.2**.

ENVIRONMENTAL EFFECTS ON PHENOTYPE

Many traits are affected by the environment as well as by genes. This may be especially true for polygenic traits. For example, adult height might be negatively impacted by poor diet or illness during childhood. Skin color is another polygenic trait. There is a wide range of skin colors in people worldwide. In addition to differences in skin color genes, differences in exposure to ultraviolet (UV) light cause some of the variations. As shown in *Figure* **12.5.3**, exposure to UV light darkens the skin.



Figure **12.5.3**: Skin on the lower part of the arm is much darker in color than protected skin near the top due to the effects of UV radiation.

PLEIOTROPY

Some genes affect more than one phenotypic trait. This is called **pleiotropy**. There are numerous examples of pleiotropy in humans. They generally involve important proteins that are needed for the normal development or functioning of more than one organ system. An example of pleiotropy in humans occurs with the gene that codes for the main protein in collagen, a substance that helps form bones. This protein is also important in the ears and eyes. Mutations in the gene result in problems not only in bones but also in these sensory organs, which is how the gene's pleiotropic effects were discovered.

Another example of pleiotropy occurs with sickle cell anemia. This recessive genetic disorder occurs when there is a mutation in the gene that normally encodes the red blood cell protein called hemoglobin. People with the disorder have two alleles for sickle-cell hemoglobin, so named for the sickle shape (Figure **12.5.4**) that their red blood cells take on under certain conditions such as physical exertion. The sickle-shaped red blood cells clog small blood vessels, causing multiple phenotypic effects, including stunting of physical growth, certain bone deformities, kidney failure, and strokes.

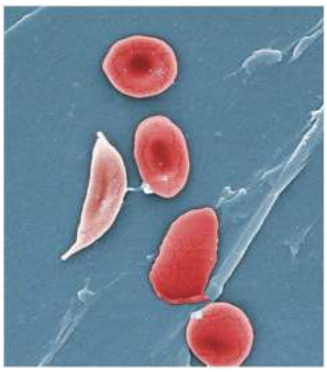


Figure **12.5.4**: The sickle-shaped red blood cell on the left is shown next to several normal red blood cells for comparison.

EPISTASIS

Some genes affect the expression of other genes. This is called **epistasis**. Epistasis is similar to dominance, except that it occurs between different genes rather than between different alleles for the same gene.

Albinism is an example of epistasis. A person with albinism has virtually no pigment in the skin. The condition occurs due to an entirely different gene than the genes that encode skin color. Albinism occurs because a protein called tyrosinase, which is needed for the production of normal skin pigment, is not produced due to a gene mutation. If an individual has albinism mutation, he or she will not have any skin pigment, regardless of the skin color genes that were inherited.

FEATURE: MY HUMAN BODY

Do you know your ABO blood type? In an emergency, knowing this valuable piece of information could possibly save your life. If you ever need a blood transfusion, it is vital that you receive blood that matches your own blood type. Why? If the blood transfused into your body contains an antigen that your own blood does not contain, antibodies in your blood plasma (the liquid part of your blood) will recognize the antigen as foreign to your body and cause a reaction called agglutination. In this reaction, the transfused red blood cells will clump together, as shown in the image below. The agglutination reaction is serious and potentially fatal.

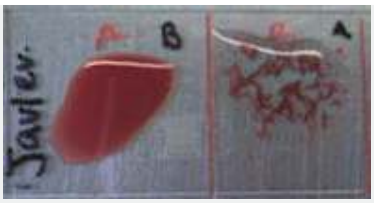
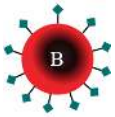
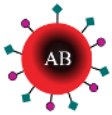


Figure **12.5.5**: Two samples of the same blood are shown here. The sample on the left is mixed with anti-B antibodies; the sample on the right is mixed with anti-A antibodies. Agglutination by the anti-A antibodies on the right shows that the sample is type A blood.

Knowing the antigens and antibodies present in each of the ABO blood types will help you understand which type(s) of blood you can safely receive if you ever need a transfusion. This information is shown in the table below for all of the ABO blood types. For example, if you have blood type A, this means that your red blood cells have the A antigen and that your blood plasma contains anti-B antibodies. If you were to receive a transfusion of type B or type AB blood, both of which have the B antigen, your anti-B antibodies would attack the transfused red blood cells, causing agglutination.

