BIO 50: ANATOMY AND PHYSIOLOGY



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Anatomy and Physiology (Zingg)

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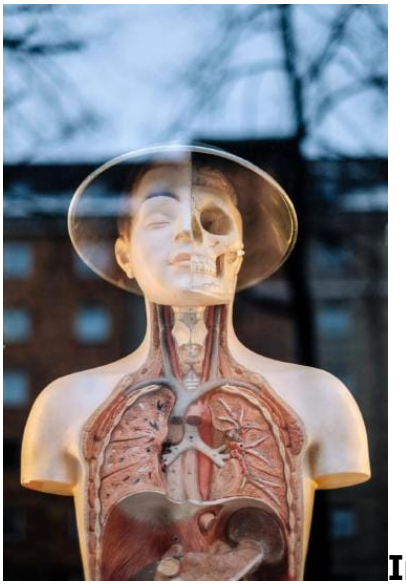
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1.1: Defining Anatomy

Human anatomy is the study of the structure of the human body.

Master this section and you'll be able to:

- Define Anatomy
- Outline the two major subtypes of anatomy
- Give a very brief overview of the history of human anatomy



Introduction to Anatomy

Anatomy is defined as the study of **body structure**. It describes the structure and location of the different components of an organism to provide a framework for understanding. Human anatomy studies the way that every part of a human, from molecules to bones, interacts to form a functional whole. The history of anatomy has been an evolving understanding of organs and structures in the body. Beginning in Ancient Greece and developing through the Middle Ages and the Renaissance, methods of studying anatomy have advanced dramatically. This field has moved from examination of animals and cadavers through invasive dissection to the technologically complex techniques developed in the 20th century, such as non-invasive imaging and radiology. For a little more detail, review the bottom of this page.

Generally, medical and biology students learn about the human body from anatomical models, skeletons, textbooks, diagrams, photographs, lectures, and tutorials. Nurses, medical and dental students also learn through the dissection and inspection of cadavers. A thorough working knowledge of anatomy is required for all medical professionals, especially surgeons and doctors working in diagnostic specialties such as radiology.

There are two major types of anatomy:

1) Gross Anatomy

Gross (or macroscopic) anatomy is the study of structural features visible to the naked eye, such as internal organs and external details. Gross anatomy can be further subdivided into three different fields:

- ## Surface Anatomy

This is the study of the external body and anatomical features without dissection. It focusses on the **external features** of the body that can be seen or felt through the skin and how they relate to deeper internal structures.

A simple example of surface anatomy is **finding your collarbone (clavicle) by feeling just below your neck.** You can feel the hard bone that runs horizontally from your neck to your shoulder — that is your clavicle. This is surface anatomy in action: using what you can see or touch on the outside of your body to understand what is underneath.

Another example of surface anatomy is identifying the **location of the heart by using external landmarks on the chest**. For instance, a clinician can locate the **apex of the heart** by finding the space between the **5^{th} and 6^{th} ribs on the left side of the chest, just below the nipple line**. This helps guide where to place a stethoscope to listen for heart sounds or where to perform CPR.

- ## Regional Anatomy

This type of anatomy focuses on specific external and internal regions of the body (such as the head or chest) and how different systems work together in that region.

An example of regional anatomy is the study of the **thoracic region** of the body. In this approach, you would examine **all the structures within the chest area** — including the **lungs, heart, ribs, thoracic vertebrae, esophagus, blood vessels, nerves, and muscles** — as a single unit, rather than studying each system (like the respiratory or circulatory system) separately.

Regional anatomy is widely used in medical schools because it is easier to apply to a clinical setting than systemic anatomy. It is especially useful in medical fields like surgery or radiology, where professionals need to understand how different structures in a particular area relate to one another in real-life situations. The major anatomy textbook, Gray's Anatomy, for example, has recently been reorganized from a systems format to a regional format to reflect this preference.

- ## Systemic Anatomy

Systemic anatomy, finally, focuses on the anatomy of different organ systems, such as the respiratory or nervous system.

In this course we will use the systemic approach to study anatomy. This type of studying anatomy is widely used in introductory general anatomy courses because it breaks down the complexity of the human body into manageable, logical parts. It also studying anatomy by **organ systems**, makes it easier for beginners to learn and understand how each system works as a whole. For example, studying the **digestive system** all at once — from the mouth to the intestines — helps you see how the structures are connected and how they function together.

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2) Microscopic Anatomy

Within microscopic anatomy, two topics of study are of great importance:

- ## Cytology

Cytology is the study of **cells**. It focuses on how individual cells operate, divide, and interact with their environment.
For example, in a **Pap smear**, cytology is used to examine cells from the cervix to check for abnormalities that might indicate cancer or infection.

- ## Histology

Histology is the study of **tissues**. Tissues are **groups of cells that work together to perform specific functions.** Histology looks at how cells are organized within tissues and how those tissues form organs.
For example, examining a **biopsy of skin tissue** under a microscope to check for signs of disease (like cancer or inflammation) is an application of histology.

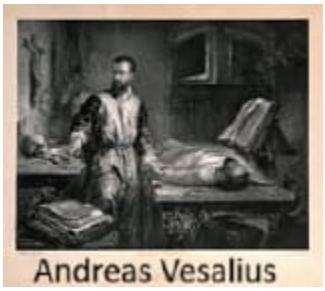
A Very Brief (and Fun) History of Anatomy & Physiology

🦴 **Ancient Times** – People in Egypt and Mesopotamia started learning about the body, mostly through trial, error, and guesswork. The *Ebers Papyrus* (c. 1550 BCE) gave early medical advice, providing interventions for common health issues of the time....some helpful, some not so. For example: It included **willow bark as a remedy for general aches and pains**. Willow bark is the progenitor of aspirin. A little less on target was the advice for birth control: A pessary was made from a paste of dates, acacia, and honey. This pessary was smeared onto wool and then used intravaginally to prevent conception.

🧠 **Classical Greece (c. 400 BCE)** – Hippocrates became the "Father of Medicine," promoting the idea that diseases had natural causes (not angry gods). Anatomy was still a mystery, though—dissection was a big no-no.



🐒 **Galen's Era (c. 150 CE)** – A Roman doctor who got most of his info from animal dissection. He got a *lot* wrong but dominated medical thinking for over 1,000 years.
One major example of what **Galen** got wrong was his belief that **blood was produced in the liver and consumed by the body** rather than circulated. Galen thought that blood moved through the body in a back-and-forth motion and was used up like fuel. He did not understand that the heart pumped blood in a closed circulatory system.
It was not until **William Harvey**'s work in the 1600s that scientists realized blood **circulates continuously through the body**, pumped by the heart.



📚 **The Renaissance (1500s)** – Human dissection became more accepted. *Andreas Vesalius* published beautifully detailed anatomy books based on actual cadavers—finally correcting Galen's mistakes. Go team science!

🔬 **1600s–1800s** – Microscopes were invented, opening up a whole new microscopic world. Physiology grew as scientists began to explore how organs, tissues, and cells *functioned*, not just how they looked.

💉 **20th Century and Beyond** – T**echnologies like X-rays, CT scans, and MRIs** revolutionized how we see inside the living body. Now we can study anatomy and physiology without making a single cut!



Figure 1.1.1: **Rembrant's "The Anatomy Lesson of Dr. Nicolaes Tulp"**. Human anatomy is the study of the structure of the human body, from the microscopic to the macroscopic.

Anatomy is closely related to **physiology** (study of function), **biochemistry** (chemical processes of living things), **comparative anatomy** (similarities and differences between species), and **embryology** (development of embryos).

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1.2: Levels of Organization

Living organisms are made up of four levels of organization: cells, tissues, organs, and organ systems.

Master this section and you'll be able to:

- Order and explain the six levels of organization for the human body

Six Levels of Organization

An organism is made up of six levels of organization: atoms and molecules, cells, tissues, organs, organ systems, and organism. These levels reduce complex anatomical structures into groups; this organization makes the components easier to understand.

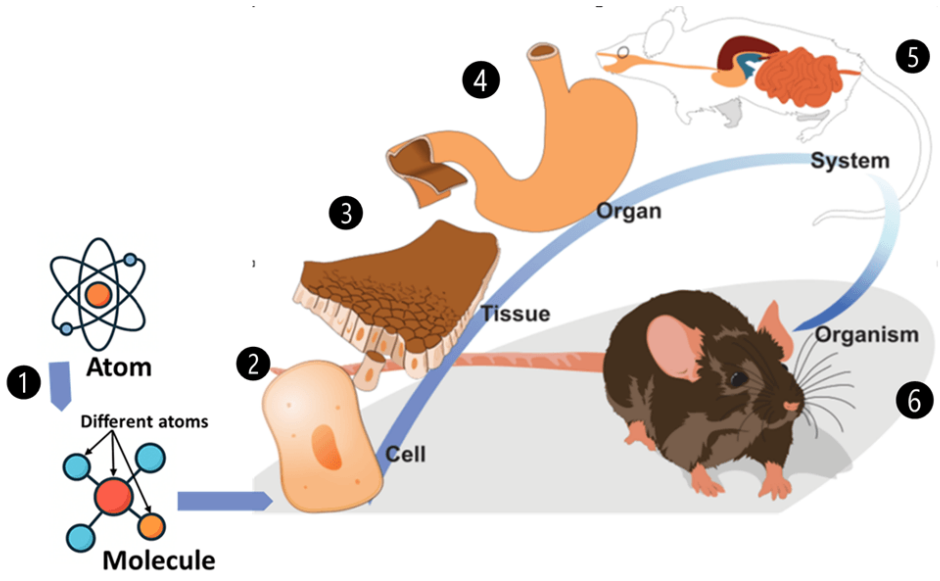


Figure 1.2.1: **Levels of Organization in Animals**. An **organism** contains **organ systems** made up of **organs** that consist of **tissues**, which are in turn made up of **cells**. The cells, finally, are made up of **molecules** and ultimately **atoms**.

Level 1: Atoms and Molecules – The Chemical Building Blocks of Life

Everything around you — your phone, your clothes, the air you breathe, and even your body — is made of **matter**. **Matter** is anything that takes up space and has weight. All matter is made up of tiny particles called **atoms,** the smallest building blocks of all materials (specific types or forms of matter). There are many different types of atoms, and each type of atom is called an **element** and chemists have given these elements different names (e.g.: oxygen, carbon, hydrogen, iron etc.).

Here is a simple summary of this chemical level:

- **Matter:** anything that has weight and takes up space.
- **Elements:** the “ingredients” of matter, each made of only one kind of atom.
- **Atoms:** the super-tiny particles that make up elements, and therefore all matter!

Wait, it gets more complex: atoms themselves are made up of subatomic particles (not covered here). However, we do need to talk about what happens when atoms **combine to form molecules.** For example, the combination of oxygen (O) and hydrogen (H) atoms forms a **water molecule (H_2O)**.

- A **molecule** is when two or more atoms join together through some kinds of chemical bonds (not covered here). It can be just two atoms like O_2 (the oxygen we breathe), three atoms H_2O (the water we drink and use for countless other things), or many atoms, such as table sugar $C_{12}H_{22}O_{11}$.

- Finally, large complex molecules formed by **Hundreds (or thousands) of** atoms are called **macromolecules**. The main types of macromolecules in living organisms are **proteins, nucleic acids (DNA and RNA), carbohydrates, and lipids.** They are collectively called "organic molecules" because of their carbon (C) skeleton or sometimes also "**biomolecules**", as they play crucial roles in the structure and function of the cells in our body.

In summary:

The **atomic level** is the most basic level of structural organization and includes individual atoms like carbon, hydrogen, oxygen, and nitrogen which are the building blocks of all matter.

The **molecular level** involves combinations of atoms forming molecules essential for life: such as oxygen, water, and the biomolecules.

Level 2: Cells – The Tiny Living Units That Make Up All Life

A cell is the basic **unit of life** and the **smallest unit capable of reproduction**. While cells vary greatly in their structure and function based on the type of organism and the location within the organism, all cells have a few things in common. Cells are made up of organic molecules, contain nucleic acids (such as DNA and RNA), are filled with fluid called cytoplasm, and have a membrane made out of lipids. Cells also contain many structures within the cytoplasm called organelles, which perform various cellular functions.

Cells are either **prokaryotic** (no nucleus, the DNA is in the cytoplasm) in bacteria and archaea (another group of single-celled organisms), or **eukaryotic** (with a nucleus containing the DNA) in plants, animals, protists, and fungi.

In humans, most cells combine to form tissues, but some cells are found independent of solid tissues and have their own functions. A red blood cell found circulating in the bloodstream carrying oxygen throughout the human body is an example of an independent cell.

Level 3: Tissues – Teams of Cells with a Common Purpose

Tissues are a **group of similar cells** of the same origin **that carry out a specific function together**. Humans have four different types of basic tissues:

1. **Epithelial** tissues make up the outer layers of organs, such as the skin or the outer layer of the stomach.
2. **Connective** tissues such as bone tissue are made up of fibrous cells and give shape and structure to organs.
3. **Muscle** tissue is made up of cells that can contract together and allow animals to move.
4. **Nervous** tissue is made of specialized cells that transmit information through electrochemical impulses, such as the tissue of nerves, the spinal cord, and the brain.

Level 4: Organs – Specialized Structures Built for Specific Jobs

Organs are made up of two or more types of tissues working together to perform a particular function. Most organs include:

- **Parenchyma** – the functional tissue that performs the organ's main job

- **Stroma** – the supportive connective tissue that provides structure and framework

- **Epithelial tissue** – often involved in lining surfaces or forming protective barriers

Organs can be **solid** (like the liver or brain) or **hollow** (like the intestines or bladder), and they vary widely in both size and complexity. Common examples include the heart, lungs, and brain.

Level 5: Organ Systems – Teamwork in the Human Body

Think of an organ system as a team of organs working together to get one big job done. The human body has **eleven different organ systems**, and each one has its own area of expertise. For example, the **digestive system** includes organs like the pancreas, stomach and intestines, all working together to break down food and absorb nutrients.

Most organ systems focus on a few specific tasks, but some body functions are so complex they need **multiple systems to collaborate**. Take **blood pressure**, for instance: it is regulated not just by the **circulatory system**, but also by the **urinary system** (hello, kidneys!) and the **nervous system**, which helps coordinate it all like a master controller.

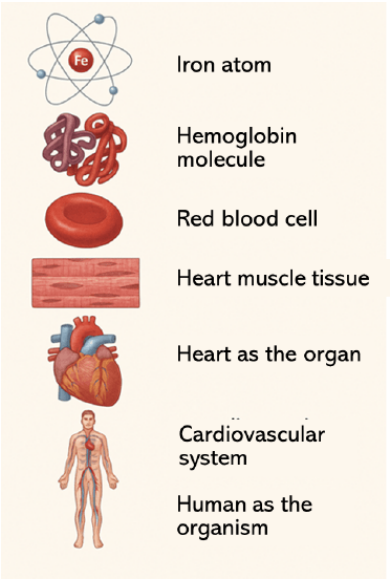
The bottom line? Your body runs on teamwork!

Level 6: Organism – The Complete Package

An **organism** is a **living, functioning whole,** the result of all the previous levels of biological organization working together. From atoms to molecules, to cells, to tissues, to organs, to organ systems... it all leads up to **you** (or any other living being)!

At this level, everything is integrated: your **cells** carry out chemical reactions, your **tissues** perform specialized roles, your **organs** work in systems, and those systems cooperate to keep you alive, growing, and responding to the world around you.

Whether it is a human, a dog, a tree, or a bacterium, an organism is a **complete, independent living thing,** able to carry out all the processes that define life, like metabolism, reproduction, response to stimuli, and homeostasis.



Specific Example:

A **cell** in this system is the **red blood cell**, which carries oxygen throughout the body. The **cardiac muscle tissue** in the heart is made of many similar muscle cells working together to help the heart contract. The **heart**, made up of several types of tissues, functions as an **organ** that pumps blood. This organ is part of the larger **organ system**, the **circulatory system**, which includes the heart, blood, and blood vessels. Inside each red blood cell is **hemoglobin**, a **macromolecule** that binds to oxygen—allowing the cell to perform its vital job.

Fig. 1.2.2: **The Six Levels of Biological Organization – Circulatory System Example**

The figure on the right illustrates using the circulatory system as an example, the six levels of biological organization at work:

1. **Atoms and Molecules:** The **iron (Fe) atom** is a key part of the **hemoglobin molecule**. Because oxygen (O_2) binds to iron (Fe), red blood cells are able to carry oxygen throughout the body.

2. **Cell:** A **red blood cell (RBC).** RBCs are specialized for transporting oxygen and carbon dioxide.

3. **Tissue: Cardiac muscle tissue** contracts, enabling the heart to pump blood.
4. **Organ:** The **heart**, a muscular organ that pumps blood through the body.
5. **Organ System:** The cardiovascular system includes te heart, blood, and blood vessels, which all work together to move blood through the body.
6. **Organism:** A complete human body, where all systems — including the circulatory system — interact to maintain life and homeostasis.

Summary

From smallest to largest:

- **Atom:** The smallest unit of matter that still has the properties of an element. Atoms are the basic building blocks of everything (both living and nonliving) including all parts of the human body.
- **Molecule:** A group of two or more atoms bonded together, like water (H_2O) or oxygen (O_2). A group of two or more atoms bonded together. Molecules can be simple, like oxygen (O_2), or more complex, like water (H_2O). They make up all the substances in your body and the world around you.
- **Macromolecule:** A very large molecule made up of many atoms, often formed by smaller molecules linked together. Macromolecules like proteins, DNA, and starch are essential for life because they carry out vital functions in the body.
- **Cell**: The smallest unit of life capable of independent reproduction. Generally contains nucleic acid, cytoplasm, a cell membrane, and many other proteins and structures.
- **Tissue**: A group of similar cells that come from the same origin and work together to carry out a specific function in the body. Examples are muscle tissue helping you move or nervous tissue sending signals.
- **Organ**: A structure made of different tissues that work together to perform physiological functions.
- **Organ system**: A group of organs and tissues that work together to perform specific functions.
- **Organism:** A complete living thing made up of various organ systems working together to carry out all the processes needed for life, such as breathing, moving, growing, and reproducing.

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1.3: Anatomical Terminology

Master this section and you'll be able to:

- Demonstrate the anatomical position
- Describe the human body using directional and regional terms

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

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

Anatomical Position

To begin, anatomists use a **standard reference position** so that everyone describes the body in the same way. Just as maps are typically drawn with north at the top, the body is described using a standard “map” called the **anatomical position.** In this position, the person is standing upright, feet about shoulder-width apart and parallel, toes pointing forward. The arms are at the sides of the body, and the palms face forward, as shown in the figure below.

Using this standard position reduces confusion. It does not matter how the body being described is oriented, the terms are used as if it is in anatomical position. For example, a scar in the “anterior (front) carpal (wrist) region” would be present on the palm side of the wrist. The term “anterior” would be used even if the hand were palm down on a table.

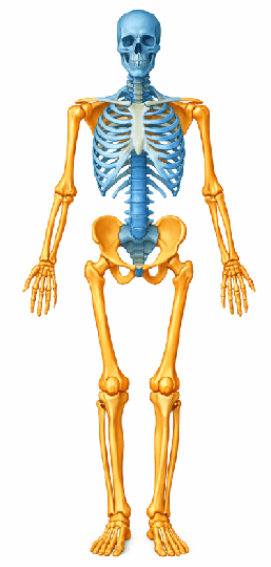


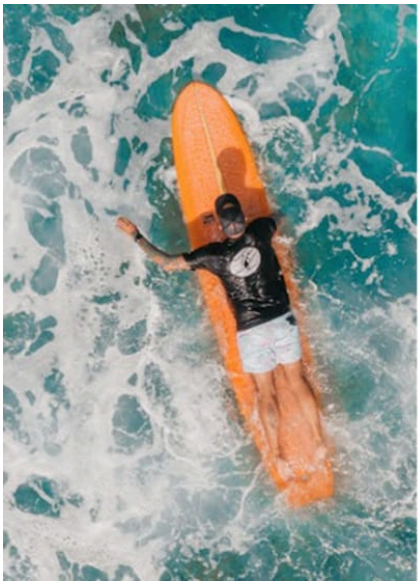
Figure 1.3.1:**Axial and Appendicular Skeleton in Anatomical Position.**
This human skeleton is shown in anatomical position, with the body standing upright, feet flat and slightly apart, arms at the sides, and palms facing forward.

The image also highlights the two major regions into which the human body is divided:

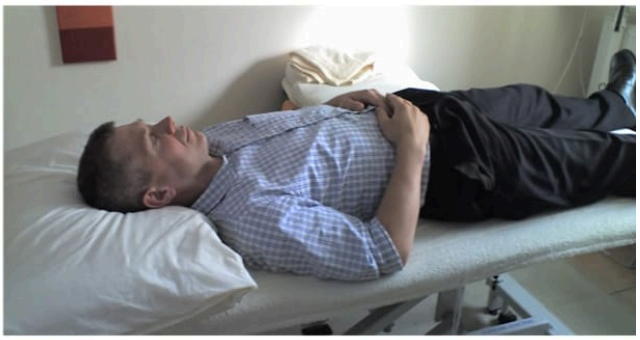
Axial region
This is the central core of the body. It includes the head, neck, and trunk. The trunk consists of the chest, abdomen, and pelvis. In Figure 1.3.1, the axial skeleton (shown in blue) includes the skull, vertebral column, ribs, and sternum, which together form the central axis of the body.

Appendicular region
This region includes the limbs that attach to the axial region. In other words, it refers to the arms and legs.
In Figure 1.3.1, the appendicular skeleton (shown in light brown) includes the shoulder girdle, upper limbs, pelvic girdle, and lower limbs. These structures attach to the axial skeleton and are primarily responsible for movement.

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



Prone



Supine

In the paragraphs above, we introduced the two broad regional categories of the body: axial and appendicular. To describe specific locations more precisely, anatomists and medical professionals use many smaller regional terms within each of these categories (see figure below).

Regional Terms

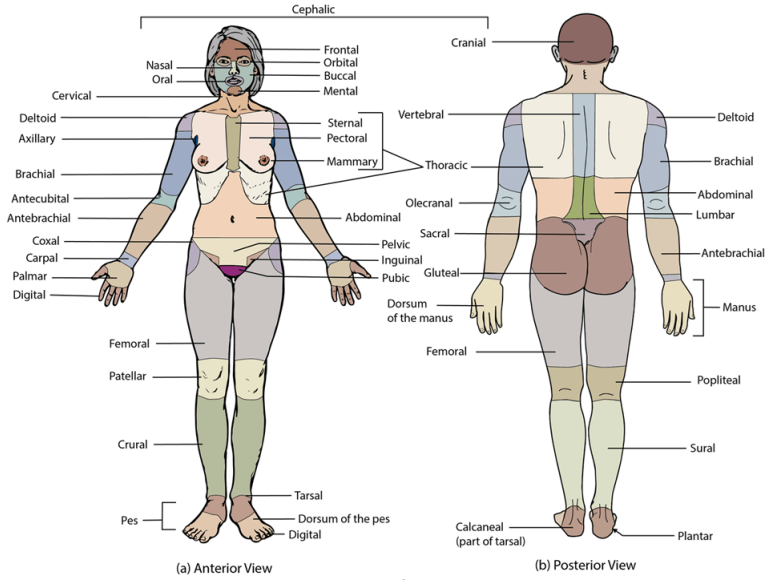


Figure 1.3.2: **Regions of the Human Body.** The human body is shown in anatomical position in an (a) anterior view and a (b) posterior view. Note that some regions are on both the anterior (a) aspect and the posterior (b) aspect, while others are on one side or the other only. *(Image credit: "Regions of the Body" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0.)*

For example:

- The **brachial region** refers specifically to the upper arm and is part of the appendicular region.
- The **abdominal region** refers to the abdomen and is part of the axial region.

Pay close attention to correct terminology.

- **Brachial** means upper arm.
- **Antebrachial** only means forearm, not “lower arm.”
- **Femoral** means thigh.
- **Crural** refers only to the area between the knee and the ankle, not the entire lower limb.

Using these specific terms allows you to describe body locations clearly and accurately.

Directional Terms

Directional terms are words used to describe the location of an anatomical structure by comparing its position to other structures within the body or within the orientation of the body itself. Certain directional anatomical terms appear throughout this and any other anatomy textbook. These terms are essential for describing the relative locations of different body structures. For instance, an anatomist might describe one band of tissue as “inferior to” another or a physician might describe a tumor as “superficial to” a deeper body structure. Commit these terms to memory to avoid confusion when you are studying or describing the locations of particular body parts.

Standard anatomical terms for direction include:

- ***Superior*** *and* ***inferior*** *(****cranial*** *and* ***caudal****)* are **used when referring to parts of the body (trunk) and the head.** Superior structures are toward the head (cranial). Inferior (or caudal = tail) describes a position below or lower than another part of the body proper; near or toward the tail (in humans, the coccyx, or lowest part of the spinal column). Examples include:

- The pelvic region is inferior to the abdominal region.
- The superior and inferior vena cava carry deoxygenated blood away from the head (superior) and from the lower body (inferior) to the heart.
- The frontal region is superior to the nasal region.

- **Anterior** (or **ventral**) is used to describe the front or direction toward the front of the body, while **posterior** (or **dorsal**) describes the back or direction toward the back of the body. Examples include:
  - The popliteal region is posterior to the patellar region.
  - The pituitary gland has an anterior and posterior part, each of which secretes different types of hormones.
  - The toes are anterior to the tarsal region.

- ***Lateral*** is used to describe anything closer to the sides of the body (toward the arms, in the standard anatomical position), while ***medial*** is used to describe anything toward the middle of the body. In general, many structures of the human body are bilateral and symmetrical with the middle of the body, such as the lungs or the arms. Examples include:
  - The thumb (pollex) is lateral to the digits. Remember you have to think of the body in anatomical position!
  - The hallux is the medial toe.

- ***Deep*** refers to structures closer to the interior center or farther from the surface of the body. ***Superficial*** describes a position closer to the exterior surface of the body. Examples include:
  - The skin is superficial to the muscles.
  - The brain is deep to the skull.

- ***Proximal*** describes a position in a limb that is nearer to the point of attachment or the trunk of the body, while ***distal*** describes a position in a limb that is farther from the point of attachment or the trunk of the body. **When describing appendages (arms and legs) always use proximal and distal** (instead of superior and inferior). The proximal end of an appendage connects the appendage to the body, while the distal end is away from the body. Examples include:
  - The brachial region is proximal to the antebrachial region.
  - The patellar region is distal to the femoral region.

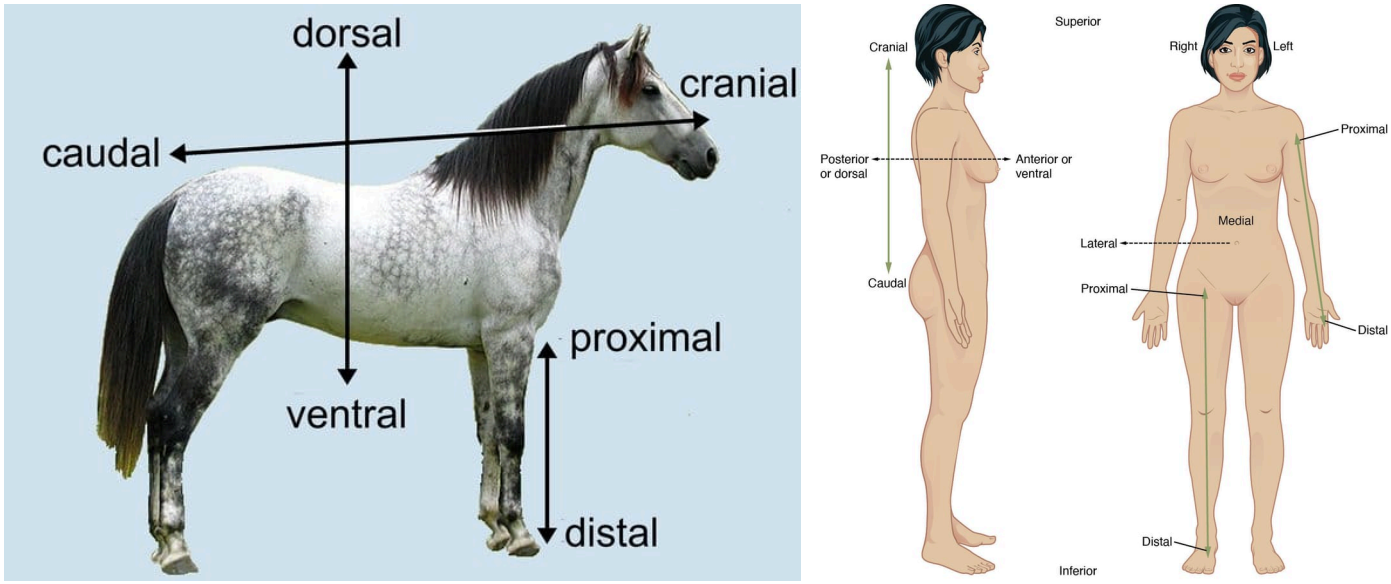


Figure 1.3.3: **Paired Directional Terms.** Comparison of a four-legged animal and a human body.

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1.4: Body Planes and Sections

There are three basic reference planes used in anatomy: the sagittal plane, the coronal plane, and the transverse plane.

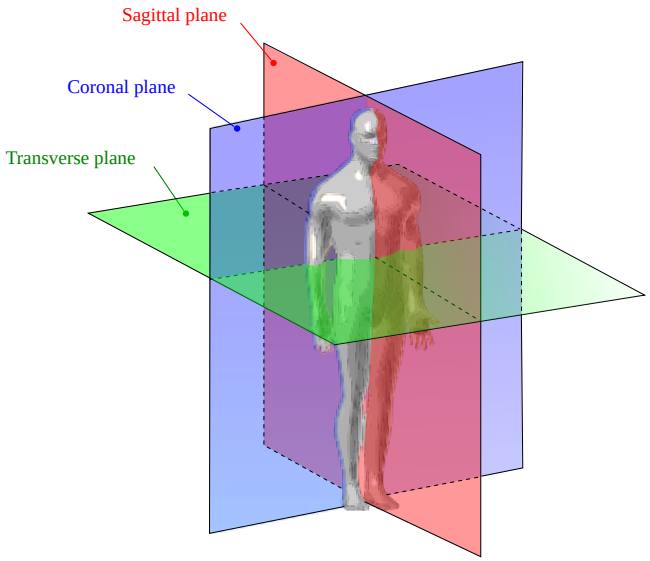
Master this section and you'll be able to:

- Identify and describe the three basic anatomical reference planes
- Understand the use of body planes in medical imaging and movement studies

What Are Body Planes?

Body planes are hypothetical geometric planes used to divide the body into sections. A section is a two-dimensional surface of a three-dimensional structure that has been cut. Modern medical imaging devices enable clinicians to obtain "virtual sections" of living bodies. We call these scans. Body sections and scans can b correctly interpreted, however, only if the viewer understands the plane along which the section was made. A plane is an imaginary two-dimensional surface that passes through the body.

There are **three planes** commonly referred to in anatomy and medicine, as illustrated in the figure below:



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

- *A **frontal or coronal plane*** divides the body or organ into an **anterior** (ventral or front) portion and a **posterior** (dorsal or rear) portion. The name "coronal plane" makes sense when you think that the term "coronal" comes from the word “corona” which is Latin for “crown.”

- *A **transverse plane*** is the plane that divides the body or organ horizontally into **upper** (cranial or head) and **lower** (caudal or tail) portions. It is also known as **cross-section or axial plane.** It is typically a horizontal plane through the center of the body or organ and is parallel to the ground.

Applications of Body Planes

Body planes are not just abstract concepts, they have real-world applications in medicine, anatomy, and embryology. One of

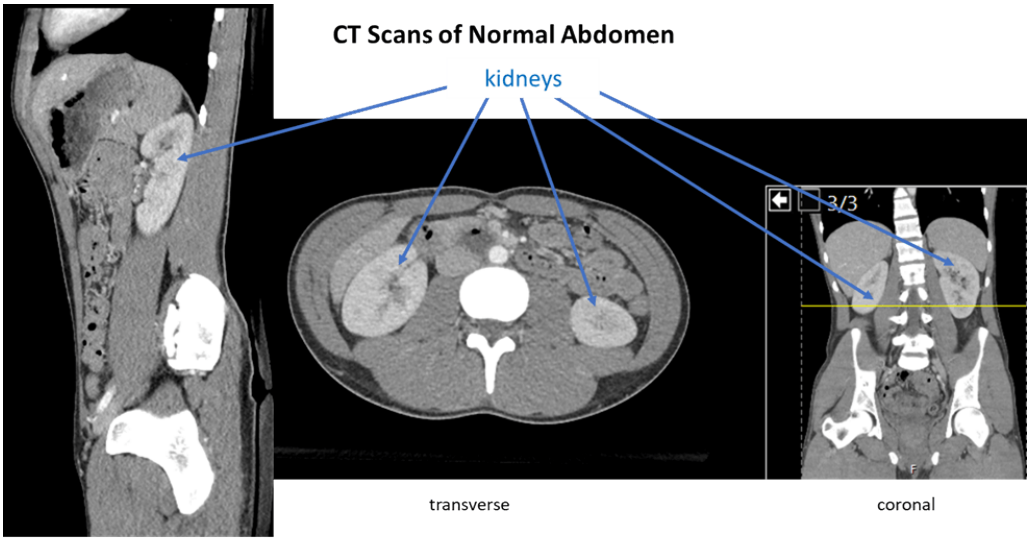
their most important uses is in **medical imaging**, such as **ultrasound** (sonography), **CT** (computer tomography) **scans, MRI** (magnetic resonance imaging) **scans,** and **PET (**Positron Emission Tomography) **scans**.

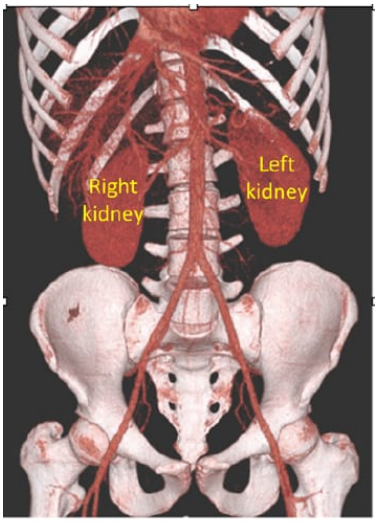
Most imaging is done with the patient lying down during the scan, but medical professionals still refer to the body as if it were in the **standard anatomical position** (facing forward with arms at the sides and palms facing forward). They then use the body planes — **sagittal, coronal,** and **transverse** — to create a **3D map of the body,** helping them pinpoint the location of organs and problems (abnormalities) inside the body more accurately.

These planes also help to reveal and diagnose small internal structures, such as tumors, cysts, or other abnormalities, within a single organ, like the brain, liver, or kidney. By viewing the organ from different angles and in slices, radiologists can better understand the size, shape, and exact location of the issue, which is essential for accurate diagnosis and treatment planning.

Body planes are also essential for understanding **how the body moves**. In biomechanics and kinesiology, the **X-Y-Z coordinate system** is used to analyze movement. For example, if you lift your leg forward, that motion happens in the **sagittal plane**. Raising your arms out to the sides involves the **coronal plane**, and rotating your torso engages the **transverse plane**. By knowing which plane a limb moves through and how far it travels, scientists and physical therapists can model and measure **range of motion**, joint flexibility, and even diagnose movement limitations.

Lastly, body planes play a key role in understanding **developmental anatomy**. During **embryonic development**, the orientation of body planes changes as the organism grows and differentiates. For instance, the **coronal plane** in an early human embryo starts out **horizontal**, but becomes **vertical** as the embryo matures into a fetus. The developing human is called an embryo from fertilization up to the end of the eight week of pregnancy. From week 9 until birth, the developing human is called a fetus.





Model skeleton with blood vessels and kidneys

Images by Mikael Häggström, M.D.

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1.5: Body Cavities

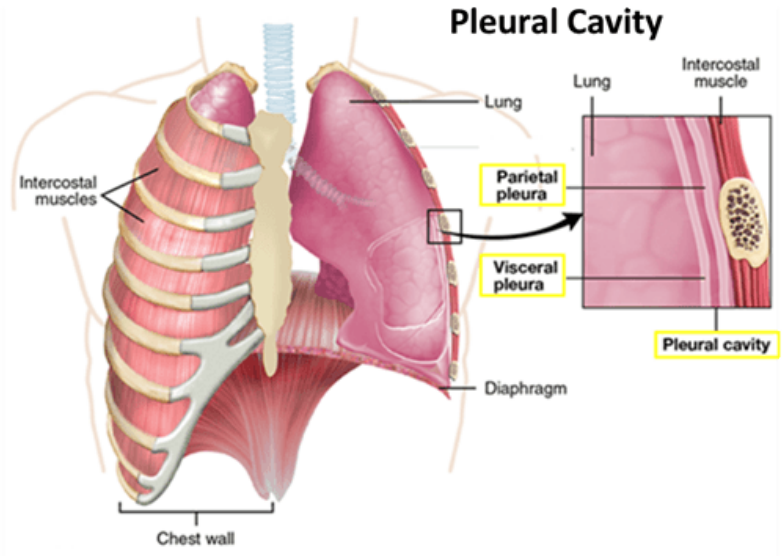
Vertebrates have fluid-filled spaces called body cavities that contain the organs.

Master this section and you'll be able to:

- Distinguish between the dorsal and the ventral body cavities, identifying their subdivisions and representative organs found in each.

By the broadest definition, a body cavity is any fluid-filled space in a multicellular organism. Blood vessels are not considered cavities but may be held within the body cavities. Most cavities provide room for the organs to adjust to changes in the organism's position. They usually contains protective membranes and sometimes bones that protect the organs.

Overview of Body Cavities



The human body has several major cavities that **protect internal organs** and allow them to **move and change shape**. The two primary body cavities — the **dorsal** and **ventral** cavities — remain when internal organs are removed (see details below).

In addition to these, there are **smaller cavities** formed by **serous membranes**.
A **serous membrane** (or *serosa*) is a **thin, slippery tissue** that lines certain internal body cavities and covers the organs within them. Each serous membrane has **two layers**:

- **Parietal layer**: lines the **walls** of the cavity
- **Visceral layer:** covers the **surface of the organs**

Between these two layers is a small amount of **serous fluid**, which reduces **friction** so the organs can move smoothly against each other — like when your lungs expand or your heart beats.
Examples are the **pleural cavity** (around the lungs; *see image on the right*), the **pericardial cavity** (around the heart), and the peritoneal cavity (around abdominal organs).

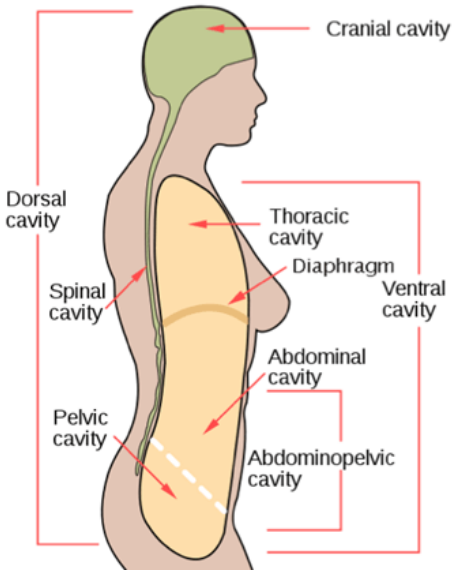
As mentioned above, the body has two major cavities, each of which is further divided into smaller compartments. These cavities house and protect delicate internal organs. The **ventral cavity**, in particular, is designed to accommodate significant changes in the size and shape of organs as they function. For example, the lungs, heart, stomach, and intestines can expand and contract as needed, without interfering with surrounding tissues or disrupting the activity of nearby organs

🟦 Dorsal Body Cavity (toward the back)

The dorsal cavity, in the back of the body, contains the primary organs of the nervous system, specifically the brain and the spinal cord. Just as the brain and spinal cord make up a continuous, uninterrupted structure, the cranial and spinal cavities that house them are also continuous. This cavity is surrounded by bone for protection (skull bones and the vertebral column), and by cerebrospinal fluid, a colorless fluid produced by the brain, which cushions the brain and spinal cord.

• Cranial Cavity

The cranial cavity is the portion of the dorsal cavity consisting of the space inside the skull. This cavity contains the brain, the meninges of the brain, and cerebrospinal fluid



• Spinal (Vertebral) Cavity

The The spinal or vertebral cavity is the posterior portion of the dorsal cavity and contains the structures within the vertebral column. These include the spinal cord, the meninges of the spinal cord, and the fluid-filled spaces between them. This is the most narrow of all body cavities, sometimes described as threadlike.

🟦 Ventral Body Cavity

The **ventral cavity** is the large internal space located at the **front of the body**. It contains many of the body's major organ systems, and the organs housed within it are collectively referred to as the **viscera**.

This cavity is divided into two main subdivisions: the **thoracic cavity** and the **abdominopelvic cavity**. Each of these is further subdivided, as described below.

Separating the thoracic and abdominal cavities is the **diaphragm**, a sheet of muscle that plays a vital role in breathing by helping move air in and out of the lungs.

• Thoracic Cavity

The thoracic cavity is found within the rib cage in the torso. It houses the primary organs of the cardiovascular and respiratory systems, such as the heart and lungs, but also includes organs from other systems, such as the esophagus and the thymus gland. The thoracic cavity is lined by two types of **serous membranes**, the **pleura** lining the pleural cavity and the lungs, and the **pericardium** lining the pericardial cavity and the heart. *(See above).*

- **Pleural Cavities (2)**

  Each houses a **lung,** and is lined with the pleura, both visceral and parietal.

- **Pericardial Cavity –**

  Contains the **heart,** and is lined with the pericardium, both visceral and parietal.

- **Abdominopelvic Cavity**

Located below the diaphragm, it is the **largest** cavity in the body. Although there is **no physical membrane** separating the abdominal and pelvic regions, the space is commonly divided into two parts for anatomical and clinical purposes.

- **Abdominal Cavity**

  The abdominal cavity is not contained within bone and houses many organs of the **digestive** (like the stomach, liver, intestines) and **renal** systems, as well as some organs of the endocrine system, such as the adrenal glands.

- **Pelvic cavity**

  The pelvic cavity is contained within the pelvis and houses the bladder, the reproductive system, and part of the large intestine.

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1.6: Abdominopelvic Regions

The abdomen is subdivided into four quadrants and nine areas.

Master this section and you'll be able to:

- Identify and differentiate the quadrants and regions within the abdominopelvic area of the body.

To make it easier to study and talk about the organs in the abdomen, anatomists and healthcare professionals divide the abdominopelvic cavity into smaller areas. These divisions help identify and describe the location and function of specific organs. They are also useful for doctors when trying to figure out what might be causing abdominal pain or other symptoms, and to help determine the appropriate treatment.

The two most widely used systems for dividing the abdominopelvic area are:

- **Four quadrants:** a simple way to us in everyday medical practice.
- **Nine regions:** a more detailed map of the area. It is often used in anatomy and in analyzing imaging.

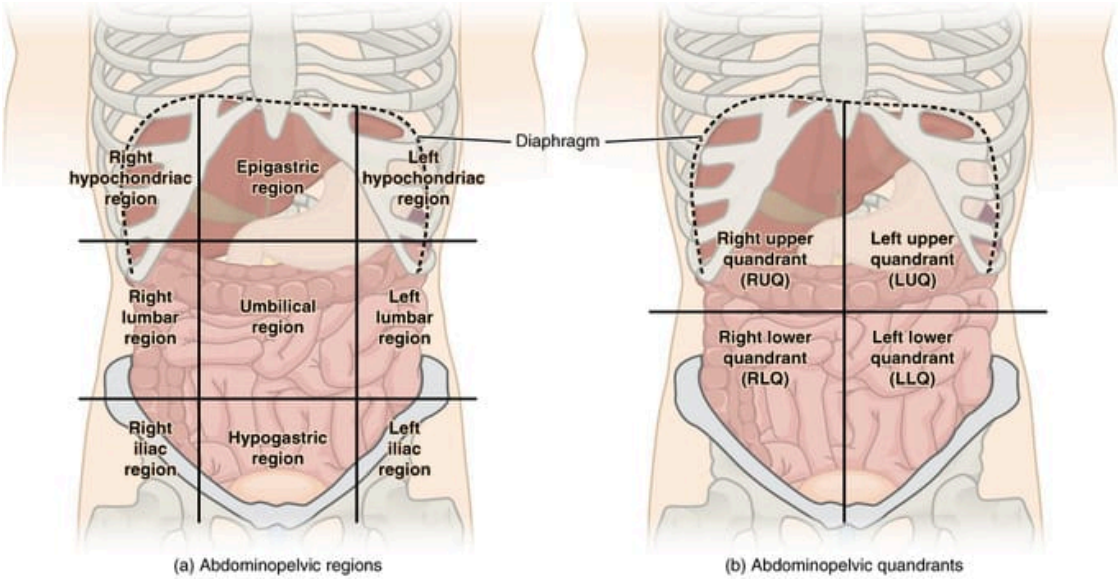
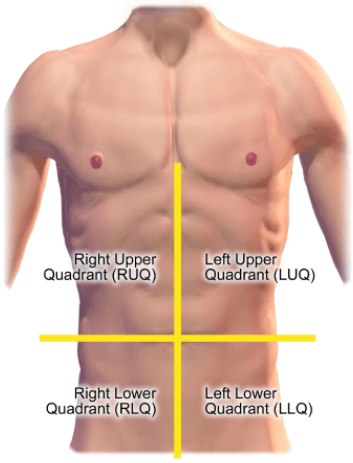


Figure 1.6.1: **Abdominal nine divisions (a) and quadrant regions (b)**. The abdomen is subdivided into four quadrants and nine regions.



Abdominopelvic Quadrants

Four Quadrants

The abdominopelvic region can be divided into four quadrants. These quadrants are defined by the **intersection of the midsagittal plane with the transverse plane** (through the navel).