Table **12.5.2**: Antigens and antibodies in ABO blood types

Characteristics	Type A	Type B	Type AB	Type O
Red Blood Cell				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red Blood Cells	 A antigen	B antigens	 A and B antigens	None

You may have heard that people with blood type O are called universal donors and that people with blood type AB are called universal recipients. People with type O blood have neither A nor B antigens in their blood, so if their blood is transfused into someone with a different ABO blood type, it causes no immune reaction. In other words, they can donate blood to anyone. On the other hand, people with type AB blood have no anti-A or anti-B antibodies in their blood, so they can receive a transfusion of blood from anyone. Which blood type(s) can safely receive a transfusion of type AB blood, and which blood type(s) can be safely received by those with type O blood?

REVIEW

1. What is non-Mendelian inheritance?
2. Explain why the human ABO blood group is an example of a multiple allele trait with codominance.
3. What is incomplete dominance? Give an example of this type of non-Mendelian inheritance in humans.
4. Explain the genetic basis of human skin color.
5. How may the human trait of adult height be influenced by the environment?
6. Define pleiotropy, and give a human example.
7. What is the difference between pleiotropy and epistasis?
8. Which of the following terms best matches each trait description? Choose only the one term that best fits each trait. (codominance; multiple allele trait; Mendelian trait; polygenic trait)
   A. A trait controlled by four genes.
   B. A trait where each allele of a heterozygote makes an equal contribution to the phenotype.
   C. A trait controlled by a single gene that has three different versions.
   D. A trait controlled by a single gene where one allele is fully dominant to the only other allele.
9. People with type AB blood have:
   A. anti-O antibodies
   B. anti-A and anti-B antibodies
   C. A and B antigens
10. *True or False*. People with type O blood cannot receive a blood transfusion from anyone besides others with type O blood.
11. *True or False*. People with type O blood can be heterozygous for this trait.

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12.6: GENETIC DISORDERS

POLLY WHO?

Each hand in Figure **12.6.1** has an extra pinky finger. This is a condition called polydactyly, which literally means "many digits." People with polydactyly may have extra fingers and/or toes, and the condition may affect just one hand or foot or both hands and feet. Polydactyly is often genetic in origin and may be part of a genetic disorder that is associated with other conditions.



Figure **12.6.1**: Polydactyly

WHAT ARE GENETIC DISORDERS?

Genetic disorders are diseases, syndromes, or other conditions that are caused by mutations in one or more genes or by chromosomal alterations. Genetic disorders are typically present at birth, but they should not be confused with congenital disorders, which are any disorders, regardless of cause, that are present at birth. Some congenital disorders are not caused by genetic mutations or chromosomal alterations. Instead, they are caused by problems that arise during embryonic or fetal development or during the process of birth. An example of a nongenetic congenital disorder is fetal alcohol syndrome. This is a collection of birth defects, including facial anomalies and intellectual disability, caused by maternal alcohol consumption during pregnancy.

GENETIC DISORDERS CAUSED BY MUTATIONS

Table **12.6.1**: Autosomal and X-linked genetic disorders

Genetic Disorder	Direct Effect of Mutation	Signs and Symptoms of the Disorder	Mode of Inheritance
Marfan syndrome	defective protein in connective tissue	heart and bone defects and unusually long, slender limbs and fingers	autosomal dominant
Sickle cell anemia	atypical hemoglobin protein in red blood cells	sickle-shaped red blood cells that clog tiny blood vessels, causing pain and damaging organs and joints	autosomal recessive
Vitamin D-resistant rickets	lack of a substance needed for bones to absorb minerals	soft bones that easily become deformed, leading to bowed legs and other skeletal deformities	X-linked dominant
Hemophilia A	reduced activity of a protein needed for blood clotting	internal and external bleeding that occurs easily and is difficult to control	X-linked recessive

Table **12.6.1** lists several genetic disorders caused by mutations in just one gene. Some of the disorders are caused by mutations in autosomal genes, others by mutations in X-linked genes. Which disorders would you expect to be more common in males than females?

Very few genetic disorders are controlled by dominant mutant alleles. A dominant allele is expressed in every individual who inherits even one copy of it. If it causes a serious disorder, affected people may die young and fail to reproduce. Therefore, the mutant dominant allele is likely to die out of the population.

A recessive mutant allele, such as the allele that causes sickle cell anemia or cystic fibrosis, is not expressed in people who inherit just one copy of it. These people are called carriers. They do not have the disorder themselves, but they carry the mutant allele and their offspring can inherit it. Thus, the allele is likely to pass on to the next generation rather than die out.

GENETIC DISORDERS CAUSED BY CHROMOSOMAL ALTERATIONS

As we learned in the Cell Reproduction chapter, mistakes may occur during meiosis that results in **nondisjunction**. This is the failure of replicated chromosomes to separate properly during meiosis. Some of the resulting gametes will be missing all or part of a chromosome, while others will have an extra copy of all or part of the chromosome. If such gametes are fertilized and form zygotes, they usually do not survive. If they do survive, the individuals are likely to have serious genetic disorders.

Table **12.6.2** lists several genetic disorders that are caused by atypical numbers of chromosomes. Most chromosomal disorders involve the X chromosome. The X and Y chromosomes are the only chromosome pair in which the two chromosomes are very different in size. This explains why nondisjunction of the sex chromosomes tends to occur more frequently than nondisjunction of autosomes.

Table **12.6.2**: Genetic Disorders Caused by Atypical Numbers of Chromosomes

Genetic Disorder	Genotype	Phenotypic Effects
Down syndrome	extra copy (complete or partial) of chromosome 21 (see figure below)	developmental delays, distinctive facial appearance, and other physical and developmental conditions (see figure below)
Turner's syndrome	one X chromosome but no other sex chromosome (XO)	Chromosomally female with short height and infertility (inability to reproduce)
Triple X syndrome	three X chromosomes (XXX)	Chromosomally female with mild developmental delays and menstrual irregularities
Klinefelter's syndrome	one Y chromosome and two or more X chromosomes (XXY, XXXY)	Chromosomally male with problems in sexual development and reduced levels of the male hormone testosterone

DIAGNOSING AND TREATING GENETIC DISORDERS

A genetic disorder that is caused by a mutation can be inherited. Therefore, people with a genetic disorder in their family may be concerned about having children with the disorder. A genetic counselor can help them understand the risks of their children being affected. If they decide to have children, they may be advised to have prenatal ("before birth") testing to see if the fetus has any genetic disorders. One method of prenatal testing is amniocentesis. In this procedure, a few fetal cells are extracted from the fluid surrounding the fetus *in utero*, and the fetal chromosomes are examined. Down syndrome and other chromosomal alterations can be detected in this way.

The symptoms of genetic disorders can sometimes be treated or prevented. For example, in the genetic disorder called **phenylketonuria (PKU)**, the amino acid phenylalanine builds up in the body to harmful levels. PKU is caused by a mutation in a gene that normally codes for an enzyme needed to break down phenylalanine. The buildup of PKU can lead to serious health problems, such as intellectual disability and delayed development, among other serious problems. Babies in the United States and many other countries are screened for PKU soon after birth. If PKU is diagnosed, the infant can be fed a low-phenylalanine diet. This prevents the buildup of phenylalanine and the health problems associated with it. With a low phenylalanine diet, most symptoms of the disorder can be prevented.

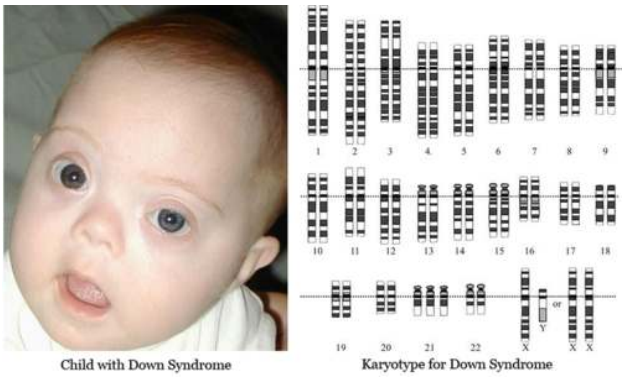


Figure **12.6.2**: Trisomy 21 (Down Syndrome) Karyotype. A karyotype is a picture of a cell's chromosomes. Note the extra chromosome 21. A child with Down syndrome, exhibiting a characteristic facial appearance.