- ### Right Upper Quadrant

  The right upper quadrant contains the right portion of the liver, the gallbladder, right kidney, a small portion of the stomach, the duodenum, the head of the pancreas, portions of the ascending and transverse colon, and parts of small intestine. Pain in this region is associated with **infection and inflammation in the gallbladder and liver** or peptic **ulcers in the stomach.**

- ### Left Upper Quadrant

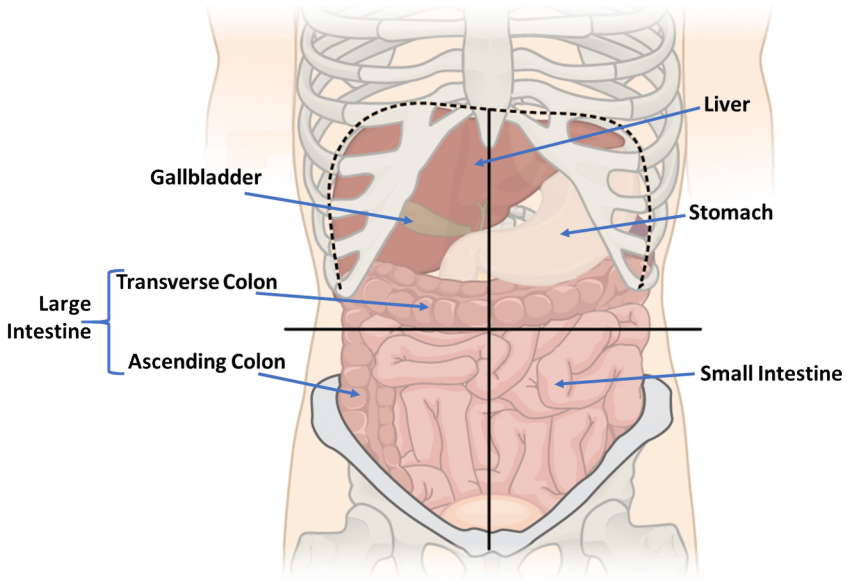
  The left upper quadrant is the location of the left portion of the liver, part of the stomach, the pancreas, left kidney, spleen, portions of the transverse and descending colon, and parts of the small intestine. Pain in this region is often associated with malrotation of the small intestines and/or colon. **Malrotation of the small intestine and colon** is a **congenital condition**, meaning it happens during fetal development, when the intestines **do not rotate properly** as they form in the abdomen.

- ### Right Lower Quadrant

  The right lower quadrant contains the cecum, appendix, part of the small intestines, the right half of the female reproductive system, and the right ureter which carries urine from the kidney to the bladder. Pain in this area is most commonly associated with **appendicitis**.

- ### Left Lower Quadrant

  The left lower quadrant houses the majority of the small intestine, some of the large intestine, the left half of the female reproductive system, and the left ureter. Pain in this region is generally associated with **colitis** (inflammation of the large intestine) as well as **pelvic inflammatory disease and ovarian cysts** in females.



Nine Regions

The nine divisions of the abdominopelvic region are smaller than the four quadrants, allowing for a more detailed discussion. These divisions are marked by **two parasagittal and two transverse planes centered around the navel.** Most organs are part of multiple regions, including the gallbladder, duodenum, stomach, kidneys, spleen, small intestine and colon.

- ### Right Hypochondriac Region

  The right hypochondriac region contains the right portion of the liver, the gallbladder, the right kidney, and parts of the small intestine.

- ### Left Hypochondriac Region

  The left hypochondriac region contains part of the spleen, the left kidney, part of the stomach, the pancreas, and parts of the colon.

- ### Epigastric Region

  The epigastric (above stomach) region contains the majority of the stomach, part of the liver, part of the pancreas, part of the duodenum, part of the spleen, and the adrenal glands. This region pushes out when the diaphragm contracts during breathing.

- ### Right Lumbar Region

  The right lumbar region consists of the gallbladder, the right kidney, part of the liver, and the ascending colon.

- ### Left Lumbar Region

  The left lumbar region consists of the descending colon, the left kidney, and part of the spleen.

- ### Umbilical Region

  The umbilical region contains the umbilicus (navel), and many parts of the small intestine, such as part of the duodenum, the

jejunum, and the ileum. It also contains the transverse colon (the section between the ascending and descending colons) and the bottom portions of both the left and right kidney.

- ## Right Iliac Region

  The right iliac region contains the appendix, cecum, and the right iliac fossa. It is also commonly referred to as the right inguinal region. Pain in this area is generally associated with appendicitis.

- ## Left Iliac Region

  The left iliac region contains part of the descending colon, the sigmoid colon, and the left iliac fossa. It is also commonly called the left inguinal region.

- ## Hypogastric Region

  The hypogastric region (below the stomach) contains the organs around the pubic bone. These include bladder, part of the sigmoid colon, the anus, and many organs of the reproductive system, such as the uterus and ovaries in females and the prostate in males.

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1.7: Defining Physiology

Human physiology is the study of the mechanical, physical, and biochemical processes that support the body's function.

Master this section and you'll be able to:

- Describe physiology in the context of living systems.

🧠🚑📚 Introduction to Physiology

Now we are moving on into Physiology, the study of how the human body *works*.

While anatomy tells us *what and where* body parts are, physiology explains *how* those parts **function.** For physiology, you study the mechanisms of the human body, specifically how organs, tissues, cells, and molecules work together to keep you alive, balanced, and (usually) running smoothly.

As you might imagine, understanding anatomy is essential to comprehending physiology because **structure and function are deeply connected**. You cannot fully understand *how* something works (physiology) without first knowing *its structure* (anatomy). For example, to understand how the heart pumps blood, you need to know its chambers, valves, and vessels. To grasp how the lungs exchange gases, you must first understand their structure and location.

In short: **anatomy provides the map — physiology explains the journey.**

Whether you are planning a career in **emergency medical services**, **nursing**, **psychology**, or you are just checking off a **general education requirement**, anatomy and physiology are surprisingly relevant:

- **For future EMTs and paramedics**, physiology is your lifeline. It helps you recognize what's happening inside a patient's body when vitals change, organs fail, or the body goes into shock. When seconds count, understanding how the body works can make a big difference.
- **For psychology majors**, physiology offers a deeper understanding of the *mind-body connection*. It explains how hormones, brain chemistry, and nervous system activity shape thoughts, emotions, and behavior: from stress and sleep to mental illness and therapy.
- **For general ed students**, physiology helps you better understand the one thing you take with you everywhere: *your body*. What actually happens when you work out? Why do you feel jittery after too much caffeine? How does your immune system fight off a cold? Even if you are not planning a health career, understanding your body makes you a more informed, healthier human being.

At the center of it all is **homeostasis -** the body's constant effort to maintain internal balance. Whether you are managing stress, caring for others, or just trying to survive another hard semester, this quiet, behind-the-scenes balancing act is what keeps you functioning.

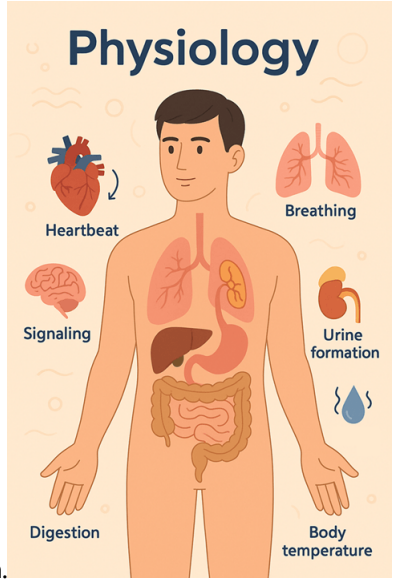
In this class, we will explore how body systems communicate, respond, and adapt, laying the foundation not only for careers in healthcare and psychology, but also for living well in your own skin. Since this is an introductory course, we will only scratch the surface of each topic, but you will still gain a solid overview of how the human body works and why it matters. Think of it as your first guided tour through the fascinating world of your body!

Examples of Physiology in Action

1. **Your heart beating faster when you exercise**
   → This involves cardiovascular physiology: your body increases heart rate and blood flow to deliver more oxygen to your muscles.

2. **Breathing more rapidly when you are anxious**

→ This touches on respiratory and nervous system physiology, showing how emotions affect breathing rate via the autonomic nervous system.



3. **Digesting food after a meal**
   → Digestive physiology covers how your body breaks down food into nutrients and absorbs them into the bloodstream.

4. **Sweating on a hot day**
   → This is thermoregulatory physiology: your body maintaining temperature (homeostasis) by releasing heat through sweat.

5. **Your kidneys adjusting urine concentration**
   → Renal physiology helps the body balance water and electrolytes, especially when you are dehydrated or overhydrated.

6. **Hormone release during stress (like cortisol and adrenaline)**
   → This involves endocrine physiology: how glands secrete hormones that affect many systems, including metabolism and mood.

7. **Muscle contraction when you lift something heavy**
   → Muscular and neuromuscular physiology explain how electrical signals from your brain activate muscle fibers.

8. **Maintaining blood sugar levels between meals**
   → Metabolic physiology looks at how hormones like insulin and glucagon regulate energy availability.

9. **The brain sending signals to pull your hand away from a hot stove**
   → Nervous system physiology explains the rapid communication between sensory neurons, the spinal cord, and muscles.

10. **Fighting off an infection**
    → Immune physiology explores how your body detects and destroys pathogens using specialized white blood cells and signaling molecules.

Homeostasis

Homeostasis refers to the body's ability to maintain a stable internal environment despite changes in the external surroundings. This internal stability is essential for normal physiological function and, ultimately, for survival. The body achieves this by continuously **regulating factors such as temperature, pH, blood pressure, and oxygen levels.**

Maintaining homeostasis requires constant monitoring and communication between body systems, primarily through the **nervous and endocrine systems**. The **nervous system**, especially the **brain** (and more specifically the **hypothalamus**), detects changes and initiates rapid, short-term responses using **electrical signals** and **neurotransmitters**. At the same time, the **endocrine system** provides slower but longer-lasting regulation by releasing **hormones** into the bloodstream from specialized glands like the pancreas, adrenal glands, and thyroid.

For example, if **blood oxygen levels drop**, the brain signals the respiratory muscles to increase the breathing rate, boosting oxygen intake. Simultaneously, it may signal the heart to beat faster to deliver oxygen more efficiently to tissues. Once oxygen levels are returned to normal, the brain reduces these signals, allowing breathing and heart rate to return to normal. This regulatory process is known as **negative feedback**, a key mechanism in homeostatic regulation.

Interaction of Body Systems

Physiology traditionally views the human body as a collection of systems, like specialized departments on a highly coordinated team. Each team member has its own roles and responsibilities. However, just like a real team, no department works in isolation. Every body system contributes to the stability of the entire team, and the health of the organism depends on how well these systems communicate and collaborate to maintain **homeostasis**.

Although we often divide the body into systems (such as muscular, nervous, or digestive), these divisions are somewhat arbitrary. Many "team members" wear multiple hats. For example, the **heart** not only pumps blood but also helps regulate hormones. The **kidneys** filter waste *and* help manage blood pressure. Depending on how you organize the team — by function, development, or purpose — the lineup might change.

One clear example of teamwork is between the **nervous and the endocrine systems.** Their collaboration blends the fast-acting signals of the nervous system with the longer-lasting effects of hormones from the endocrine system. Together, they coordinate many essential physiological processes to keep the body running smoothly.

Sometimes, though, parts of the team break down. The study of **pathophysiology** looks at what happens when systems fail to function properly. When communication breaks down, roles are confused, or key players underperform, resulting in disease and symptoms.

Understanding physiology means learning how the team works in harmony. Understanding pathophysiology means figuring out what happens when that harmony is lost.

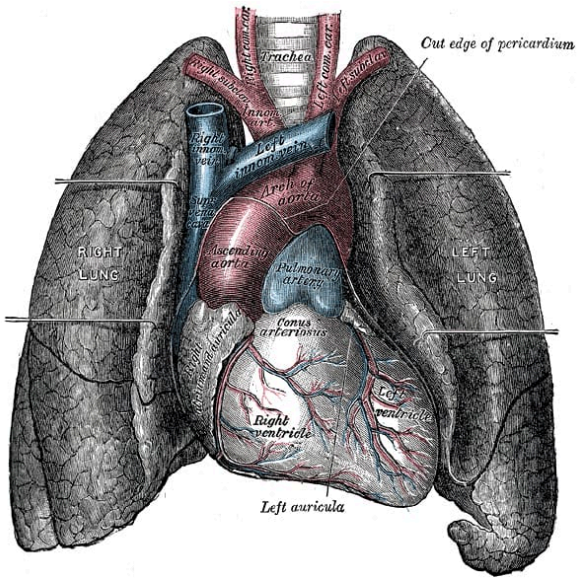


Figure 1.7.1: **The human heart and lungs**. Anatomy and physiology are complimentary disciplines as the structure of body systems often influences system.

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1.8: WHAT THE HUMAN BODY NEEDS TO STAY ALIVE

1.8.1: Basic Life Processes and Functions
1.8.2: Survival Needs

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1.8.1: Basic Life Processes and Functions

Master this section and you'll be able to:

- Explain the importance of organization and boundaries in maintaining internal stability and function in the human body.
- Describe how anabolic and catabolic reactions contribute to metabolism. Include the production and use of ATP.
- Identify the characteristics of life. Focussing on responsiveness and movement, give at least two examples of how organ systems support these functions.
- Compare and contrast growth, differentiation, and reproduction.

The human body is composed of multiple organ systems, each with specialized functions and distinct roles in maintaining physiological balance. Together, these systems work to support overall health and survival. For example, the **respiratory system** is responsible for gas exchange, while the **circulatory system** transports blood throughout the body. These individual functions contribute to broader life-sustaining processes that are considered defining characteristics of living organisms.

Let's take a look at six such functions:

1) Organization and Maintaining Boundaries

Maintaining boundaries is fundamental for the organization and survival of all living things, especially at the cellular level. Without a stable boundary, cells could not control their internal environment, making life-sustaining processes impossible. To stay alive, the human body must keep its internal environment separate from the outside world — and even separate different parts inside the body. This is called **maintaining boundaries**, and it is a key part of the body's overall **organization**.

A human body consists of **trillions of cells** organized in a way that maintains distinct internal compartments. The **plasma membrane** plays a vital role in maintaining the life of a cell by acting as a **physical barrier** that separates the internal environment from the outside world. It is **selectively permeable**, meaning it carefully controls what enters and leaves the cell — helping maintain **homeostasis** even when external conditions change. In addition to protection, the membrane also allows for **communication and exchange**, enabling the movement of nutrients, waste, and chemical signals. This balance of separation and interaction helps the cell regulate its **internal conditions**, such as pH, ion levels, and metabolic activity, and protects it from harmful substances and pathogens.

In your body, every cell maintains its own boundary, and together, these boundaries allow tissues, organs, and organ systems to function in an organized, coordinated way.

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

2) Metabolism: Your Body's Energy Game Plan

According to the **first law of thermodynamics**, energy cannot be created or destroyed, it can only **change forms**. That means your body's job is not to make energy out of thin air, but to **take in energy from food**, convert it into usable fuel, and then use that fuel to power everything from muscle movement to cell repair.

Your body handles this through a pair of constantly running chemical reactions: **anabolism** and **catabolism**.

- **Anabolism** is like building with Legos: your body takes smaller, simpler molecules (like amino acids from food) and **uses energy** to build larger, more complex structures (like proteins).

- **Catabolism** is the opposite: it **breaks down** big molecules (like glucose or fat) into smaller ones (ultimately carbon dioxide

and water), thereby **releasing energy** your body can use.

Together, these two processes make up your **metabolism** — the total of all the chemical reactions happening in your body, all the time, to keep you alive and functioning. Whether you are sleeping, eating, or running late to class, metabolism is working behind the scenes to keep your body in business.

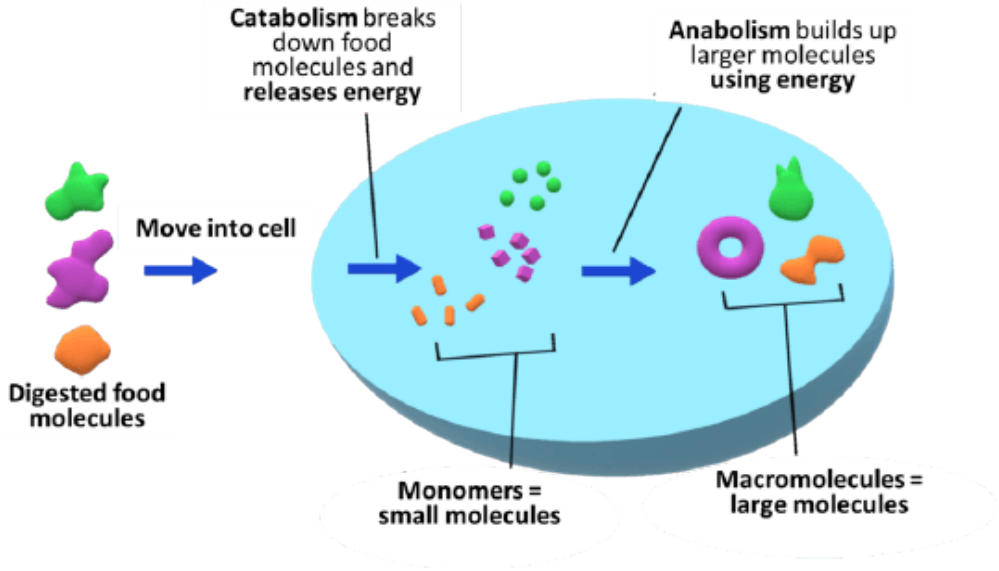


Figure 1.8.1.1: **Anabolism & Catabolism.** Both anabolism and catabolism occur simultaneously and continuously to keep you alive.

Your body is made up of trillions of cells, and each one depends on a special molecule called **adenosine triphosphate (ATP)** to get its work done. Often described as **the cell's "energy currency**," ATP stores and delivers energy where and when it is needed. As food is broken down through **catabolic reactions**, cells use the released energy to produce ATP. This ATP can then be stored — like saving money for later — or spent right away to power essential tasks such as muscle contraction, nerve signaling, or building new molecules during anabolic reactions.

3) Responsiveness

Responsiveness is the ability of an organism to adjust to changes in its internal and external environments. An example of responsiveness to external stimuli could include moving toward sources of food and water and away from perceived dangers. Changes in an organism's internal environment, such as increased body temperature, can cause the responses of sweating and the dilation of blood vessels in the skin in order to decrease body temperature, as shown by the runners in Figure 1.8.1.2

4) Movement

Human movement includes not only actions at the joints of the body, but also the motion of individual organs and even individual cells. As you read these words, red and white blood cells are moving throughout your body, muscle cells are contracting and relaxing to maintain your posture and to focus your vision, and glands are secreting chemicals to regulate body functions. Your body is coordinating the action of entire muscle groups to enable you to move air into and out of your lungs, to push blood throughout your body, and to propel the food you have eaten through your digestive tract. Consciously, of course, you contract your skeletal muscles to move the bones of your skeleton to get from one place to another (as the runners are doing in Figure 1.8.1.2), and to carry out all of the activities of your daily life.



Figure 1.8.1.2: **Marathon Runners.** Runners demonstrate two characteristics of living humans—responsiveness and movement. Anatomic structures and physiological processes allow runners to coordinate the action of muscle groups and sweat in response to rising internal body temperature. (credit: Phil Roeder/flickr)

5) Development, Growth and Reproduction

Development includes the process of **cell differentiation**, where unspecialized cells become specialized in both structure and function to carry out specific roles in the body. Differentiation is essential not only during early development but also throughout life, as it supports the body's ability to grow, heal, and adapt.

Development also encompasses **growth** and **repair.** Both depend on cell division and differentiation. **Growth** refers to an increase in body size and occurs in several ways: by increasing the number of cells, expanding the extracellular (non-cellular) materials such as the mineral content of bones, and, to a limited extent, enlarging individual cells.

Reproduction, finally, is the biological process by which new organisms are produced from parent organisms. In humans, this function is carried out by the male and female reproductive systems. Since all complex organisms eventually die, reproduction i essential to ensure the continuation of the species.

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1.8.2: Survival Needs

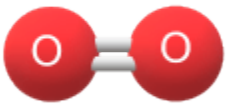
To sustain human life, certain physiological needs include air, water, food, shelter, sanitation, touch, sleep and personal space.

Master this section and you'll be able to:

- Explain the five essential requirements for human survival.
- Describe how the absence or deficiency of each affects physiological function.
- Analyze the physiological consequences of environmental changes, such as dehydration, hyper- or hypothermia, and high altitude or deep-sea conditions.

Survival Needs

While the development of tools, plumbing systems and food preservation have enabled modern man to live life with many creature comforts, the truth remains that the requirements for human survival are quite basic.



1)

Mount Everest North Face as seen from the path to the base camp.

Oxygen Availability

Oxygen, within a particular range of pressure, concentration, and purity, is essential for **aerobic cellular respiration**, the process by which cells **generate ATP**, the primary energy currency of the body. Insufficient oxygen delivery (hypoxia) rapidly impairs organ function, particularly in the brain. Without oxygen, brain damage begins in minutes and death quickly follows.

2) Food Availability

Our food must be adequate in calorie and nutritional standards in order to sustain life. A continuous supply of nutrients is necessary and can be categorized into:

- **Macronutrients,** specifically carbohydrates, lipids, and proteins. These macronutrients provide the energy necessary for cellular processes and the structural components for growth and repair.
- **Micronutrients,** such as vitamins and minerals are critical for enzymatic activity, nerve conduction, immune function, and metabolic regulation.

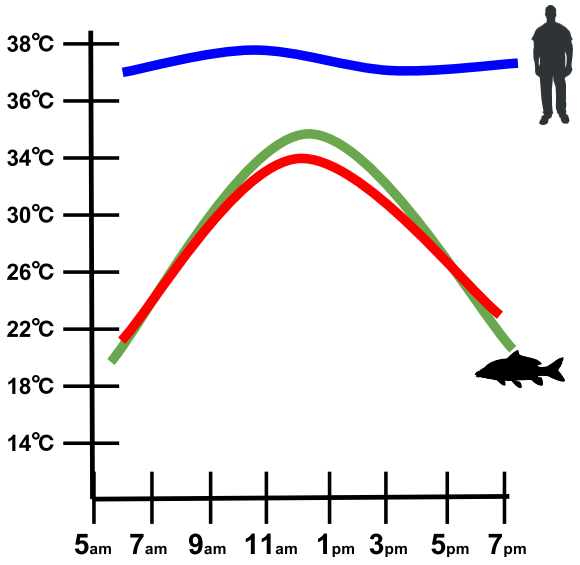
3) Water Availability

Access to a safe, clean, and adequate water supply is absolutely necessary for human survival. Indeed, water is as critical as oxygen. It serves as the solvent for biochemical reactions, assists in thermoregulation, and facilitates nutrient transport and waste elimination. Even mild **dehydration** can lead to headaches, dizziness, fatigue, and impaired cognitive function. Severe dehydration affects blood volume, **reduces blood pressure**, and can lead to **organ failure** and **death**.

⚠️ *Fun-but-Scary Fact:* You can survive **weeks without food**, but only a **few days without water**. Water is *not optional!* It

is a top priority for survival.

The typical survival time for a human without water is about **three days (72 hours)**. However, this can vary significantly depending on several factors. In some cases, individuals may survive anywhere from **two to seven days** without water. Environmental conditions play a major role — extreme heat and dry climates accelerate water loss through sweat and evaporation, while cooler, more humid environments may slow dehydration. Other influencing factors include a person's **level of physical activity**, **age**, **overall health**, **body size and fat reserves**, and their **hydration status before water deprivation** begins. These variables determine how quickly dehydration sets in and how long the body can continue to function without adequate fluid intake.



4) Stable Body Temperature

Enzymatic reactions and physiological processes in our body are optimized around a core temperature of approximately 37°C (98.6°F).

- **Hyperthermia** can denature proteins and disrupt cellular integrity. It begins when **core body temperature rises above 38.3°C (101°F)** and becomes dangerous above **40°C (104°F)**.
  - Around ~38–40°C (100.4–104°F) **heat exhaustion** often kicks in, leading to heavy sweating, weakness, and dizziness.
  - Above 40°C (104°F) **heat strokes** start build up and cause organ failure, altered mental status, and is a medical emergency.

- **Hypothermia** on the other hand impairs organ systems by slowing down metabolic activity. It occurs when **core body temperature drops below 35°C (95°F)**.
  - **Mild hypothermia:** 32–35°C (89.6–95°F) causes vasoconstriction, shivering, and confusion.
  - **Moderate hypothermia**: 28–32°C (82.4–89.6°F) slows the metabolism and decreased consciousness.
  - **Severe hypothermia**: <28°C (<82.4°F) will ultimately lead to cardiac arrest and death.

5) Appropriate Atmospheric Pressure

Atmospheric pressure is the force of the air around us — and, believe it or not, your ability to breathe depends on it. This pressure helps create the **differences in air pressure** that your body needs to move oxygen into your blood and get rid of carbon dioxide. Atmospheric pressure enables adequate ventilation and gas exchange in the lungs. A sufficient pressure gradient is required for oxygen to diffuse into the blood and for carbon dioxide to be expelled. Changes in barometric pressure, such as at high altitude, can hinder respiratory efficiency.

Here is the short version of how it works:

- **Oxygen** moves from areas of **higher pressure (the air in your lungs)** to areas of **lower pressure (your blood)**.

- **Carbon dioxide** does the opposite. It moves from your blood (where it is higher) into your lungs to be exhaled.
  This only works if the pressure **outside your body** is high enough to keep this gas exchange going. (Don't worry, if you do not totally understand this now, we will cover it in more detail when we study the respiratory system).

Even though the percentage of oxygen in the air (about 21%) stays the same no matter where you are, the **air pressure** changes with altitude. As you go higher — like climbing a mountain — the atmospheric pressure drops. This causes the **partial pressure of oxygen** (the amount of pressure oxygen alone exerts) to drop too. When that happens, it becomes harder for oxygen to move from your lungs into your blood because the **pressure difference** that drives gas exchange is too small. Less oxygen gets into your bloodstream, and that affects your whole body, right down to your **mitochondria**, which are the tiny structures in cells that use oxygen to make energy.

For example, at around 5500 meters (18,000 feet), approximately the hight of the Mt. Everest North Base Camp, the **oxygen pressure** is only about **half** of what it is at sea level. At the top of Mount Everest (about 8900 meters or 29,000 feet), it is only about **30%** of sea level. This drop in oxygen availability can cause symptoms all the symptoms of **hypoxia**. And if your body cannot adapt or you do not use supplemental oxygen, it can become life-threatening.

On the flip side, in situations with **too much pressure** (like deep-sea diving), other problems can occur, such as too much oxygen or nitrogen entering the blood, which also is dangerous.

Bottom line: atmospheric pressure is not just about the weather! Your life depends on it, because **without the right pressure, your body cannot get the oxygen it needs to survive**.



Figure 1.8.2.1: Mount Everest North Face as seen from the path to the base camp.

Beyond the five key requirements for maintaining homeostasis and supporting basic survival, humans also depend on other factors to thrive.

- **Shelter** is critical for protection from extreme heat, cold, sun, and precipitation, conditions that could otherwise lead to hypothermia or hyperthermia.
- **Sanitation** helps prevent disease by safely removing waste and reducing exposure to harmful toxins and pathogens.
- **Sleep** is vital for physical and cognitive restoration. Ideally seven to eight uninterrupted hours per night are needed.
- Adequate **space** reduces overcrowding by promoting mental well-being and maintenance of healthy social structures.
- Finally, **touch** is also a fundamental human need. As humans have evolved to interact in community settings, both hunting and gathering in groups, touch (as in a caring caress) is often considered a basic human survival need. In fact, studies have shown that physical contact fosters bonding, reduces stress, and even supports immune function, especially in infants and young children and is therefore essential to the early growth and development of healthy humans.



Figure 1.8.2.2: **Sleeping Child.** Adequate sleep is necessary to sustain life.

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1.9: Maintaining Balance — Homeostasis and the Power of Negative Feedback

Homeostasis is maintained by the body's responses to adverse stimuli, ensuring maintenance of an optimal physiological environment.

Master this section and you'll be able to:

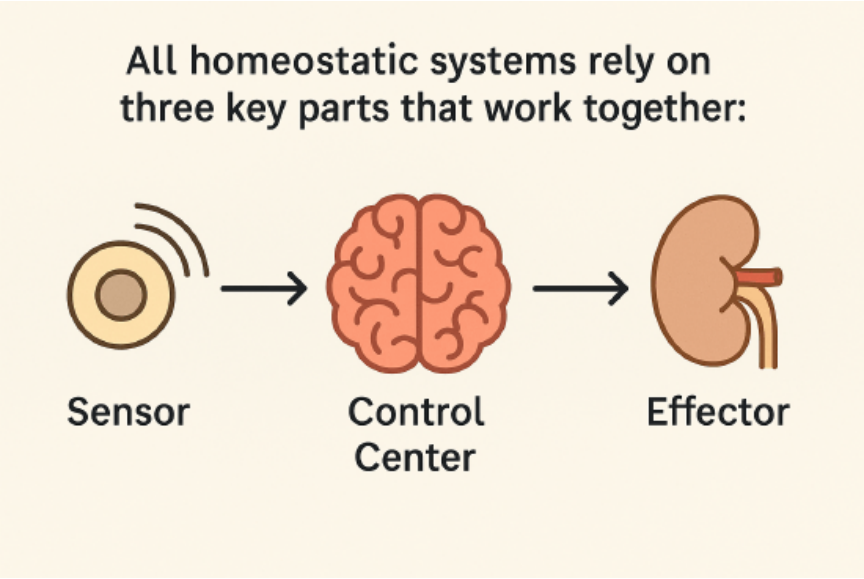
- Define the concept of homeostasis and explain its importance for maintaining a stable internal environment.
- Identify key physiological variables (e.g., temperature, blood pressure, blood glucose) that are regulated to maintain homeostasis.
- Describe the roles of sensors, control centers, and effectors in maintaining homeostasis.
- Explain how homeostasis is a dynamic process involving constant monitoring and adjustment, rather than a static "set point."

The Concept of Homeostasis

Homeostasis is the process the body uses to keep its internal environment stable, even when conditions outside (or inside) the body change. Factors like **body temperature, blood pH, blood pressure, and fluid levels** must stay within a narrow, healthy range for the body to function properly.

The body constantly monitors these internal conditions and makes adjustments as needed. Most of these adjustments happen through **negative feedback loops**, which are the body's main tool for maintaining balance. These loops work by detecting a change and triggering a response that reverses or counteracts that change, helping to bring things back to normal.

All homeostatic systems rely on **three key parts** that work together:



- **Sensor (or receptor):** This part detects a change in the environment — either inside or outside the body. For example, *peripheral chemoreceptors* can sense changes in the pH of your blood.
- **Control center (or integrating center):** This part receives the information from the sensor and decides how to respond. The *hypothalamus* in the brain is a great example — it helps regulate body temperature, heart rate, blood pressure, hunger, and even sleep cycles.

- **Effector:** This is the organ or tissue that carries out the response to restore balance. For instance, if your blood pressure drops, your *kidneys* may retain more water to help bring it back up.

These three components — **sensor, control center, and effector** — are the foundation of every homeostatic response. To coordinate these complex changes, the body uses **feedback loops**. As mentioned above, most of the time, these are **negative feedback loops**, which act to reverse a change and bring things back to normal. In certain situations, **positive feedback loops** temporarily amplify a change until a specific goal is reached. *See the next page for an overview of positive feedback loops.*

Negative Feedback

Negative feedback is the body's way of fixing a problem by turning things down or reversing a change. It helps bring body systems back to their normal range when something goes off track, or in other words: the output of a negative feedback system reduces the activity that causes that output.

A great example is **blood pressure regulation**. Your blood vessels have special sensors called **baroreceptors** that can tell if your blood pressure is too high or too low. These sensors send a message to the **hypothalamus**, a part of your brain that acts like a *smart control center,* managing many subconscious, automatic body functions. The hypothalamus always monitors and adjusts things to help you stay healthy and stable, meaning to maintain **homeostasis**.

If your blood pressure is **too high**, the hypothalamus tells your **heart, blood vessels,** and **kidneys** (the effectors) to take action. Your heart rate slows down, your blood vessels widen (**vasodilation**), and your kidneys let go of more water. All of these changes help bring your blood pressure back down to normal.

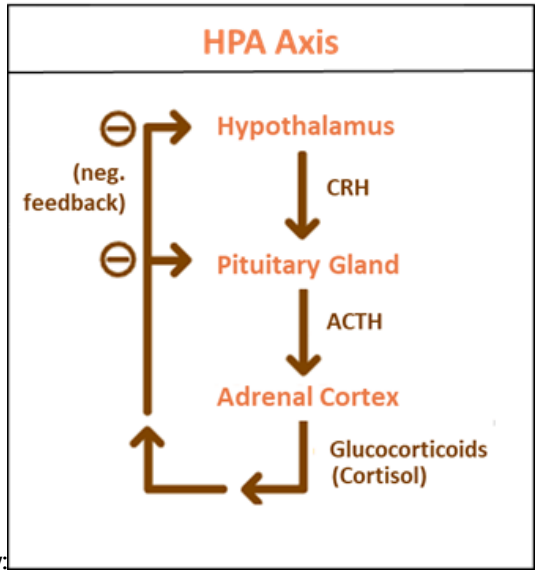
If your blood pressure is **too low**, the process works in the opposite direction. Your blood vessels tighten (**vasoconstriction**), your heart beats faster, and your kidneys hold on to more water. Again, this brings your blood pressure back up to where it should be.

It is called "negative feedback" because the body reverses the direction of the change to bring things back into balance.

Examples of Negative Feedback to Maintain Homeostasis

1) Hypothalamic – Pituitary – Adrenal (HPA) Axis

When your body is under **stress** — whether it is physical, emotional, or even from skipping meals — it needs to respond in a way that keeps you functioning. One of the key systems that kicks into action is called the **HPA axis**. It is a chain reaction involving three major parts of your body:

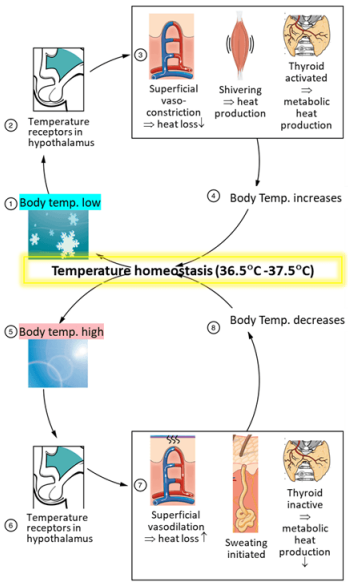


1. **CRH (Corticotropin-Releasing Hormone)** is released by the **hypothalamus.**
2. CRH travels to the **pituitary gland** (also in the brain), which then releases **ACTH (Adrenocorticotropic Hormone)** into the bloodstream.
3. ACTH travels through your blood to the **adrenal glands** (which sit on top of your kidneys), signaling them to release **glucocorticoids**, the most important of which is **cortisol** — often called the "stress hormone."

This whole process looks like a **chain of command.** Cortisol helps your body deal with stress by increasing blood sugar (for energy), suppressing non-essential functions (like digestion or reproduction), and reducing inflammation.

Once enough cortisol is in your bloodstream, it signals the hypothalamus and pituitary to **stop making CRH and ACTH** — this is a classic example of a **negative feedback loop**. The system shuts itself off when the job is done, so you do not end up with too much cortisol, which could be harmful over time.

> **Stress** → Hypothalamus releases **CRH** → Pituitary releases **ACTH** → Adrenal glands release **glucocorticoids** (like cortisol)



2) Body Temperature Control

Temperature control is another great example of a **negative feedback loop**. Peripheral (skin) and central thermoreceptors sense an increase or decrease in body temperature and send that information to the **hypothalamus**, the brain's temperature control center. If the temperature is too high or too low, the hypothalamus sends signals to various **effectors** to bring the body back to its normal temperature—about **37°C (98.6°F)**.

🥵 If the body gets **too hot**, the hypothalamus:

- Triggers **sweat glands** to release sweat, cooling the skin
- Causes **vasodilation**, where blood vessels near the surface widen to release more heat

🥶 If the body gets **too cold**, the hypothalamus:

- Makes **muscles shiver** to generate heat
- Causes **vasoconstriction**, narrowing the blood vessels to keep heat inside the body

This process is more complex than it seems, because the **hypothalamus can actually change the set point**. For example,

during a fever, it raises the body's temperature on purpose to help fight off infection.

Both **internal changes** (like an infection) and **external factors** (like cold weather) can trigger negative feedback responses that help the body maintain a safe and stable temperature.

See the image on the right to review how your body uses negative feedback to control temperature.

💡 Key Takeaways:

✅ **Homeostasis is the body's built-in balancing act.**
It uses sensors, a control center (usually the brain), and effectors (like organs or glands) to monitor and adjust internal conditions (like temperature and blood pressure) so they stay within a healthy range.

✅ **Negative feedback is the body's main strategy to stay stable.**
When something changes (like body temp or blood pressure), the body responds by reversing that change—bringing things back to normal. This "fix-it" system is used constantly to maintain balance and health.

✅ **Negative feedback loops shut themselves off when the job is done.**
This makes them *self-regulating* and helps prevent overcorrection. For example, when cortisol levels rise enough to deal with stress, the body stops producing more, a perfect example of a built-in "off switch."

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1.10: Positive Feedback Loops

Positive feedback amplifies a change rather than restoring balance.

Master this section and you'll be able to:

- Distinguish between negative and positive feedback mechanisms.
- Identify the key components of a positive feedback loop.
- Describe how childbirth illustrates a positive feedback loop and explain how the process is normally terminated.
- Explain how blood clotting functions as a positive feedback mechanism and how the response is shut off.
- Explain why negative feedback predominates in maintaining homeostasis, whereas positive feedback are sparingly used.

Positive Feedback: What It Is and Why It Matters

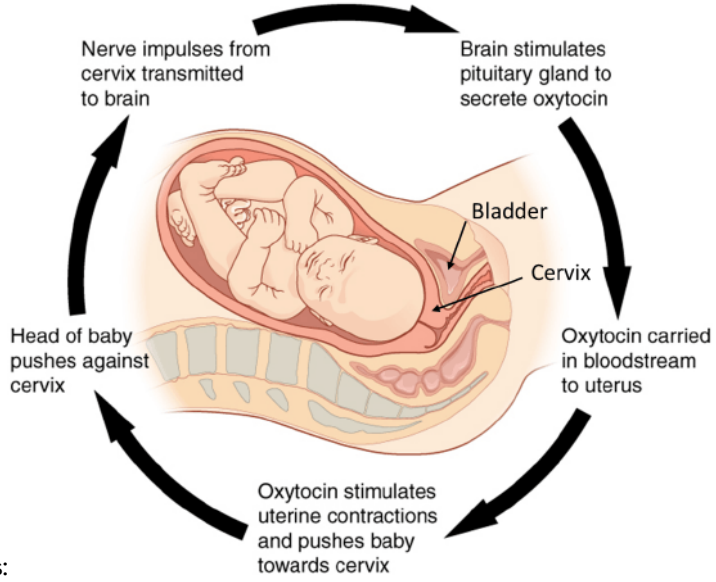
Positive feedback is a physiological mechanism in which the body **amplifies a change rather than reversing it**. Unlike negative feedback, which works to restore balance and maintain homeostasis, **positive feedback pushes the body further in the direction of the initial change,** and the system moves farther away from the normal range.

This might sound like a bad idea, but in certain situations, positive feedback is essential to maintain homeostasis. It allows the body to complete specific processes quickly and efficiently. Therefore, positive feedback in the body is normal only when there is a definite end point.

Examples of Positive Feedback

🤰 1. Childbirth (Labor Contractions)

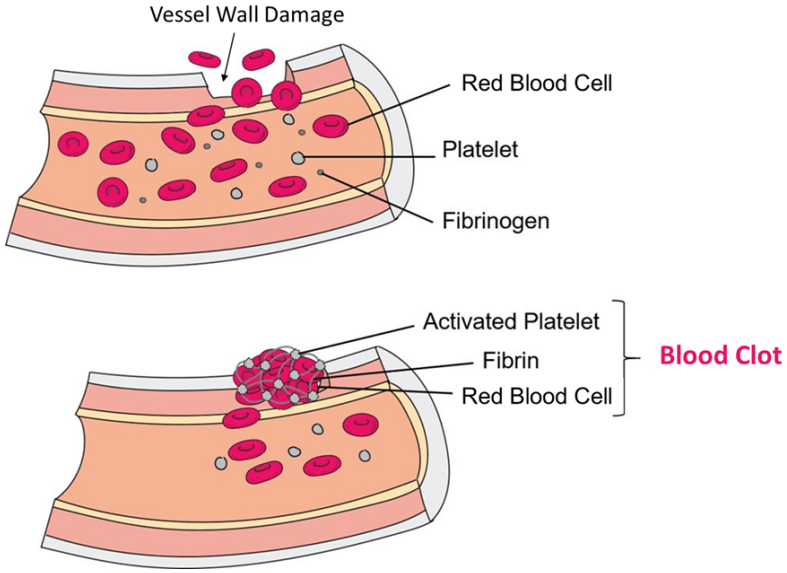
Childbirth is one of the clearest and most commonly used examples of a positive feedback loop in human physiology. It follows a straightforward, self-amplifying process with a clear starting point, increasing intensity, and a definite conclusion. At full term, maintaining the body's current state is no longer beneficial. Major physiological changes are needed to deliver the baby. Once labor begins, it must progress quickly, because delays can put both the mother and baby at risk. The strong muscular contractions of the uterus during labor are controlled by a positive feedback loop, which causes the contractions to become stronger and more frequent until the baby is born.



Here is how it works:

1. **Trigger**: Labor begins when the baby's head pushes against the **cervix**, causing it to **stretch**.
2. **Signal**: This stretching activates stretch receptors and sends nerve signals **to the brain** (specifically the pituitary gland), which responds by releasing the hormone **oxytocin**.
3. **Response**: Oxytocin increases the strength and frequency of **uterine contractions**.
4. **Amplification**: These contractions push the baby harder against the cervix, which causes more stretching, more nerve signals, more oxytocin, and therefore stronger contractions.
5. **Loop continues**: This cycle of increasing pressure and increasing hormone release continues until the baby is born.
6. **Loop ends**: This loop continues until the baby is born, at which point **the pressure on the cervix stops**, oxytocin levels drop, and contractions subside.

2. Blood Clotting



A second well-known example of a positive feedback loop is the **blood clotting process**, which helps the body respond to severe

injuries like a deep cut or puncture. In this situation, the most immediate threat is **excessive blood loss**, which can cause **a dangerous drop in blood pressure** and reduced **perfusion** — that is, reduced delivery of oxygen and nutrients — to the brain and other vital organs. If perfusion drops too low, vital organs begin to shut down, and the person may die.

To prevent this, the body launches a rapid, **localized coagulation** (= blood clotting) response.

Here's how it works:

1. **Injury occurs**: A blood vessel is damaged, and the body detects the break in the vessel wall.
2. **Platelets rush in**: Platelets (small cell fragments in the blood) stick to the injured site and release **chemical signals**.
3. **Amplification**: These chemicals attract **more platelets** to the area, which then release even more signals to recruit **even more platelets**.
4. **Clot forms**: This growing pile of platelets and clotting factors rapidly forms a **plug** that seals the break and stops the bleeding.
5. **Loop ends**: The process continues until the clot is large enough to seal the injury. Once a clot is formed and the damage is repaired, the positive feedback loop of coagulation is terminated through a combination of mechanisms, including the activation of specific inhibitors and negative feedback pathways.

In short, **positive feedback in blood clotting helps the body respond quickly and powerfully to blood vessel injury—but only until the job is done.**

💡 Key Takeaways:

✅ **Not all feedback is negative — sometimes the body uses positive feedback, too.**
Although rare, positive feedback temporarily *amplifies* a change to reach a specific goal (e.g., childbirth or blood clotting). After that goal is met, the loop stops.

✅ **Positive feedback loops are not used for everyday regulation.**
They are used for **short-term, goal-driven processes** that need to be completed efficiently. Once the goal is met (e.g., stopping bleeding or delivering a baby), the loop naturally shuts off.

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2: CELLS AND MEMBRANE TRANSPORT

2.1: Inorganic Chemistry Overview

2.2: Organic Chemistry Review

2.2.1: Types of Biological Macromolecules

2.2.2: Protein Synthesis

2.3: Cell Anatomy — Introduction

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2.1: Inorganic Chemistry Overview

Atoms are made up of particles called protons, neutrons, and electrons, which are responsible for the mass and charge of atoms.

Master this section and you'll be able to

- Define the term element and distinguish between atom and element.
- Describe the basic structure of an atom, including the relative location, charge, and mass of its subatomic particles.
- Distinguish between the terms atomic number and mass number.
- Explain what an ion is.

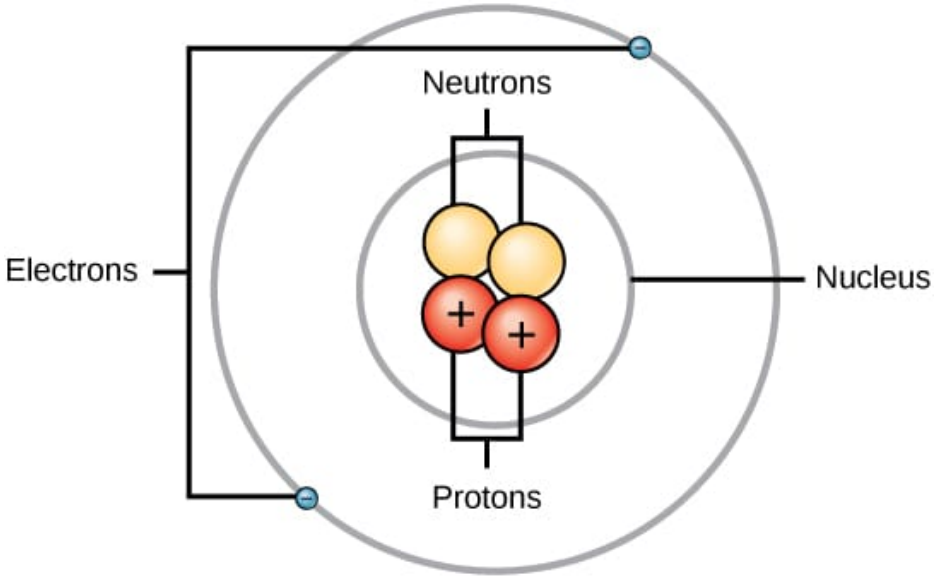
Atoms and Subatomic Structure: The Foundation of Matter

Matter is anything that has mass and takes up space. All things in the universe (i.e. living and non-living things) are considered to be "matter". The smallest component of matter normally found is the **atom**. Therefore, all things in the universe (including humans) are made of atoms.