CURING GENETIC DISORDERS

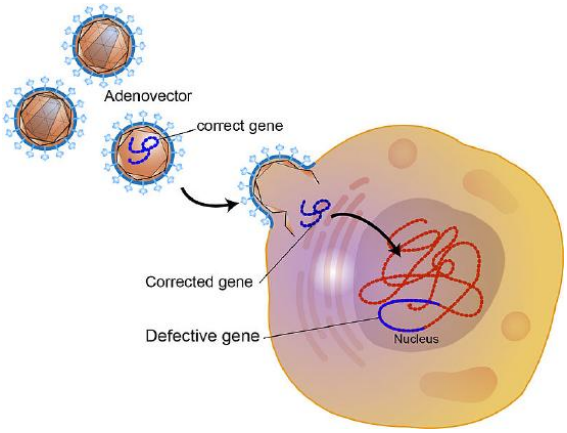


Figure **12.6.3**: Gene therapy is an experimental technique for curing a genetic disorder by changing the patient's genetic makeup. Typically, gene therapy involves introducing a normal copy of a mutant gene into the patient's cells.

Cures for genetic disorders are still in the early stages of development. One potential cure is gene therapy. **Gene therapy** is an experimental technique that uses genes to treat or prevent disease. In gene therapy, normal genes are introduced into cells to compensate for mutated genes. If a mutated gene causes a necessary protein to be nonfunctional or missing, gene therapy may be able to introduce a normal copy of the gene to produce the needed functional protein.

A gene that is inserted directly into a cell usually does not function, so a carrier called a **vector** is genetically engineered to deliver the gene (Figure **12.6.3**). Certain viruses, such as adenoviruses, are often used as vectors. They can deliver the new gene by infecting cells. The viruses are modified so they do not cause disease when used in people. If the treatment is successful, the new gene delivered by the vector will allow the synthesis of a functioning protein.

FEATURE: HUMAN BIOLOGY IN THE NEWS

Down syndrome is the most common genetic cause of intellectual disability. It occurs in about 1 in every 700 live births, and it currently affects nearly half a million Americans.

Until recently, scientists thought that the changes leading to intellectual disability in people with Down syndrome all happen before birth.

Researchers recently discovered a genetic disorder that affects brain development in people with Down Syndrome throughout childhood and into adulthood. The newly discovered genetic disorder changes communication between nerve cells in the brain, resulting in the slower transmission of nerve impulses. This finding may eventually allow the development of strategies to promote brain functioning in Down syndrome patients and may also be applicable to other developmental disabilities such as autism.

REVIEW

1. Define genetic disorder.
2. Identify three genetic disorders caused by mutations in a single gene.
3. Why are single-gene genetic disorders more commonly controlled by recessive than dominant mutant alleles?
4. What is nondisjunction? Why may it cause genetic disorders?
5. Explain why genetic disorders caused by a number of chromosomes most often involve the X chromosome.
6. How is Down syndrome detected *in utero*?
7. Use the example of PKU to illustrate how the symptoms of a genetic disorder can sometimes be prevented.
8. Explain how gene therapy works.
9. Compare and contrast genetic disorders and congenital disorders.
10. Explain why parents that do not have Down syndrome can have a child with Down syndrome.
11. Hemophilia A and Turner's syndrome both involve problems with the X chromosome. What is the major difference between these two types of disorders in terms of how the X chromosome is affected?
12. Can you be a carrier of Marfan syndrome and not have the disorder? Explain your answer.
13. *True or False.* It is impossible for people to have more than three copies of one chromosome.
14. *True or False.* The gene for sickle cell anemia is on a sex chromosome.