Atoms themselves are composed of even smaller **subatomic particles** (extremely tiny things) called **neutrons, protons, and electrons.**

- **Protons** have a positive electrical charge (+),
- **electrons** have a negative electrical charge (-), and
- **neutrons** are electrically neutral, meaning they have no charge.

The **nucleus** at the center of the atom contains **protons** (positively charged) and **neutrons** (no charge). The **electrons** (negatively charged) are found in regions called **orbitals** around the nucleus. Electrons do not travel in fixed paths but are described by a probability distribution. The orbitals define the regions where an electron is most likely to be found at any given time. The different orbitals are associated with specific energy levels. See the images below for a simplified view of an atom.



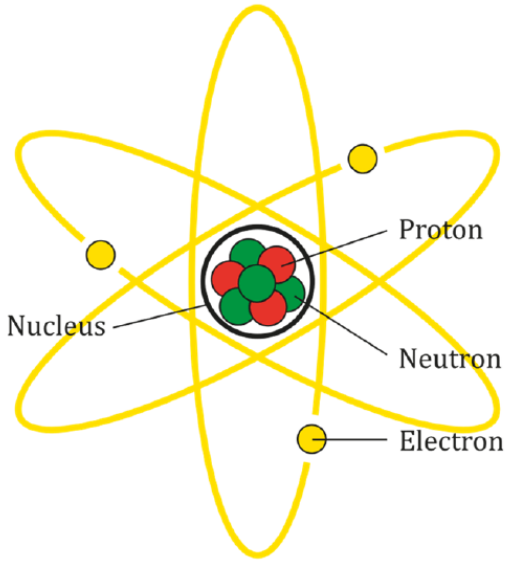


Figure 2.1.1: **Structure of an Atom — Common Planetary Representations of an Atom.** The **helium (He)** atom *in the image on the left* is made up of **2 protons** and **2 neutrons** located within the nucleus. The two electrons are in orbitals surrounding the nucleus. *The image on the right depicts* **lithium (Li)**, which has **3 protons**, **3 electrons**, and typically **4 neutrons** in its most common **isotope** (= version of an element that has the same number of protons but a different number of neutrons).

An atom in its **neutral state** has the **same number of protons and electrons**. Because protons carry a **positive charge (+)** and electrons carry a **negative charge (–)**, their charges cancel each other out, making the atom **electrically neutral**.

For example, a **neutral sodium atom (Na)** has **11 protons** and **11 electrons**. The 11 positive charges balance the 11 negative charges, resulting in an overall charge of **zero**. The most common isotope of sodium has 12 neutrons.

All atoms are made of subatomic particles — protons, neutrons, and electrons — but differ in the number of these particles, giving rise to **118 unique elements**.

🔢 Atomic Number: The Element's ID Card

All known elements in the universe are organized in a chart called the **Periodic Table of Elements**. The table arranges elements according to their chemical properties, their number of protons, and the way electrons are organized in orbital shells. Elements are symbolized by a **chemical symbol** (one- or two-letter abbreviation). Every element on the **periodic table** has a special number called the **atomic number** — it is usually shown **above the element's symbol** (like the "7" above "N" for nitrogen).
That number tells us how many **protons** are in the nucleus of each atom of that element.

💡 **Fun fact:** Because atoms are **electrically neutral**, the number of **electrons** always equals the number of **protons**. So once you know the atomic number, you also know how many electrons there are!

For example:

- **Nitrogen (N)** has an atomic number of **7**, so it has **7 protons and 7 electrons**.
- **Sodium (Na)** has an atomic number of **11**, so it has **11 protons and 11 electrons**.

✅ This rule works for **every element** in the periodic table!

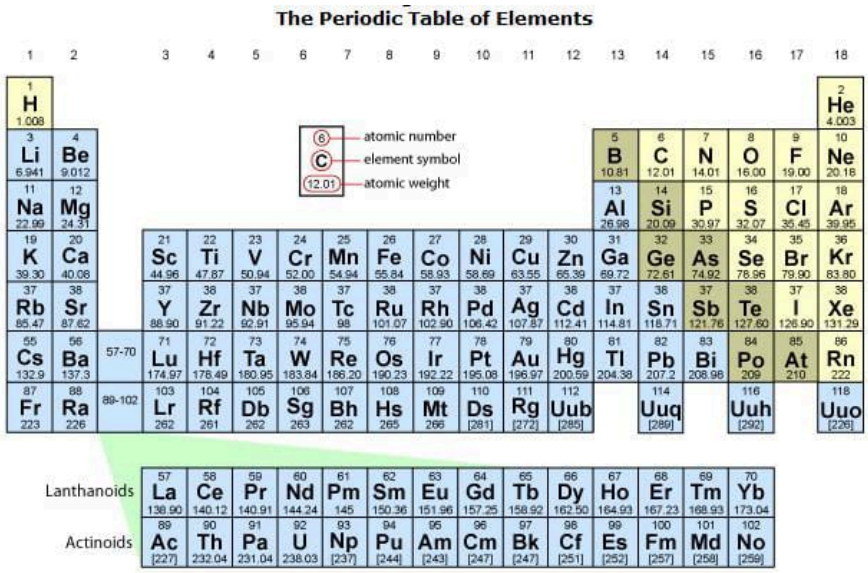


Figure 2.1.2: **Periodic Table of Elements.** The periodic table shows the **element symbols**, **atomic numbers**, and **mass numbers**. The **mass of an atom** is often referred to as its **atomic weight** on Earth — since in most cases, we can think of **atomic weight** and **mass number** as being roughly the same.

Each **element** has its own unique **physical and chemical properties** — like how it looks, how it reacts, or what it can do. These properties come from the number of **protons** in the atom.

An atom with a specific number of protons is the **smallest unit** that still shows the **characteristics of that element**. That means **all atoms of the same element** have the **same number of protons**.

The figure below shows **three different elements**, each with its own number of protons — and its own personality, so to speak!

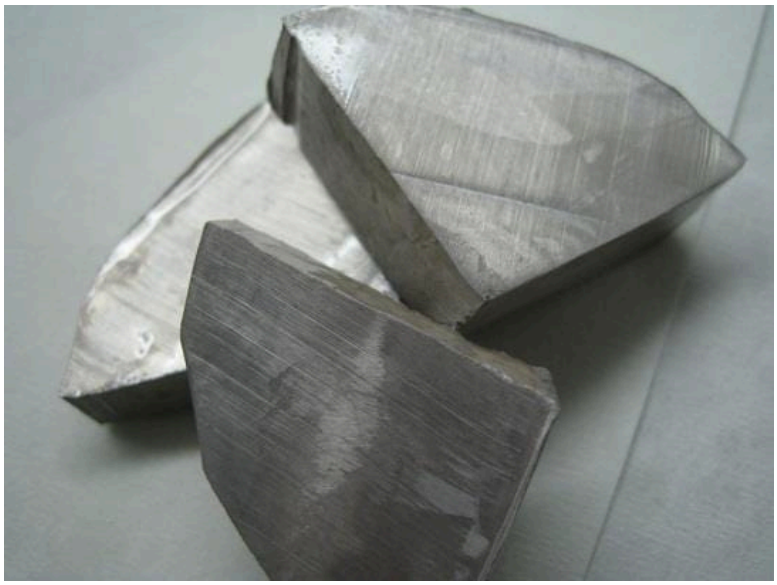






Figure 2.1.3: From left to right, images of the elements **sodium** (solid), **nitrogen** (liquid), and **oxygen** (colorless gas bubbles in the pale blue liquid). The element sodium is made of sodium atoms, the element nitrogen is made of nitrogen atoms, and the element oxygen is made of oxygen atoms.

⚖️ Atomic Mass: The Weight Behind the Atom

You now know that atoms are made up of three main subatomic particles: **protons, neutrons, and electrons**. But believe it or not, scientists have discovered **many more subatomic particles** beyond these three. Do not worry though — we will not dive into those here!

Protons and neutrons each have a mass of approximately **one atomic mass unit (amu)** and are located at the center of the atom, forming the **nucleus**. **Electrons** occupy regions called **orbitals** or **electron clouds** surrounding the nucleus, organized into **energy shells**. Because electrons are so small — about **1/1836 the mass of a proton** — their mass is often considered **negligible (effectively zero)** in most calculations.

When it comes to **atomic mass** (how "heavy" an atom is), **only protons and neutrons really matter**. We can therefore say, the number of **neutrons** affects the mass of the atom, but not its charge.

- A **proton** and a **neutron** each weigh about **1 atomic mass unit (amu)** — basically the same weight.
- **Electrons** are like tiny lightweights — about **1/1800 the mass** of a proton or neutron! Because they are so small, we usually **ignore their mass** when calculating the atom's total mass.

➡️ Summary:

Atomic Number = Number of protons

Atomic Mass = Atomic Weight = Number of protons + Number of neutrons

Charge of an Atom = protons (+) and electrons (–)

Charge & Mass of Subatomic Particles			
	Charge	**Mass (amu)**	**Location**
Proton	+1	1	nucleus
Neutron	0	1	nucleus
Electron	–1	0	orbitals

Atoms Are Mostly Empty Space... So Why Don't We Fall Through Things?

Believe it or not, **over 99% of an atom is empty space**! Protons and neutrons are packed into the tiny nucleus, and the much smaller electrons zoom around it — but most of the atom is just... nothing.

So, if atoms are mostly empty, why do **solid things feel solid**?

It all comes down to **electrons**. Electrons are **negatively charged** and hang out in the outer regions of atoms. When atoms get close, their electrons **repel** each other — kind of like trying to push the same poles of two magnets together.

These repelling forces (called **intermolecular forces**) keep atoms from overlapping. That is why you **do not fall through your chair**, even though both you and the chair are made mostly of empty space!

🔋 Sometimes atoms **gain or lose electrons**, becoming **ions — charged versions of atoms.** This changes how strongly they interact with other atoms and affects many things in biology, like nerve signals and muscle movement.

Interactive: Build an Atom: Build an atom out of protons, neutrons, and electrons, and see how the element, charge, and mass change. Then play a game to test your ideas!

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2.2: ORGANIC CHEMISTRY REVIEW

2.2.1: Types of Biological Macromolecules
2.2.2: Protein Synthesis

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2.2.1: Types of Biological Macromolecules

Biological macromolecules, the large molecules necessary for life, include carbohydrates, lipids, nucleic acids, and proteins.

Master this section and you'll be able to

- Define the terms organic compound and macromolecule, and compare an organic compound with an inorganic compound.
- Distinguish between monomers and polymers.
- Identify the four major classes of biological macromolecules.

Introduction to the Types of Biological Macromolecules

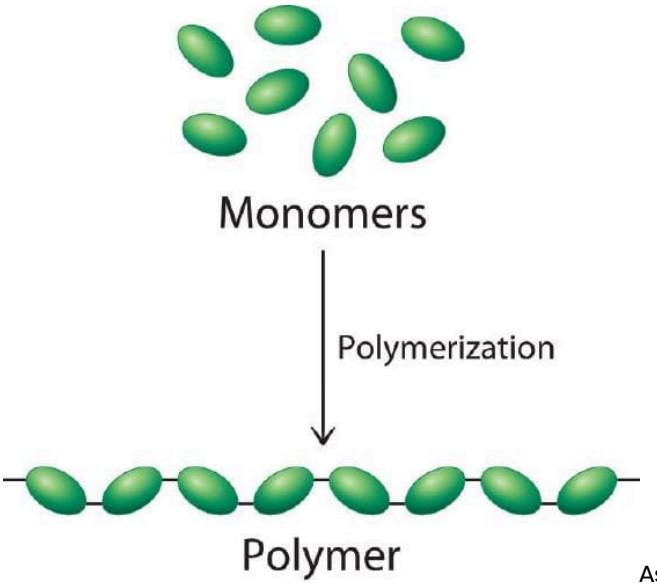
All living matter, as well as the parts, products, and remains of living organisms, is composed of **organic compounds**. These organic compounds consist of large molecules, commonly referred to as **biological macromolecules** or, more simply, as **biomolecules**. The main thing that makes these molecules special is that they always contain **carbon atoms (C)** as well as **hydrogen atoms (H)** attached to the carbon. Think of the carbon atoms as the "backbone" of these molecules — like the spine in your body. Hydrogen atoms are attached to the carbon, like arms or legs. In addition, different organic compounds may be joined by other elements, such as oxygen (O), nitrogen (N), or phosphorus (P) to name just a few.

This means that you, other animals, plants, bacteria, and fungi are all remarkably similar at the molecular level, being constructed from variations of the same types of biomolecules.

In short:

- **Organic compounds:** Carbon-based molecules that typically **contain carbon-hydrogen bonds** and form the backbone of living organisms, including carbohydrates, lipids, proteins, and nucleic acids.
    - **Biological macromolecules (biomolecules)** are large, complex molecules that serve as the building blocks of living things.
    - **All organisms** — from humans to bacteria — are fundamentally similar at the molecular level, despite their visible differences.
- **Inorganic compounds:** Molecules that generally do not contain carbon-hydrogen bonds and include essential substances like water, salts, acids, and bases.
    - **Carbon dioxide (CO_2):** Even though it has carbon, it does not have hydrogen, so it is not organic.
    - **Water (H_2O):** It has hydrogen, but not carbon, so it is not organic.
    - **Salt (sodium chloride, NaCl):** It does not have carbon or hydrogen, so it not organic.

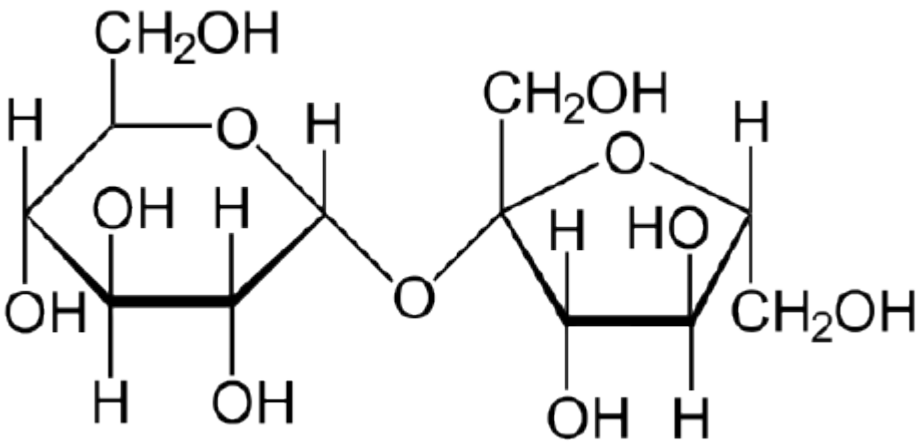
Monomers vs. Polymers



As you have seen, biomolecules are the VIPs of cell structure and function. Most of the big, important molecules in living things (called macromolecules) are actually **polymers**, which means they are made by snapping together lots of smaller, repeating units (building blocks) called **monomers**. Think of monomers as the Lego bricks of life: simple on their own, but incredibly powerful when combined in creative ways.

A great real-life example? **Proteins.** These essential polymer molecules are made by linking together long chains of **amino acids**, which are their monomers. You have only 20 types of amino acids to work with, yet your body can combine them in thousands of different ways to build everything from enzymes that speed up chemical reactions to structural proteins like keratin in your hair and nails. It is like making everything from a paperclip to a jet engine using just 20 kinds of building blocks.

You can also see this concept with **carbohydrates**. Table sugar (sucrose) is a **disaccharide** (a small polymer) made of two monomers: glucose and fructose. Link more sugar monomers together and you get **polysaccharides** like starch (found in potatoes and pasta) or glycogen (found in your muscle cells). The prefixes help you keep track: "**mono-**" means one, "**di-**" means two, and



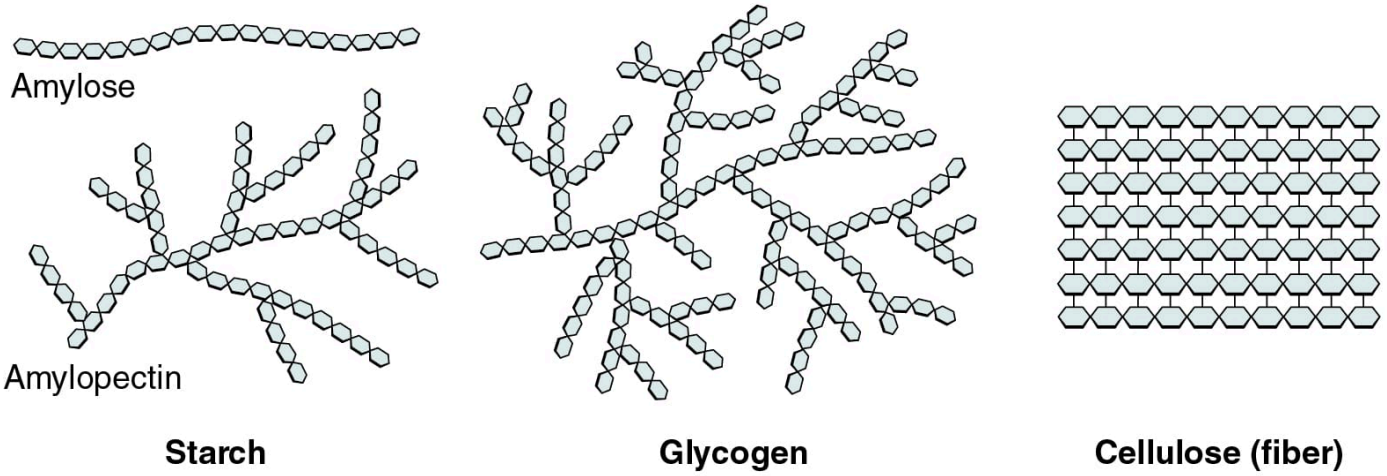
"**poly-**" means many.

In the image on the right, you can see the **sucrose** molecule (commonly known as **table sugar)**: The two **monosaccharides** (glucose on the left and fructose on the right), both simple sugars/carbohydrates are joined to make the **disaccharide sucrose**.

In the image below, you can see polymers that are made up of the monomers glucose:

Amylose (upper left) forms a single chain and amylopectin (below it) is a branched chain. They are the two important polymers that make up **starch**. Starch is a polymer of glucose found in **plants**. You can see that **glycogen**, also a polymer of glucose — but

in animals — is even more highly branched than amylopectin. Starch and glycogen are used for **energy storage**. Finally, cellulose, again a polymer of glucose, has every other glucose monomer upside down.



Interactive Polymerization Reaction Chamber:

The Four Major Classes of Biological Macromolecules

Cells may be tiny, but they are packed with some pretty amazing molecules that keep everything running smoothly. These molecules fall into four major categories:

- **Carbohydrates (COHs):** A broad class of biomolecules that includes **monosaccharides** (the simplest sugars, e.g. glucose and fructose); **disaccharides** (two sugars linked together, e.g. sucrose = glucose + fructose); and **polysaccharides** (complex COHs made up of long chains of many sugar units, e.g. starch, glycogen, cellulose).

- **Lipids:** A diverse group of hydrophobic biomolecules that includes **fats** (triglycerides, used for long-term energy storage), **phospholipids** (major components of cell membranes), and **steroids** (such as cholesterol and hormones). Unlike carbohydrates, lipids are not built from repeating monomer units but are typically made from fatty acids and glycerol.

- **Nucleic Acids:** Two types of biomolecules that store and transmit genetic information. They include **DNA** (deoxyribonucleic acid), which holds the instructions for building proteins, and **RNA** (ribonucleic acid), which helps carry out those instructions. Nucleic acids are made up of **nucleotide** monomers, each consisting of a sugar, a phosphate group, and a nitrogenous base.

- **Proteins:** A wide array of large, complex biomolecules made up of **amino acid** monomers linked in specific sequences. Proteins can be **fibrous** (providing structural support, e.g. collagen) or **globular** (involved in dynamic functions like enzymes, hormones, and antibodies). The unique shape of a protein determines its specific function within the body, from muscle contraction to cell signaling.

Each group plays a unique and essential role in human biology, whether it is providing energy, building structures, storing information, or helping chemical reactions happen at lightning speed. Without a steady supply of these biomolecules in your diet, cells simply could not do their jobs — and you could not function.

Together, these four types of macromolecules make up most of a cell's *dry* mass (meaning everything except water). But since cells are mostly water by weight, all these important molecules are essentially floating in an **aqueous** (water-based) environment. Every reaction that happens in your body, whether you are breathing, blinking, or binge-watching your favorite show, is happening in water and depends on the teamwork of these four molecular VIPs.

Image below: **Living organisms are made up of chemical building blocks**: All organisms are composed of a variety of these biological macromolecules. Nutrients are the molecules that living organisms require for survival and growth but that animals and plants cannot synthesize all by themselves. Animals obtain nutrients by consuming food, while plants pull nutrients from soil.

Image below:

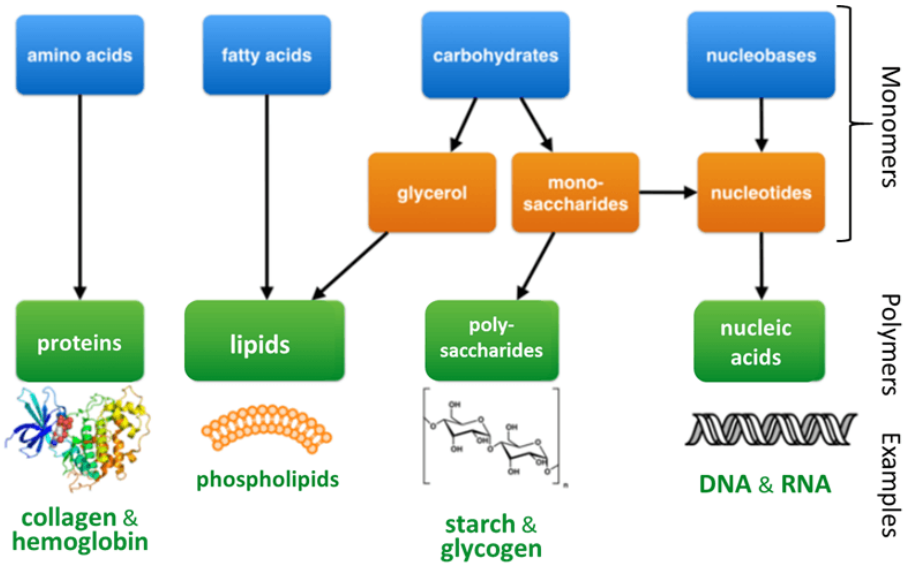


Figure 2.2.1.1: **Biological Macromolecules (or Biomolecules).** Living organisms are made up of chemical building blocks known as biomolecules. All organisms contain a variety of these essential molecules.

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2.2.2: Protein Synthesis

Genes in DNA encode proteins that do the work of the cell.

Master this section and you'll be able to

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

Blueprints and Builders: DNA, Genes, and Proteins

Earlier, we mentioned that DNA acts like a “blueprint” for the cell. That means it holds the instructions to build one of the most important molecules in your body: **proteins**. Proteins help form the structure of cells, and almost everything a cell does depends on proteins in some way.

One especially important group of proteins is called **enzymes**. Enzymes speed up the chemical reactions that cells need to survive. These reactions might involve **building** larger molecules (like during DNA replication or making microtubules) or **breaking down** larger molecules (like when your cells extract energy from food).

In short, if your cells are doing something, **proteins are probably involved**.

Just like the **genome** is all the DNA in a cell, the **proteome** is the full set of proteins the cell can make. The instructions for making these proteins come from **genes** — specific segments of DNA that carry the code to build a particular protein. This process is called **gene expression**. It is how cells turn genetic instructions into working proteins, which then shape the cell’s structure and control what it can do.

How Do Genes Build Proteins?

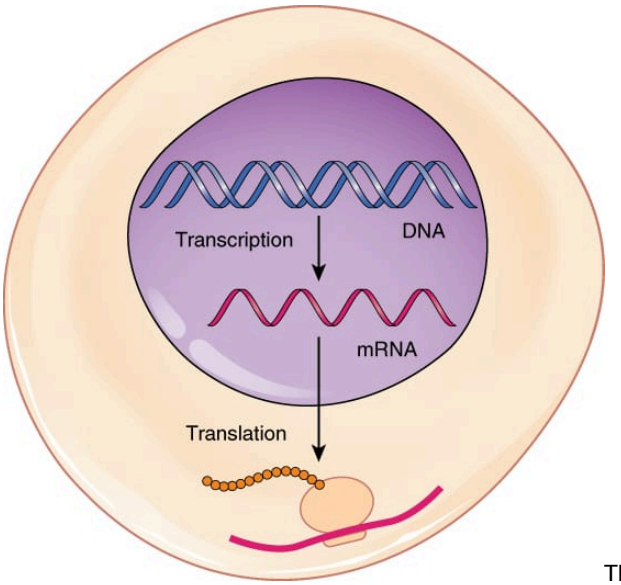
Let's break it down: As you have learned, proteins are made of long chains of smaller units called amino acids — kind of like beads on a necklace. The order of those amino acids determines what kind of protein it is and what job it will do in your body.

So how does your body know which amino acids to put together, and in what order? That is where your DNA comes in.

DNA is made of four building blocks called nucleotides, represented by the letters **A, T, C, and G**. These letters form "words" in your genetic code. Every **three-letter combination** (called a **triplet**) gives instructions to add a specific amino acid. For example, the triplet **CAC** tells your cell to add the amino acid **valine**.

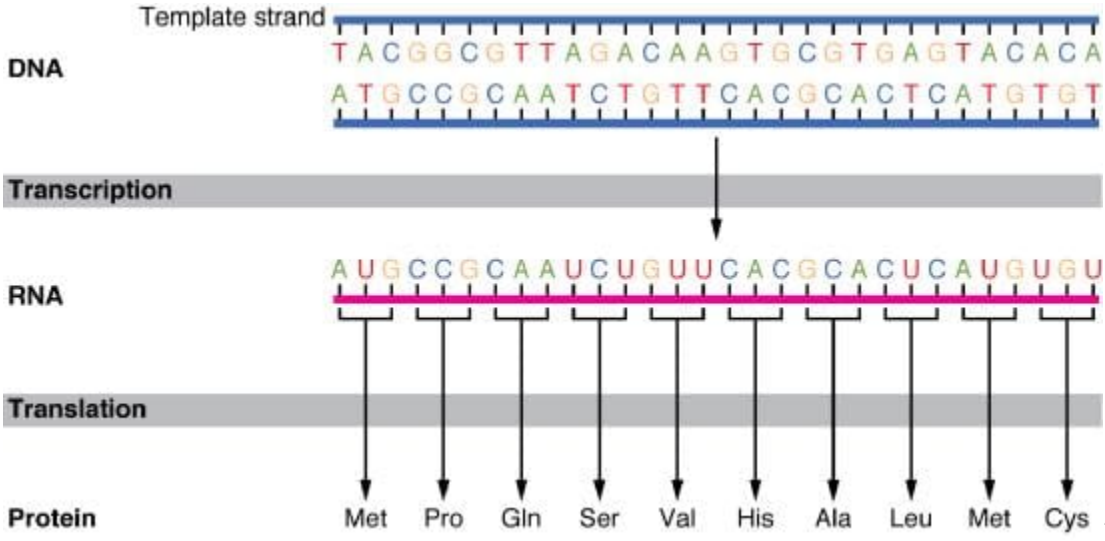
Think of it like this: just like the letters d-o-g create the word “dog,” the DNA letters C-A-C create a signal for “valine.”

A **gene** is a long string of these triplets, each one contributing an amino acid to a growing protein chain. When the full sequence is read, your body knows how to build a complete protein with the correct structure and function.



This process of going from DNA to protein happens in **two main steps** *(see image on the left)*:

1. **Transcription:** The DNA's instructions are copied into a molecule called **RNA** (kind of like making a working copy of a recipe).
2. **Translation:** That RNA copy travels to a ribosome (your cell's protein-building station), where it is read and used to assemble a chain of amino acids—the final **protein**.



The image on the right offers another artistic rendition of these two key biological steps that shows how a cell reads genetic instructions to build a protein:
Starting at the top:

The **DNA sequence** contains the genetic code. Since DNA is double-stranded, only one — the **template strand** — is used to guide the process of **transcription**. During transcription the cell makes a copy of the template strand code in the form of **messenger RNA (mRNA).** This is like writing down a recipe to take with you.

The RNA uses bases A, U, C, and G (note: **U** replaces **T** in RNA).

For the process of **translation,** each set of three RNA bases (called a **codon**) is translated into one amino acid. For example, the first codon **AUG** codes for the amino acid **methionine (Met)**, which is always the starting amino acid.

The result is a **protein**, a chain of amino acids folded into a working molecule that does jobs in your body, such as building muscle, carrying oxygen (hemoglobin), or speeding up reactions in the form of enzymes.

....*And a little more detail:*

Step 1: From DNA to RNA — How the Message Gets Out

Your DNA is stored safely inside the **nucleus** of the cell, but proteins, the workers of the cell, are built in the **cytoplasm**. So, how do the instructions get from one place to the other?

That job goes to a special messenger called **messenger RNA (mRNA)**. It is a single-stranded copy of a gene's instructions, and it travels out of the nucleus into the cytoplasm, where it helps build proteins.

Meet RNA: DNA's Close Cousin

There are different types of RNA in the cell, but the one we are focusing on is **mRNA**—the one that carries the recipe for making a protein.

RNA is very similar to DNA, but with a few important differences:

- RNA is **single-stranded**, not double-stranded like DNA.
- The sugar in RNA is **ribose**, which has one more oxygen atom than the sugar in DNA (called deoxyribose).
- RNA uses a base called **uracil (U)** instead of **thymine (T)**. So, whenever DNA has an **A**, RNA will match it with a **U**

Transcription: Copying the Code

The first step in making a protein is called **transcription**. In this step, your cell makes an **RNA copy** of the gene it needs. That is why it is called "transcription"—just like copying notes from the board in class.

Here is how it works:

1. The section of DNA that contains the needed gene **unwinds**.
2. The two strands of DNA **separate** just in that region.
3. Using one of the DNA strands as a guide (= the template strand), the cell builds an **mRNA strand** with the matching bases.

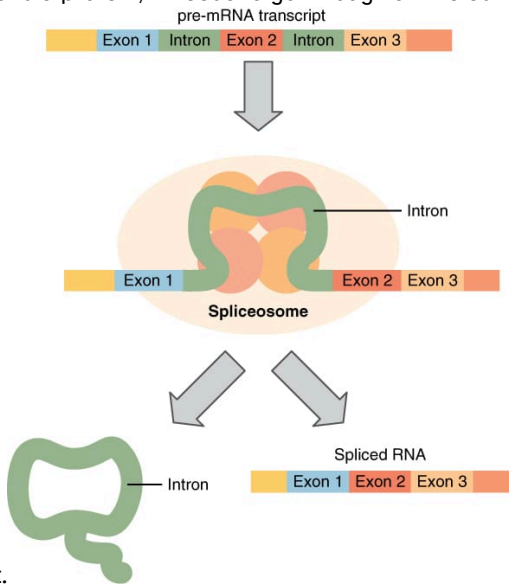
The DNA is read in **triplets**, and each triplet gets copied into a matching **three-base unit on the mRNA**, called a **codon**. Each codon will eventually tell the cell which amino acid to add to the protein chain.



In the figure on the left, you can see how a gene on the DNA molecule is transcribed by an enzyme called RNA polymerase into a complementary mRNA molecule:

Polishing the Message: What Happens Before mRNA Leaves the Nucleus

Before the mRNA can go out into the cytoplasm and help build a protein, it needs to go through a little **editing**. At this point, it is still called **pre-mRNA** because it is not quite ready yet.



One important editing step is called **splicing** *(see image on the right)*. Your DNA (and the mRNA copied from it) contains some stretches of code that **do not actually code for proteins**. These parts are called **non-coding regions**, or **introns**, and scientists are still figuring out exactly what they do. But for now, the cell snips them out.

A special structure in the cell, called a **spliceosome**, does the cutting. It removes the **introns,** the parts of the RNA that are not needed, and stitches together the **exons**, which are the useful coding parts.

- **Introns** = the "in-between" parts that get removed
- **Exons** = the parts that stay and get used to build the protein

Here is something cool: Sometimes, even **coding regions** (exons) can be spliced in different ways. This is called **alternative splicing**. By mixing and matching different exons, your cells can make **many different versions of a protein** from just one gene. That means **more variety** in what your body can build, even with a limited number of genes!

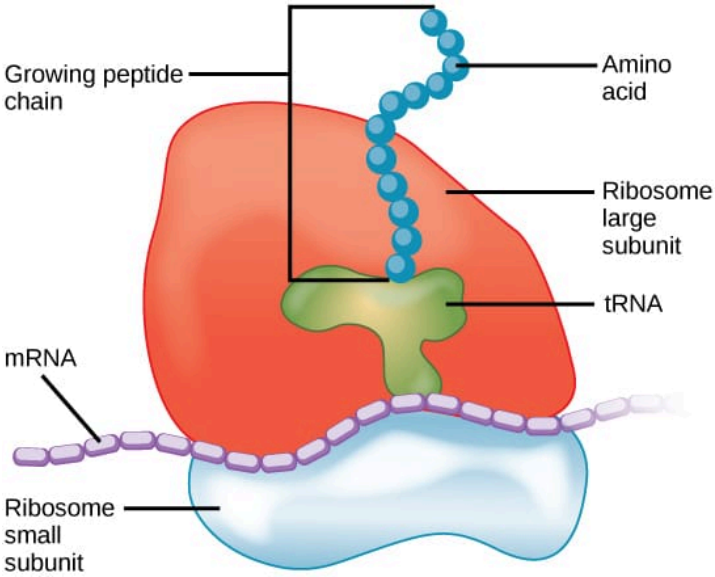
Once the mRNA is cleaned up and ready, it **leaves the nucleus** and heads into the **cytoplasm**, where the next step (translation) will turn that message into a real, working protein.

Step 2: Translation — From RNA to Protein (a.k.a. Turning the Genetic Recipe into Dinner)

Think of this step like translating a recipe written in one language (RNA) into another (protein). Each three-letter "word" on the mRNA strand is called a **codon**, and each codon stands for a specific amino acid, the building blocks of proteins. The goal of **translation** is to string these amino acids together to make a **polypeptide**, which will eventually fold into a fully functioning protein.

To pull this off, the cell needs two main tools:

1. A **translator:** someone (or something) who can read the RNA and know which amino acid goes where.
2. A **workspace:** like a kitchen counter or desk where this translation happens.



Lucky for us, the cell already has both. The translator job goes to **tRNA**, and the workspace is the **ribosome,** a protein-building machine made partly of another type of RNA called **rRNA** (ribosomal RNA). *See image on the left.*

You might remember from an earlier biology course that many ribosomes hang out on the **endoplasmic reticulum (ER)**, making it the rough ER. Each ribosome is made of two parts, a large and a small subunit. When it is time to start protein synthesis, these two parts snap together on an mRNA strand and get to work, aligning everything just right for accurate decoding. If you have never heard of that, no worries, we will cover it in some details in Module 3.

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tRNA: The Protein Builder's Uber

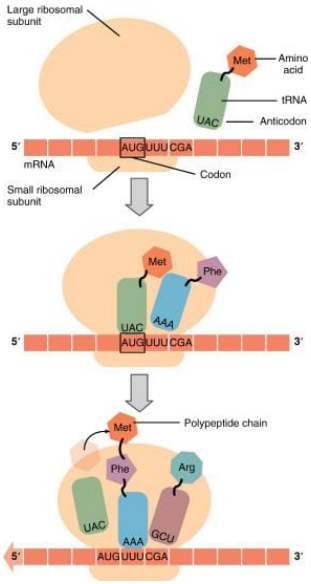
Now let's zoom in on our translator: **tRNA**, short for **transfer RNA**. These clever little molecules do the legwork (literally!) of bringing the right amino acid to the ribosome. They cruise around the cytoplasm, pick up their assigned amino acid, and deliver it to the assembly line.

But here's the cool part: each tRNA has two key features that make this possible:

- One end has a spot to **grab a specific amino acid** (like glycine, for example).
- The other end carries an **anticodon,** a three-letter sequence that **matches up with the codon on the mRNA** (like a

plug fitting into a socket).

Let's say the mRNA strand shows the codon **CGA**, which encodes the amino acid arginine. A tRNA with the anticodon **GCU** will recognize and bind to it, bringing arginine along for the ride. The ribosome helps this happen smoothly, joining the new amino acid to the growing chain one-by-one until the full protein is complete. But how does the cell know the protein is complete? When the ribosome stops translating mRNA when it reaches a special **"stop" codon.** The stop codon signals the end of translation. At that point, the finished protein is released — ready to fold into its final shape and go to work. Thus, a gene within the DNA molecule is transcribed into mRNA, which is then translated into a protein product.



In the top part of the figure on the right, you can see a large ribosomal subunit coming into contact with the mRNA that already has the small ribosomal subunit attached. A tRNA and an anticodon are in proximity. In the second panel, the tRNA also binds to the same site as the ribosomal subunits. In the bottom panel, a polypeptide chain is shown emerging from the complex.

In summary: a **gene** on DNA is first **transcribed** into mRNA, and that mRNA is then **translated** into a functional **protein**

Interactive Link

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

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2.3: Cell Anatomy — Introduction

A cell is the smallest unit of a living thing and is the basic building block of all organisms.

Master this section and you'll be able to

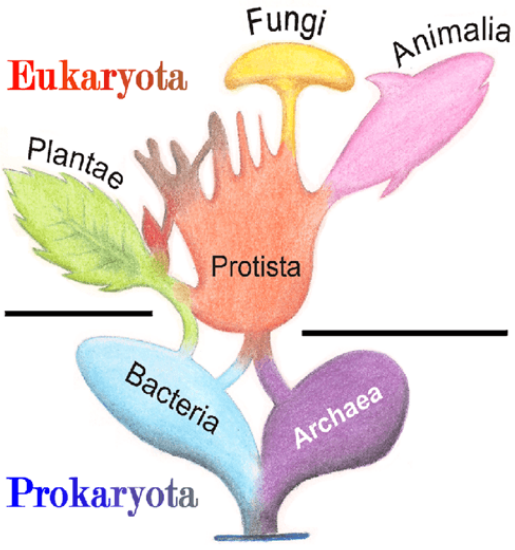
- Describe the general characteristics shared by all cells.
- Compare and contrast prokaryotic and eukaryotic cells.
- Explain why cells have different shapes.
- Summarize the main principles of the cell theory.

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

Cells as Building Blocks

A **cell** is the smallest unit of a living thing. Any living thing, whether it consists of just one cell (like bacteria) or many cells (like a human), is called an **organism**. This means that **cells are the basic building blocks of all organisms**.

When many cells of the same type work together to perform a shared function, they form a **tissue**. Multiple tissues then combine to form an **organ** (such as the stomach, heart, or brain). A group of organs that work together make up an **organ system** (like the digestive, circulatory, or nervous system). Several systems working in coordination form an entire **organism**, such as a human being.



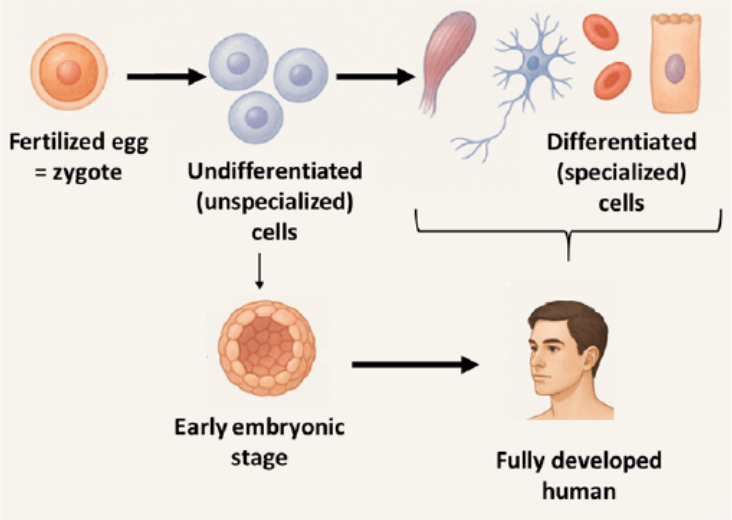
There are many different types of cells, but they all fall into one of two broad categories: **prokaryotic** or **eukaryotic cells**. Prokaryotic cells, found in organisms like bacteria, are simpler and lack a nucleus or membrane-bound organelles. In contrast, eukaryotic cells, found in animals, plants, fungi, and protists, are more complex, with a **defined nucleus and various organelles that carry out specialized functions**. Eukaryotic organisms can be unicellular or multicellular, while prokaryotic organisms are always unicellular. Below is a concise comparison of eukaryotes and prokaryotes.

Comparison of Prokaryotic and Eukaryotic Cells

Feature	Prokaryotes	Eukaryotes
Nucleus	❌ Absent	✅ Present
Organelles	❌ No membrane-bound organelles	✅ Membrane-bound organelles present
Cell Type	Always unicellular	Unicellular or multicellular
Cell Size	Small (1–10 µm)	Larger (10–100 µm)
DNA Structure	Circular DNA	Linear DNA in chromosomes
Examples	*E. coli*	*Homo sapiens*

From One Cell to Trillions

You began life as a single fertilized egg cell known as a **zygote**. From that one cell, you developed into the complex human you see in the mirror today, a body composed of **trillions of cells.** Estimates state that a human body is made up of approximately 37 trillion cells. The cells are organized into **tissues**, **organs**, and **organ systems**. This incredible transformation is made possible by two processes called **cell division (mitosis)** and **cell differentiation.**



After fertilization, the zygote started to do something remarkable: it divided. First, it split into **two** identical cells. Then **each of those two** divided again, making **four**. Those four became **eight**, then **sixteen**, and so on. This pattern of **exponential growth** continued rapidly as the **embryo** (= early stage of development in a multicellular organism) started to grow. With each round of division, more and more cells were created. Eventually, this growing collection of cells began to organize, specialize (= differentiate), and form the tissues and organs of your body. But it all started with one tiny cell, using a process called mitosis to multiply again and again.

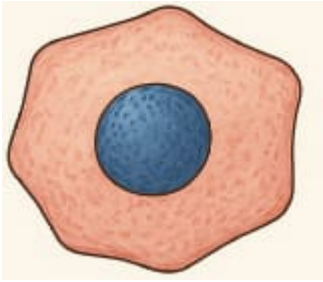
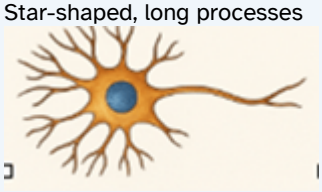
However, just multiplying cells is not enough. In the early stages of development, these new cells are **unspecialized (= undifferentiated)**, meaning they do not yet have a specific job. Over time, they undergo a process called **differentiation**, during which they become **specialized in both their structure and function**. For example, some cells become muscle cells that contract, while others become nerve cells that carry electrical signals, or red blood cells that transport oxygen.

Differentiation is guided by the cell's environment and by specific instructions in its DNA. Even though nearly all the cells in your body contain the same genetic material, different genes are turned "on" or "off" in each type of cell. This selective gene expression is what allows cells to take on unique roles, ultimately giving rise to the specialized tissues and organs that keep your body alive and functioning.

Why Cell Shape Matters

You will see this theme throughout your study of anatomy and physiology. For now, let us look at a simple comparison to illustrate the point:
a **skin cell** and a **nerve cell**. Each one is uniquely shaped to carry out its specialized role in the body.

Comparison of Two Specialized Cell Types

Cell Type	Shape	Function	Lifespan
Skin (Epithelial)	Flat, plate-like 	Forms protective barriers	Short; constantly replaced
Nerve (Neuron)	Star-shaped, long processes 	Sends fast signals across long distances	Long-lived; can last a lifetime

Just as a home is made from a variety of building materials, the human body is constructed from many cell types. In fact, there are **over 200 different types of cells** in the human body. To name just a few, these include familiar ones like:

- **Epithelial cells**, which protect the surface of the body and cover the organs and internal body cavities;
- **Neurons**, which transmit electrical and chemical signals to communicate information throughout the body;
- **Muscle cells**, which contract to produce movement and generate force; and
- **Immune cells**, which detect and respond to harmful invaders to protect the body from infection and disease.

But there are also less familiar (but equally fascinating) examples, such as the **Merkel cell,** a specialized mechanoreceptor found in the outer layer of the skin. Merkel cells play a crucial role in sensing touch and transmitting sensory information to the brain.

Each of these cell types plays a vital role during the growth, development, and day-to-day maintenance of the body.

The fact that cells in the body can have strikingly different shapes is not random. It reflects the specific job each cell is designed to do. In fact, the differences between cell shapes highlight a central concept in biology:

> **Form follows function** — the shape and structure of a cell directly relate to the job it performs.

Cells do not work in isolation. They cooperate in tissues, organs, and organ systems — each one contributing to your survival. No matter the job, every cell plays a part in keeping your body balanced.

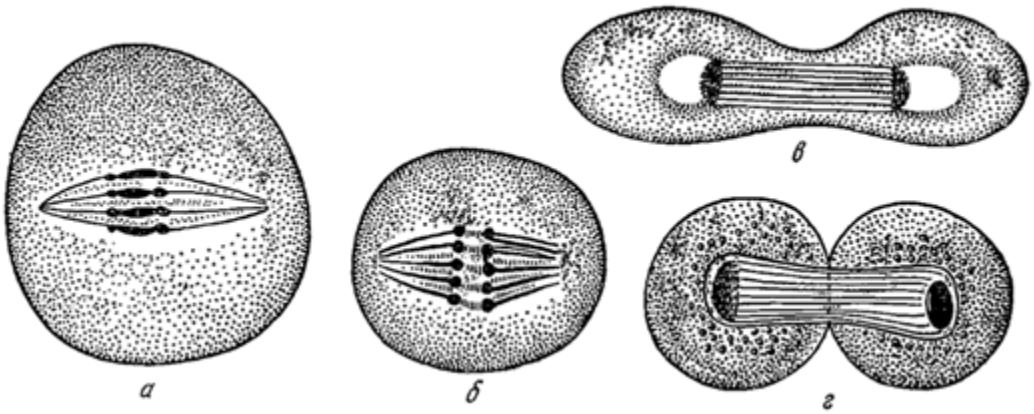


A Quick History of Cell Discovery

The first person to use the word “cell” was **Robert Hooke** in 1665. Looking at cork tissue under a microscope, he noticed tiny compartments that reminded him of *cells*, the rooms where monks lived.