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12.7: CASE STUDY CONCLUSION- CANCER AND CHAPTER SUMMARY

CASE STUDY CONCLUSION: CANCER IN THE FAMILY

Rebecca's family tree, as illustrated in Figure **12.7.1**, shows a high incidence of cancer among close relatives. But are genes the cause of cancer in this family? Only genetic testing, which is the sequencing of specific genes in an individual, can reveal whether a cancer-causing gene is being inherited in this family.

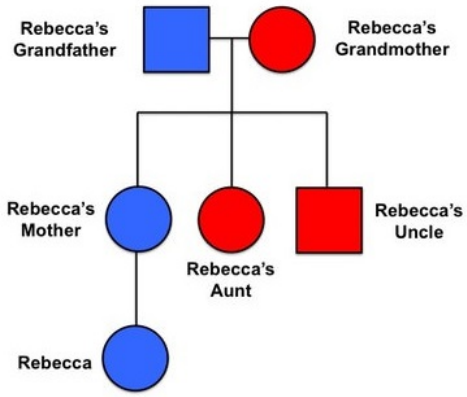


Figure **12.7.1**: Pedigree for Rebecca's family, as described at the beginning of this chapter, showing individuals with cancer (red) and those that do not have cancer (blue). Circles represent women, squares represent men.

Fortunately for Rebecca, the results of her genetic testing show that she does not have the mutations in the **BRCA1** and **BRCA2** genes that most commonly increase a person's risk of getting cancer. However, it does not mean that she doesn't have other mutations in these genes that could increase her risk of getting cancer. There are many other mutations in BRCA genes whose effect on cancer risk is not known, and there may be many more yet to be discovered. It is important to continue to study the variations in genes such as BRCA in different people to better assess their possible contribution to the development of the disease. As you now know from this chapter, many mutations are harmless, while others can cause significant health effects, depending on the specific mutation and the gene involved.

Mutations in BRCA genes are particularly likely to cause cancer because these genes encode for tumor-suppressor proteins that normally repair damaged DNA and control cell division. If these genes are mutated in a way that causes the proteins to not function properly, other mutations can accumulate and cell division can run out of control, which can cause cancer.

BRCA1 and BRCA2 are on chromosomes 17 and 13, respectively, which are autosomes. As Rebecca's genetic counselor mentioned, mutations in these genes have a dominant inheritance pattern. Now that you know the pattern of inheritance of autosomal dominant genes if Rebecca's grandmother *did* have one copy of a mutated BRCA gene, what are the chances that Rebecca's mother also has this mutation? Because it is dominant, only one copy of the gene is needed to increase the risk of cancer, and because it is on autosomes instead of sex chromosomes, the sex of the parent or offspring does not matter in the inheritance pattern. In this situation, Rebecca's grandmother's eggs would have had a 50% chance of having a BRCA gene mutation, due to Mendel's law of segregation. Therefore, Rebecca's mother would have had a 50% chance of inheriting this gene. Even though Rebecca does not have the most common BRCA mutations that increase the risk of cancer, it does not mean that her also mother does not, because there would also only be a 50% chance that she would pass it on to Rebecca. Therefore, Rebecca's mother should consider getting tested for mutations in the BRCA genes as well. Ideally, the individuals with cancer in a family should be tested first when a genetic cause is suspected so that if there is a specific mutation being inherited, it can be identified and the other family members can be tested for that same mutation.

Mutations in both BRCA1 and BRCA2 are often found in Ashkenazi Jewish families. However, these genes are not linked in the chromosomal sense, because they are on different chromosomes and are therefore inherited independently, in accordance with Mendel's law of independent assortment. Why would certain gene mutations be prevalent in particular ethnic groups? If people within an ethnic group tend to produce offspring with each other, their genes will remain prevalent within the group. These may be genes for harmless variations such as skin, hair, or eye color, or harmful variations such as the mutations in the BRCA genes. Other genetically based diseases and disorders are sometimes more commonly found in particular ethnic groups, such as cystic fibrosis in people of European descent and sickle-cell anemia in people of African descent. You will learn more about the prevalence of certain genes and traits in particular ethnic groups and populations in the chapter on *Human Variation.*

As you learned in this chapter, genetics is not the sole determinant of phenotype. The environment can also influence many traits, such as adult height and skin color. The environment also plays a major role in the development of cancer. 90 to 95% of all cancers do not have an identified genetic cause and are often caused by mutagens in the environment such as UV radiation from the sun or toxic chemicals in cigarette smoke. But for families like Rebecca's, knowing their family health history and genetic makeup may help them better prevent or treat diseases that are caused by their genetic inheritance. If a person knows they have a gene that can increase their risk of cancer, they can make lifestyle changes, have early and more frequent cancer screenings, and may even choose to have preventative surgeries that may help reduce their risk of getting cancer and increase their odds of long-term survival if cancer does occur. The next time you go to the doctor and they ask whether any members of your family have had cancer, you will have a deeper understanding of why this information is so important to your health.

CHAPTER SUMMARY

In this chapter, you learned about genetics — the science of heredity. Specifically, you learned that:

- Chromosomes are structures made of DNA and proteins that are encoded with genetic instructions for making proteins. The instructions are organized into units called genes, most of which contain instructions for a single protein.
- Humans normally have 23 pairs of chromosomes. Of these, 22 pairs are autosomes, which contain genes for characteristics unrelated to sex. The other pair consists of sex chromosomes (XX in females, XY in males). Only the Y chromosome contains genes that determine sex.
- Humans have an estimated 20,000 to 22,000 genes. The majority of human genes have two or more possible versions, called alleles.
- Mendel experimented with the inheritance of traits in pea plants, which have two different forms of several visible characteristics. Mendel crossed pea plants with different forms of traits.
    - In Mendel's first set of experiments, he crossed plants that only differed in one characteristic. The results led to Mendel's first law of inheritance, called the law of segregation. This law states that there are two factors controlling a given characteristic, one of which dominates the other, and these factors separate and go to different gametes when a parent reproduces.
    - In Mendel's second set of experiments, he experimented with two characteristics at a time. The results led to Mendel's second law of inheritance, called the law of independent assortment. This law states that the factors controlling different characteristics are inherited independently of each other.
- Mendel's laws of inheritance, now expressed in terms of genes, form the basis of genetics, the science of heredity. Mendel is often called the father of genetics.
- The position of a gene on a chromosome is its locus. A given gene may have different versions called alleles. Paired chromosomes of the same type are called homologous chromosomes and they have the same genes at the same loci.
- The alleles an individual inherits for a given gene make up the individual's genotype. An organism with two of the same allele is called a homozygote, and an individual with two different alleles is called a heterozygote.
- The expression of an organism's genotype is referred to as its phenotype. A dominant allele is always expressed in the phenotype, even when just one dominant allele has been inherited. A recessive allele is expressed in the phenotype only when two recessive alleles have been inherited.
- In sexual reproduction, two parents produce gametes that unite in the process of fertilization to form a single-celled zygote. Gametes are haploid cells with only one of each pair of homologous chromosomes, and the zygote is a diploid cell with two of each pair of chromosomes.
- Mendelian inheritance refers to the inheritance of traits controlled by a single gene with two alleles, one of which may be completely dominant to the other. The pattern of inheritance of Mendelian traits depends on whether the traits are controlled by genes on autosomes or by genes on sex chromosomes.
    - Examples of human autosomal Mendelian traits include dimples and earlobe attachment. Examples of human X-linked traits include red-green color blindness and hemophilia.
- Two tools for studying inheritance are pedigrees and Punnett squares. A pedigree is a chart that shows how a trait is passed from generation to generation. A Punnett square is a chart that shows the expected ratios of possible genotypes in the offspring of two parents.
- Non-Mendelian inheritance refers to the inheritance of traits that have a more complex genetic basis than one gene with two alleles and complete dominance.
    - Multiple allele traits are controlled by a single gene with more than two alleles. An example of a human multiple allele trait is ABO blood type.
    - Codominance occurs when two alleles for a gene are expressed equally in the phenotype of heterozygotes. A human example of codominance occurs in the AB blood type, in which the I^A and I^B alleles are codominant.
    - Incomplete dominance is the case in which the dominant allele for a gene is not completely dominant to a recessive allele, so an intermediate phenotype occurs in heterozygotes who inherit both alleles. A human example of incomplete dominance is Tay Sachs disease, in which heterozygotes produce half as much functional enzyme as normal homozygotes.
    - Polygenic traits are controlled by more than one gene, each of which has a minor additive effect on the phenotype. This results in a continuum of phenotypes. Examples of human polygenic traits include skin color and adult height. Many of these types of traits, as well as others, are affected by the environment as well as by genes.
    - Pleiotropy refers to the situation in which a gene affects more than one phenotypic trait. A human example of pleiotropy occurs with sickle cell anemia, which has multiple effects on the body.
    - Epistasis is when one gene affects the expression of other genes. An example of epistasis is albinism, in which the albinism mutation negates the expression of skin color genes.
- Genetic disorders are diseases, syndromes, or other abnormal conditions that are caused by mutations in one or more genes or by chromosomal alterations.
    - Examples of genetic disorders caused by single-gene mutations include Marfan syndrome (autosomal dominant), sickle cell anemia (autosomal recessive), vitamin D-resistant rickets (X-linked dominant), and hemophilia A (X-linked recessive). Very few genetic disorders are caused by