A few years later, **Antonie van Leeuwenhoek** (1632 – 1723) invented the microscope and observed **living cells** for the first time. Over the following decades, scientists developed the **cell theory**, a fundamental concept in biology, which tells us:

- All living organisms are made of cells.
- The cell is the basic unit of life.
- All cells arise from pre-existing cells.



The illustration above depicts stages of cell division as understood by Eduard Strasburger in 1875 (Bonn, Germany).

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2.4: Components of Plasma Membranes

The plasma membrane protects the cell from its external environment, mediates cellular transport, and transmits cellular signals.

Master this section and you'll be able to

- Identify the major components of the plasma membrane (including phospholipids, proteins, cholesterol, and carbohydrates).
- Describe three key functions of the plasma membrane.

Principle Components of the Plasma Membrane

The **plasma membrane** (also known as the **cell membrane** or **cytoplasmic membrane**) is a biological membrane that separates the interior of a cell from its outside environment.

The primary function of the plasma membrane is to **protect** the cell from its surroundings. Composed of a **phospholipid bilayer with embedded proteins**, the plasma membrane is **selectively permeable** to ions and organic molecules and regulates the movement of substances in and out of cells. Plasma membranes must be very flexible in order to allow certain cells, such as red blood cells and white blood cells, to change shape as they pass through narrow capillaries.

The plasma membrane also plays a role in anchoring the cytoskeleton to provide shape to the cell, and in attaching to the extracellular matrix and other cells to help group cells together to form tissues. The membrane also maintains the cell potential.

In short, if the cell is represented by a castle, the plasma membrane is the wall that provides structure for the buildings inside the wall, regulates which people leave and enter the castle, and conveys messages to and from neighboring castles. Just as a hole in the wall can be a disaster for the castle, a rupture in the plasma membrane causes the cell to lyse and die.

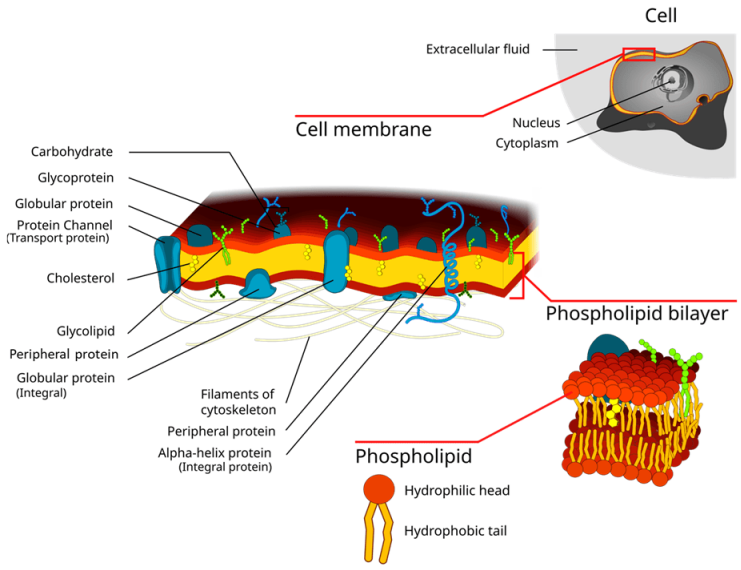


Figure 2.4.1: **The plasma membrane**. The plasma membrane is composed of phospholipids and proteins that provide a barrier between the external environment and the cell, regulate the transportation of molecules across the membrane, and communicate with other cells via protein receptors.

The Plasma Membrane and Cellular Transport

Due to the selective nature of the phospholipid bilayer (remember you learned the expression "selectively permeable" above),

cells require a range of specialized transport mechanisms to control the movement of materials across their membranes.

The movement of a substance across the selectively permeable plasma membrane can be either "**passive**"— *i.e.:* occurring without the input of cellular energy — or "**active**"— *i.e.:* its transport requires the cell to expend energy.

1. **Diffusion** and **osmosis: passive movement** of gases (such as O_2 and CO_2) and other small molecules and ions.

2. **Transmembrane protein channels** and **transporters:** transport small organic molecules such as sugars or amino acids. Transmembrane proteins can support both passive or active transport depending on the direction of movement and whether or not energy is used.

3. **Endocytosis** and **exocytosis:** are active transport processes that move large substances into our out of the cell.

    - In **endocytosis**, the cell ***engulfs*** large molecules — or even whole cells — by wrapping its membrane around them.

    - In **exocytosis**, the cell ***releases*** substances like hormones or enzymes by packaging them in a vesicle that fuses with the cell membrane.

More details to follow when we cover Cell Physiology later in this Module.

The Plasma Membrane and Cellular Signaling

Among the most sophisticated functions of the plasma membrane is its ability to transmit signals via complex proteins. These proteins can be **receptors**, which work as receivers of extracellular inputs and as activators of intracellular processes, or **markers**, which allow cells to recognize each other.

Membrane receptors provide extracellular attachment sites for effectors like hormones and growth factors, which then trigger intracellular responses. Some viruses, such as Human Immunodeficiency Virus (HIV), can hijack these receptors to gain entry into the cells, causing infections.

Membrane markers allow cells to recognize one another, which is vital for cellular signaling processes that influence tissue and organ formation during early development. This marking function also plays a later role in the "self"-versus-"non-self" distinction of the immune response. Marker proteins on human red blood cells, for example, determine blood type (A, B, AB, or O).

Again, for more details see later in the semester.

Summary of Key Points

- The principal components of the plasma membrane are lipids (phospholipids and cholesterol), proteins, and carbohydrates.
- The plasma membrane protects intracellular components from the extracellular environment.
- The plasma membrane mediates cellular processes by regulating the materials that enter and exit the cell.
- The plasma membrane carries markers that allow cells to recognize one another and can transmit signals to other cells via receptors.

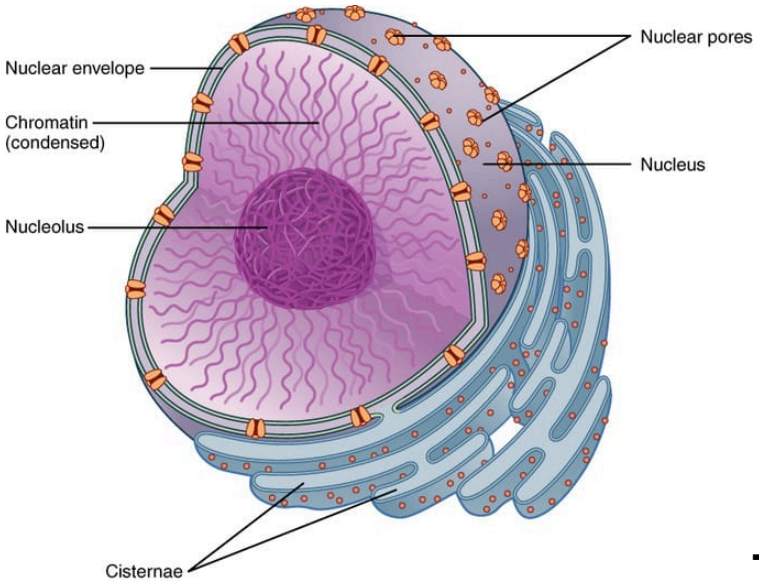
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2.5: The Nucleus

Found within eukaryotic cells, the nucleus contains the genetic material that determines the entire structure and function of that cell.

Master this section and you'll be able to

- Explain the purpose of the nucleus in eukaryotic cells (include storing DNA and directing the synthesis of ribosomes and proteins)
- Identify the nucleolus as a condensed region within the nucleoplasm where ribosome synthesis takes place
- Explain the structure and role of chromatin (including how DNA is wrapped around histone proteins and stored within the nucleoplasm).
- Describe briefly the composition and function of ribosomes.



The Nucleus

One of the biggest differences between prokaryotic and eukaryotic cells is the **nucleus** — the "command center" of the cell. As you learned earlier, **prokaryotic cells** (such as bacteria) *do not* have a true nucleus. Their **DNA (deoxyribonucleic acid)** just floats around in the cytoplasm. But **eukaryotic cells** (like our own) *do* have a **membrane-bound nucleus** that stores and protects DNA, and also helps direct important activities like making ribosomes and proteins. In fact the nucleus actually has a double-membrane

Inside this nucleus is a gel-like substance called the **nucleoplasm**, which holds the cell's **chromatin** and other substances. What is chromatin? It is the material that makes up **chromosomes,** the structures made of DNA (your genetic blueprint) and proteins.

In **prokaryotes**, DNA comes in the form of a *single circular chromosome*. In **eukaryotes**, chromosomes are *linear*, and each species has a specific number. For example, **humans have 46 chromosomes**, while cats have 38 and dogs 78. **Chromosomes** are arranged in **pairs.** Therefore, humans have

- **18 pairs of autosomes.** Any chromosome that is not a sex chromosome and carries genes that determine most of an organism's traits is called an autosome.
- **1 pair of sex chromosomes.** The sex chromosomes determine an organism's biological sex — typically **XX** for females and **XY** for males in most mammals.

To keep the long, fragile DNA organized, the DNA is wrapped around special proteins called **histones** *(see image below)*. This protein-associated DNA is what we call **chromatin.** The long DNA strands are wound around special proteins called histones, like thread wrapped around spools.

To keep the long, fragile DNA organized, it is wrapped around special proteins called **histones** (see image below). This combination of DNA and proteins is called **chromatin**. You can think of it like thread wrapped around spools — the histones help neatly package the DNA so it fits inside the cell's nucleus.

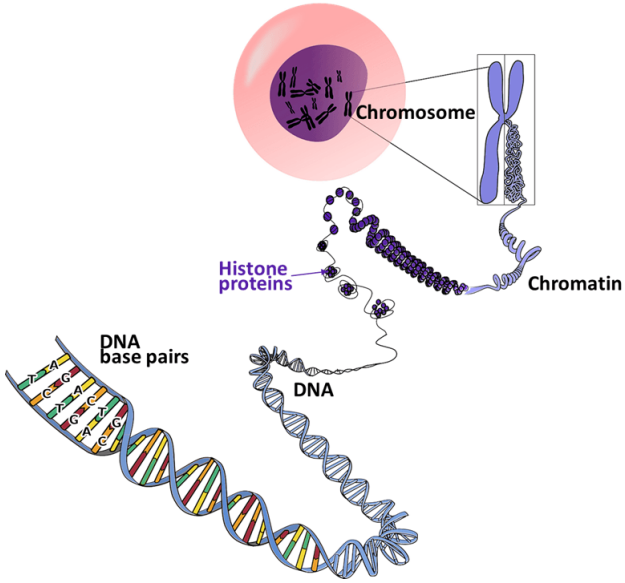


Figure 2.5.1: **Most of the time, your DNA is kept as chromatin in the nucleus.** This relaxed structure makes it easy for the cell to **read the DNA and make proteins**. But when a cell is about to **divide**, it needs to make sure each new cell gets the right amount of DNA. To do that, the chromatin **coils up tightly** into thick, visible structures called **chromosomes**.

Think of it like this:

- **Chromatin** is like a loose pile of yarn when the cell is working.
- **Chromosomes** are like neatly wrapped balls of yarn when the cell is getting ready to divide and pack things up.

Once the cell finishes dividing, the chromosomes **unwind back into chromatin** so the new cells can get back to work.

Humans have **23 different chromosomes**, but we have **two copies of each** — one from each parent. That means each cell in your body has **46 chromosomes total**. Because we have two sets, humans are called **diploid**.

Some organisms only have **one copy of each chromosome** — they are called **haploid**. Others may have **three** or even **four copies** of each chromosome, and these are called **triploid** and **tetraploid**, respectively.

The **nucleoplasm** is kind of like the cytoplasm, but just for the nucleus. It is the gel-like fluid inside the nucleus that surrounds and supports the DNA and other structures inside the nucleus.

The **nucleolus** is a dense region inside the nucleoplasm, and it is where **ribosomes are made**. Specifically, it is a concentrated area of chromatin involved in building the components of ribosomes.

Ribosomes are large structures made of **proteins and RNA (ribonucleic acid)**. They are the **organelles responsible for making proteins**. Ribosomes get their instructions from the DNA in the nucleus, where the DNA is first **transcribed into messenger RNA (mRNA)**.

The **mRNA** then travels out of the nucleus to the ribosomes. There, the ribosomes **read the mRNA code** — a sequence of nitrogenous bases — and **translate it into a specific chain of amino acids**, forming a protein.

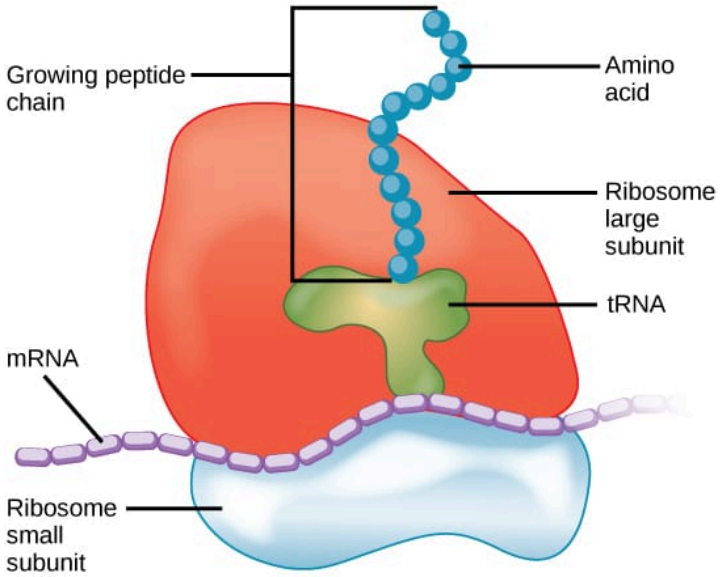


Figure 2.5.2: **Ribosomes are responsible for protein synthesis**. Ribosomes are made up of a large subunit (top) and a small subunit (bottom). During protein synthesis, ribosomes assemble amino acids into proteins.

Lastly, the boundary of the nucleus is called the **nuclear envelope**. It consists of two phospholipid bilayers: an outer membrane and an inner membrane. The nuclear membrane is continuous with the endoplasmic reticulum. **Nuclear pores** allow substances to enter and exit the nucleus

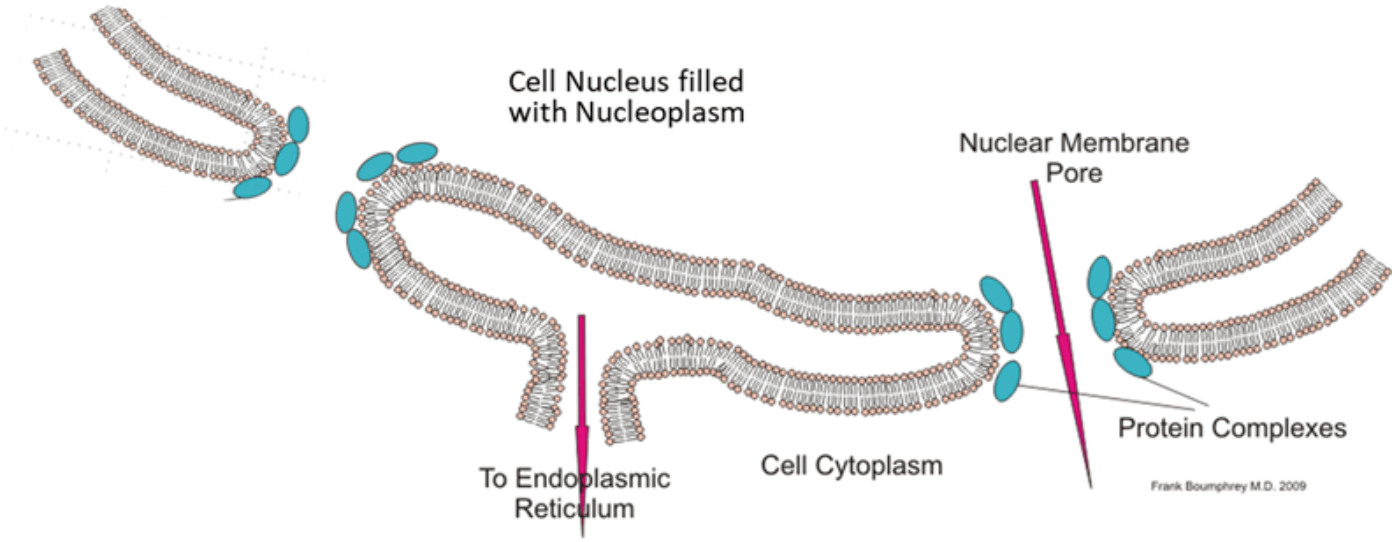


Figure 2.5.3: **Nuclear envelope with nuclear pores**. The nuclear envelope is a **double membrane** that encloses the nucleus, separating it from the cytoplasm. Each layer is made of a **phospholipid bilayer.** This is in contrast to the **cell membrane**, which has just **one bilayer**. The envelope is studded with **nuclear pores**, which act like selective gateways, allowing materials like RNA and proteins to move in and out of the nucleus while protecting the DNA inside.

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2.6: The Cytoplasm and Cellular Organelles

Inside the cell, a coordinated system of organelles works together to produce energy, build molecules, transport materials, and keep the cell alive.

Master this section and you'll be able to

- Describe the structure and function of the cellular organelles associated with the endomembrane system, including the endoplasmic reticulum, Golgi apparatus, and lysosomes
- Describe the structure and function of mitochondria

Inside the Cell

Now that you know every cell is wrapped in a protective cell membrane, let us take a tour inside and see what is going on beneath the surface.

The entire content (excluding the nucleus) within the cell membrane of a typical human cell is a busy, jelly-like interior called the **cytoplasm**, the cell's working interior. The cytoplasm includes the **cytosol**, **organelles**, and other inclusions:

- **Cytosol** is the fluid portion inside the cell, excluding organelles and other structures. It is composed primarily of water which makes up about **70%** of its volume and serves as the site for many metabolic (biochemical) reactions. The cytosol is also the liquid in which the organelles "float".

- **Organelles** are the cell's mini-organs, each with its own job to do. Just like your organs work together to keep your body functioning, the cell's organelles team up to keep the cell alive, healthy, and productive. Some organelles make proteins, some generate energy, and others help clean up cellular waste.

All **eukaryotic cells** (like those in your body) have this organized internal setup. At the center is the **nucleus**, the "command center" of the cell, which safely stores the DNA, the instructions for building and running the entire cell. So yes, even a tiny cell is like a bustling city, full of activity and teamwork—with the nucleus acting as city hall, and organelles taking on roles like power plants, recycling centers, factories, and more.

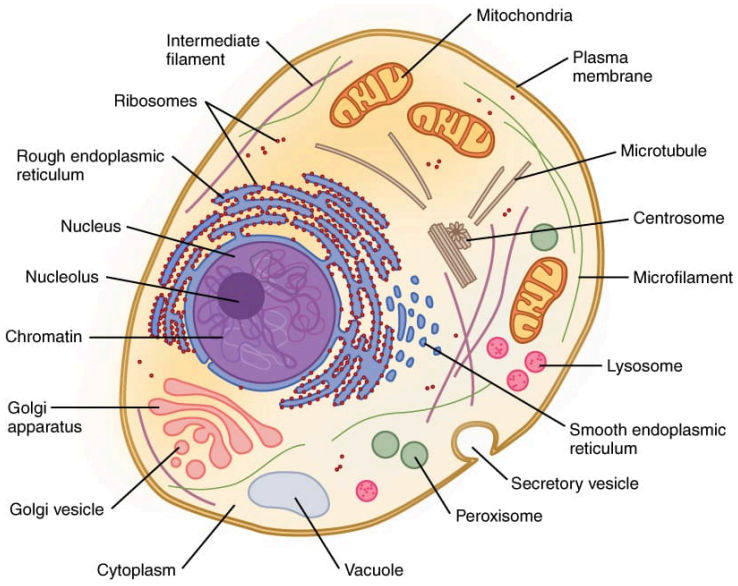


Figure 2.6.1: **Prototypical Human Cell.** While this image is not indicative of any one particular human cell, it is a general example of a human cell containing the standard organelles and internal structures.

Organelles of the Endomembrane System

The **endomembrane system** is a group of connected membranes and organelles inside eukaryotic cells that work together to perform various cellular jobs, including the task of producing, packaging, and exporting certain cellular products (proteins and lipids). Think of it as the cell's internal shipping and processing center, making sure molecules get to the right place, both inside and outside the cell. The organelles of the endomembrane system include the **endoplasmic reticulum, Golgi apparatus, and vesicles.**

Endoplasmic Reticulum 🏭🧪

The endoplasmic reticulum (ER) is a system of channels that is continuous with the nuclear membrane (or "envelope") covering the nucleus and composed of the same lipid bilayer material. The ER can be thought of as a series of winding thoroughfares similar to the waterway canals in Venice. The ER provides passages throughout much of the cell that function in transporting, synthesizing, and storing materials. The winding structure of the ER results in a large membranous surface area that supports its many functions (Figure 2.6.2).

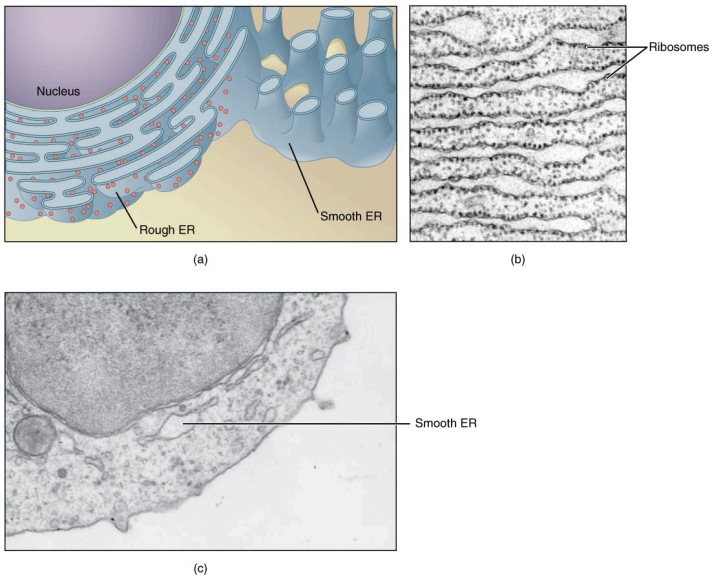


Figure 2.6.2: **Endoplasmic Reticulum (ER).** (a) The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function (source: mouse tissue). (b) Rough ER is studded with numerous ribosomes, which are sites of protein synthesis (source: mouse tissue). EM × 110,000. (c) Smooth ER synthesizes phospholipids, steroid hormones, regulates the concentration of cellular Ca++, metabolizes some carbohydrates, and breaks down certain toxins (source: mouse tissue). EM × 110,510. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

Endoplasmic reticulum can exist in two forms: **rough ER (RER)** and **smooth ER (SER)**. These two types of ER perform some very different functions and can be found in very different amounts depending on the type of cell. Rough ER is so-called because its membrane is dotted with embedded granules — organelles called **ribosomes**, giving the RER a bumpy appearance. A ribosome is an organelle that serves as the site of **protein synthesis.** It is composed of two ribosomal RNA subunits that wrap around mRNA to start the process of translation, followed by protein synthesis. Smooth ER (SER) lacks these ribosomes.