dominant mutations because these alleles are less likely to be passed on to successive generations.

- Nondisjunction is the failure of replicated chromosomes to separate properly during meiosis. This may result in genetic disorders caused by abnormal numbers of chromosomes. An example is Down syndrome, in which the individual inherits an extra copy of chromosome 21. Most chromosomal disorders involve the X chromosome. An example is Klinefelter's syndrome (XXY, XXXY).
- Prenatal genetic testing, for example, by amniocentesis, can detect chromosomal alterations *in utero*. The symptoms of some genetic disorders can be treated or prevented. For example, symptoms of phenylketonuria (PKU) can be prevented by following a low-phenylalanine diet throughout life.
- Cures for genetic disorders are still in the early stages of development. One potential cure is gene therapy, in which normal genes are introduced into cells by a vector such as a virus to compensate for mutated genes.

CHAPTER SUMMARY REVIEW

1. Which sentence is correct?
   A. Different alleles of the same gene are located at the same locus on homologous chromosomes.
   B. Different alleles of the same gene are located at different loci on homologous chromosomes.
   C. Different genes of the same alleles are located at the same locus on homologous chromosomes.
   D. Different alleles of the same gene are located at different loci on the same chromosome.
2. A person has a hypothetical *Aa* genotype. Answer the following questions about this genotype.
   A. What do *A* and *a* represent?
   B. If the person expresses only the phenotype associated with *A*, is this an example of complete dominance, codominance, or incomplete dominance? Explain your answer. Also, describe what the observed phenotypes would be if it were either of the two incorrect answers.
3. Explain how a mutation that occurs in a parent can result in a genetic disorder in their child. Be sure to include which type of cell or cells in the parent must be affected in order for this to happen.
4. What is an allele that is not expressed in a heterozygote called?
5. *True or False*. Sex is determined by a gene on an autosome.
6. *True or False*. In sexual reproduction, parents and offspring are never identical.
7. *True or False*. In humans, a gamete will have 23 chromosomes.
8. *True or False*. The expression of an organism's phenotype produces its genotype.
9. *True or False*. It is entirely likely for a gene to have more than two alleles.
10. Mendel's law of independent assortment states that
    A. two factors of the same characteristic separate into different gametes.
    B. there are dominant and recessive factors.
    C. factors controlling different characteristics are inherited independently of each other.
    D. there are two factors that control inheritance.
11. Linked genes:
    A. are on homologous chromosomes.
    B. are on the same chromosome.
    C. are on adjacent chromosomes.
    D. are on non-homologous chromosomes.
12. A woman has red-green color blindness, which is an X-linked recessive trait. Her husband does not have red-green color blindness. Which of the following is correct?
    A. Half of their daughters will have red-green color blindness.
    B. All of their daughters will have red-green color blindness.
    C. All of their sons will have red-green color blindness.
    D. All of their children will have red-green color blindness.
13. Which of the following is an example of Mendelian inheritance?
    A. A trait that has three alleles
    B. A trait that is controlled by two genes
    C. A trait that is controlled by a single gene with one dominant and one recessive allele
    D. A trait that has two alleles, both of which are expressed equally in the phenotype

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