One of the main functions of the smooth ER is in the **synthesis of lipids**. The smooth ER synthesizes phospholipids, the main component of biological membranes, as well as steroid hormones. For this reason, cells that produce large quantities of such hormones, such as those of the female ovaries and male testes, contain large amounts of smooth ER. In addition to lipid synthesis, the smooth ER also sequesters (i.e., stores) and regulates the concentration of cellular Ca^{++}, a function extremely important in cells of the nervous system where Ca^{++} is the trigger for neurotransmitter release. The smooth ER additionally performs a detoxification role, breaking down certain toxins.

In contrast with the smooth ER, the primary job of the rough ER is the synthesis and modification of proteins destined for the cell membrane or for export from the cell. For this protein synthesis, many ribosomes attach to the ER (giving it the studded

appearance of rough ER). Typically, a protein is synthesized within the ribosome and released inside the channel of the rough ER, where sugars can be added to it (by a process called glycosylation) before it is transported within a vesicle to the next stage in the packaging and shipping process: the Golgi apparatus.

The Golgi Apparatus: The Cell's Post Office 🏣

The **Golgi apparatus** is like the cell's own post office. It **sorts, modifies, and ships** the proteins and other products that arrive from the rough endoplasmic reticulum (RER).

This organelle looks like a stack of **flattened, squishy pancakes** — each "pancake" is actually a **membrane-bound sac**. Like the ER, the Golgi apparatus is made of membranes, but it is arranged in a more compact, stacked form.

The Golgi apparatus has **two distinct sides**, each with a different job:

- One side **receives** incoming products in **vesicles** (tiny membrane bubbles).
- Inside the Golgi, those products are **processed and sorted.** Some are modified with sugars or other molecules.
- Then, they are **repackaged into new vesicles** and sent out from the opposite side.

If a product is meant to be **exported out of the cell**, the vesicle carrying it will move to the **cell membrane**, **fuse with it**, and **release its cargo** outside the cell. The cargo is thereby secreted in a process called **exocytosis** (Figure 2.6.3).

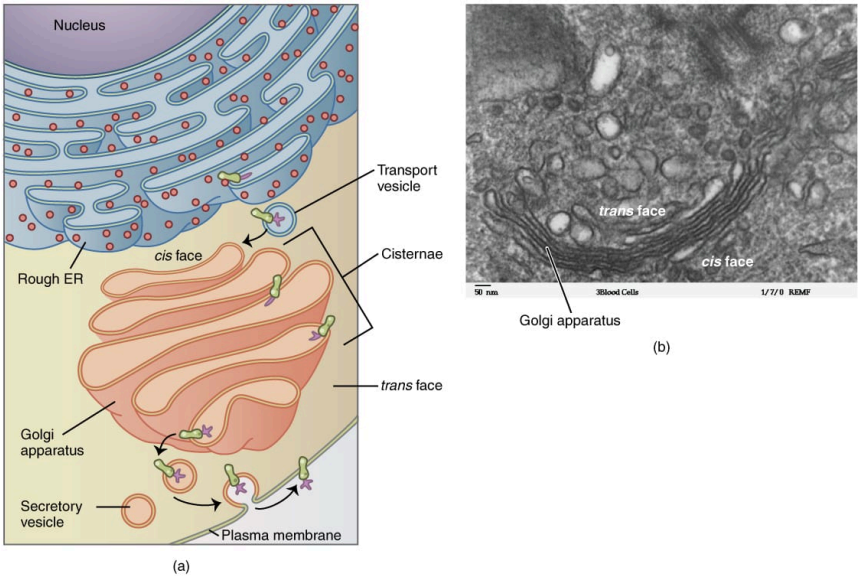


Figure 2.6.3: **Golgi Apparatus.** (a) The Golgi apparatus manipulates products from the rough ER, and also produces new organelles called lysosomes. Proteins and other products of the ER are sent to the Golgi apparatus, which organizes, modifies, packages, and tags them. Some of these products are transported to other areas of the cell and some are exported from the cell through exocytosis. Enzymatic proteins are packaged as new lysosomes (or packaged and sent for fusion with existing lysosomes). (b) An electron micrograph of the Golgi apparatus.

Lysosomes: The Cell's Recycling and Demolition Crew 🗑️🔧💣

Some of the proteins packaged by the Golgi apparatus include **digestive enzymes** that stay **inside** the cell. These enzymes are packaged inside special **vesicles** known as **lysosomes.**

A **lysosome** is a **membrane-bound organelle** filled with **enzymes that break down** unwanted or damaged parts of the cell — like a worn-out organelle. Think of lysosomes as the cell's **garbage disposal** or even a **demolition crew** that clears out old, unsafe structures.

The process of a cell "cleaning up" its own components is called **autophagy**, which literally means **"self-eating."**

Lysosomes are also key players in **defense against invaders**. When immune cells like **white blood cells** engulf (or **phagocytize**) harmful bacteria, the engulfed bacteria are sent to a lysosome, where they are **broken down and destroyed** by enzymes. Because of this, **defense cells are packed with lysosomes** to help them do their job.

But lysosomes are not always so tidy. In **severely damaged or dying cells**, lysosomes may **burst open** and release their enzymes into the cell's interior. This results in the **destruction of the entire cell**, a process called **autolysis** ("self-destruction"). Unlike **apoptosis** (a clean and controlled form of cell death), **autolysis is messy,** it can spill damaging enzymes into the surrounding tissue, especially during trauma, severe infection, or after death.

Interactive Link

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

Mitochondria: The Cell's Power Plant ⚡

In addition to the jobs performed by the endomembrane system, the cell has many other important functions. Just as you must consume nutrients to provide yourself with energy, so must each of your cells take in nutrients, some of which convert to chemical energy that can be used to power biochemical reactions.

A **mitochondrion** (plural: **mitochondria**) is a **bean-shaped, membrane-bound organelle** known as the **"energy transformer"** of the cell. Just like the nucleus, each mitochondrion has **two membranes**:

- An **outer membrane** (made of a lipid bilayer),
- And a highly folded **inner membrane** (also made of a lipid bilayer), which forms winding structures called **cristae**.

These folds give the inner membrane a **large surface area**, which is important because this is where the critical steps of **cellular respiration** take place.

During cellular respiration, mitochondria use **oxygen** and **nutrients** (like glucose) to produce **ATP (adenosine triphosphate)** — the molecule that powers almost all of the cell's work. Think of ATP as the **"energy currency"** your cells spend to do anything from contracting muscles to sending nerve signals.

Because your body constantly needs energy, **mitochondria are always working**. Some cells need more energy than others, so they have more mitochondria:

- **Muscle cells** need lots of ATP to keep contracting, so they are **packed** with mitochondria.
- **Nerve cells** also need a steady supply of ATP to run their sodium-potassium pumps, and a single neuron may contain **over a thousand mitochondria**.
- In contrast, a **bone cell**, which is less active metabolically, might have **just a few hundred mitochondria**.

And yes, **this is why you need to breathe**! Oxygen is essential for your mitochondria to keep the ATP flowing in the process called **aerobic respiration**!

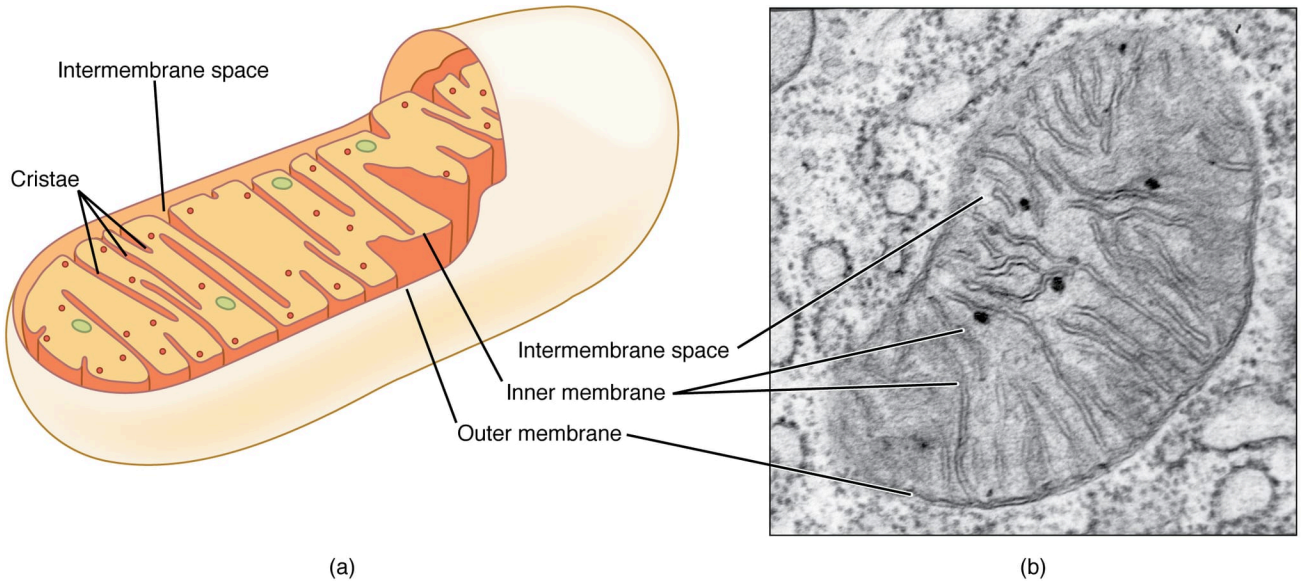


Figure 2.6.4: **Mitochondrion.** The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. Along the inner membrane are various molecules that work together to produce ATP, the cell's major energy currency. (b) An electron micrograph of mitochondria. EM × 236,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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2.7: Cytoskeleton and Cell Extensions

The cytoskeleton is a protein fiber network that supports cell shape, movement, and internal transport.

Master this section and you'll be able to

- Explain the three components of the cytoskeleton, including their composition and functions

The Cytoskeleton: The Cell's Support and Transport Network

If all the organelles were removed from a cell, the plasma membrane and cytoplasm would not be the only components left. Within the cytoplasm there would still be ions and organic molecules, plus a network of protein fibers called the cytoskeleton. The cytoskeleton runs through the cell and the fibers help the cell to

- **Keep its shape**
- **Move** (like crawling or changing form)
- **Reproduce**
- **Transport materials**

Just like your **bony skeleton** holds your body up and gives it shape, the **cytoskeleton** helps a cell keep its structure and stay stable. But it does a lot more than just provide support!

There are **three main types of protein fibers** within the cytoskeleton:

1) Microtubules

As their name implies, **microtubules** are **small hollow tubes made of a globular (round) protein called tubulin**. Even though they only have a diameter of about 25 nm (nanometers), microtubules are the widest components of the three types of cytoskeletal fibers. They help the cell **keep its shape and stay sturdy**, especially by **resisting compression**, so the cell does not get squished or collapse under pressure. They also hold organelles in place and act as "tracks" along which vesicles move through the cell. Finally, during cell division, microtubules pull replicated chromosomes to opposite ends of a dividing cell. Microtubules can dissolve and reform quickly. ,

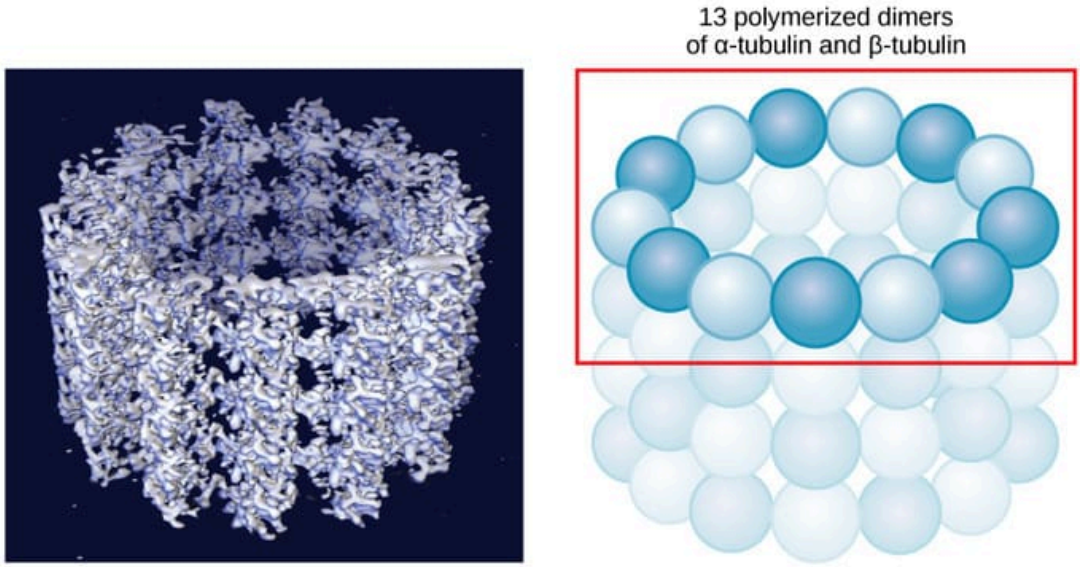


Figure 2.7.1: **Microtubule Structure**. In this image, you can see that the microtubules are hollow with walls that are made of stacks of 13 polymerized dimers of **α-tubulin and β-tubulin** (right image). The left image shows the molecular structure of the tube.

Microtubules are also the structural elements of **flagella, cilia,** and centrioles (the latter are the two perpendicular bodies of the centrosome which is used during cell division). In animal cells, the centrosome is the microtubule-organizing center.

- **Cilia** are tiny, hair-like structures that beat rhythmically in waves. In the **respiratory tract**, they are found on top of the epithelial cells and sweep out mucus, dust, and bacteria to keep the lungs clean. **Cilia in the fallopian tubes** help move egg cells from the ovary toward the uterus. A flagellum (plural = flagella) is an appendage larger than a cilium and specialized for cell locomotion. The only flagellated cell in humans is the sperm cell that must propel itself towards female egg cells.

- **Flagella** (singular = **flagellum**), are longer, whip-like structures that allow the cells to **swim**. In humans, the **only cell with one flagellum is the sperm cell**, which uses it to swim toward an egg.

2) Intermediate Filaments

Intermediate filaments are named such, because their thickness falls **between** that of microfilaments and microtubules. They are made of strong, fibrous proteins like **keratin**, which are **twisted together like the strands of a rope**. This rope-like structure gives the cell strength and helps it **hold its shape**.

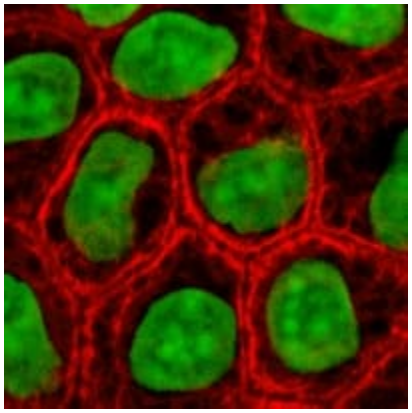
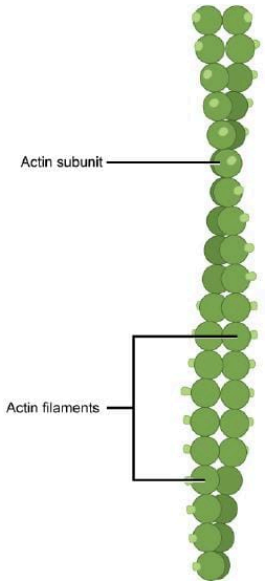


Figure 2.7.2: **Stained Keratin Intermediate filaments**. Keratin cytoskeletal intermediate filaments are concentrated around the edge of the cells and merge into the surface membrane. This network of intermediate filaments from cell to cell holds together tissues like skin.

While **microtubules resist compression** (squeezing forces), **intermediate filaments resist tension,** the **pulling or stretching forces** that might try to tear the cell apart. For example, skin cells are constantly being pushed, pulled, and stretched, and intermediate filaments help them stay intact.

However, intermediate filaments do more than just strengthen the cell:

- they **anchor organelles** in place inside the cell,
- and they **connect neighboring cells** by forming special junctions, which helps tissues stay strong and connected.



3) Microfilaments

Microfilaments are the **thinnest** type of cytoskeletal fibers — much thinner than microtubules, with a diameter of about 7 nm. They are made mostly of a globular (round) protein called **actin**, which forms **long, twisted chains** (see image on the right). For this reason, microfilaments are also known as actin filaments. Microfilaments function in cellular movement.

In **muscle cells**, actin filaments team up with another protein called **myosin** to make muscles contract. The actin filaments (called **thin filaments**) get **pulled by thicker myosin filaments**, causing the muscle cell to shorten or contract. We will study the mechanics of the muscle movement in more detail in a future module.

Microfilaments also provide some rigidity and shape to the cell. They can depolymerize (disassemble) and reform quickly, **thus enabling a cell to change its shape and move.** White blood cells (your body's infection-fighting cells) make good use of this ability. They can move to the site of an infection and engulf the pathogen.

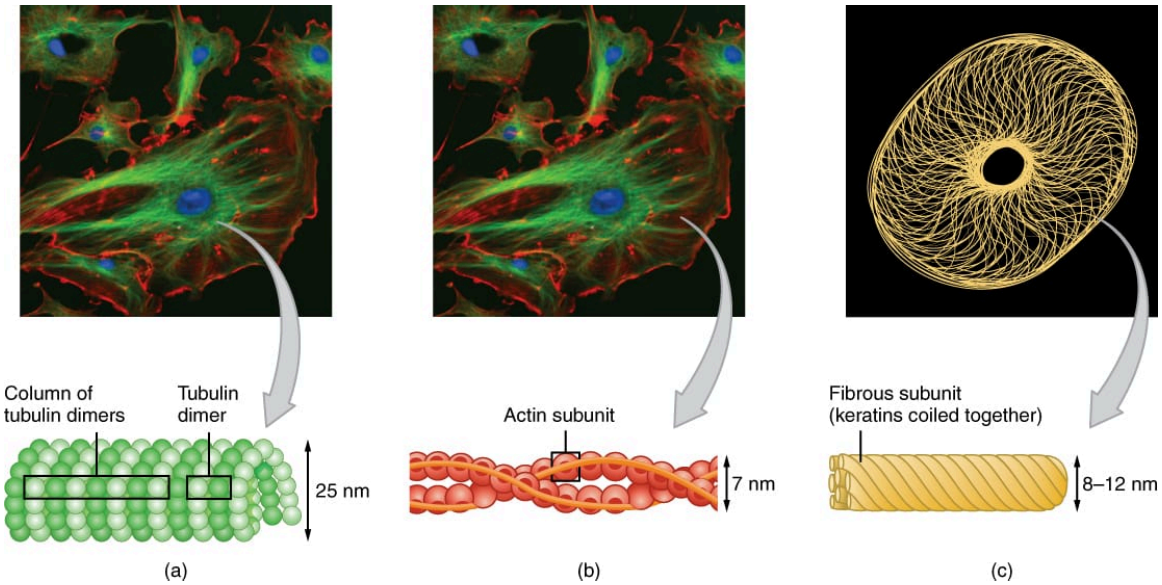


Figure 2.7.3: **The Three Components of the Cytoskeleton.** The cytoskeleton consists of (a) **microtubules**, (b) **microfilaments**, and (c) **intermediate filaments.** The cytoskeleton plays an important role in maintaining cell shape and structure, promoting cellular movement, and aiding cell division.

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2.8: Stem Cells and Cellular Differentiation

From a single fertilized egg, stem cells and the process of cellular differentiation give rise to the many specialized cell types that form, maintain, and repair the human body.

Master this section and you'll be able to

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

How does a complex organism such as a human develop from a single cell — a fertilized egg — into the vast array of cell types such as nerve cells, muscle cells, and epithelial cells that characterize the adult? Throughout development and adulthood, the process of cellular differentiation leads cells to assume their final morphology and physiology. Differentiation is the process by which unspecialized cells become specialized to carry out distinct functions.

Stem Cells

A stem cell is an **unspecialized (undifferentiated) cell** that can divide without limit as needed and can, under specific conditions, differentiate into specialized cells. Stem cells are divided into several categories according to their potential to differentiate.

The first embryonic cells that arise from the division of the **zygote** (the single cell formed when a sperm fertilizes an egg, marking the start of a new organism) are the ultimate stem cells; these stems cells are described as **totipotent** because they have the potential to differentiate into any of the cells needed to enable an organism to grow and develop.

The embryonic cells that develop from totipotent stem cells and are precursors to the fundamental tissue layers of the embryo are classified as **pluripotent ("pluri-"** comes from Latin and means **"many")**. A pluripotent stem cell is one that has the potential to differentiate into any type of human tissue but cannot support the full development of an organism. These cells then become slightly more specialized, and are referred to as **multipotent** cells.

A multipotent stem cell has the potential to differentiate into different types of cells within a given cell lineage or small number of lineages, such as a red blood cell or white blood cell.

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

Stem cells are unique in that they can also continually divide and regenerate new stem cells instead of further specializing. There are different stem cells present at different stages of a human's life. They include the embryonic stem cells of the embryo, fetal stem cells of the fetus, and adult stem cells in the adult. One type of adult stem cell is the epithelial stem cell, which gives rise to the keratinocytes in the multiple layers of epithelial cells in the epidermis of skin. Adult bone marrow has three distinct types of stem cells: hematopoietic stem cells, which give rise to red blood cells, white blood cells, and platelets (Figure 2.8.1:); endothelial stem cells, which give rise to the endothelial cell types that line blood and lymph vessels; and mesenchymal stem cells, which give rise to the different types of muscle cells.

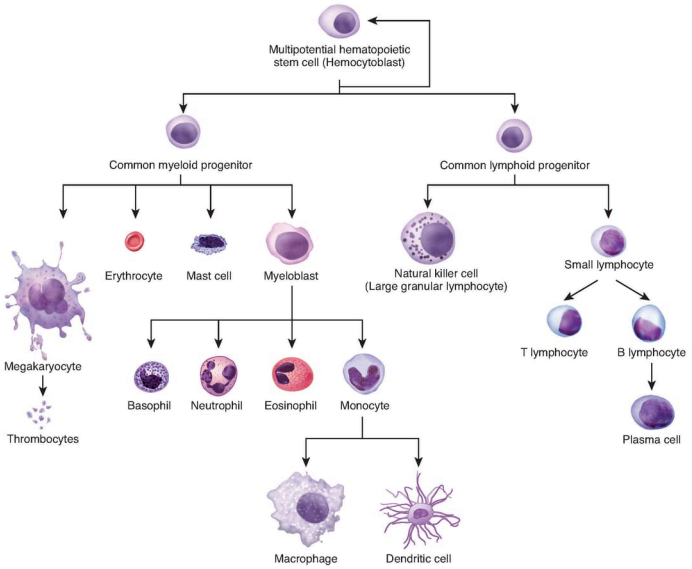


Figure 2.8.1: **Hematopoiesis.** The process of hematopoiesis involves the differentiation of multipotent cells into blood and immune cells. The multipotent hematopoietic stem cells give rise to many different cell types, including the cells of the immune system and red blood cells.

Differentiation

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

In order for a cell to differentiate into its specialized form and function, it need only manipulate those genes (and thus those proteins) that will be expressed, and not those that will remain silent. The primary mechanism by which genes are turned "on" or "off" is through transcription factors. A transcription factor is one of a class of proteins that bind to specific genes on the DNA molecule and either promote or inhibit their transcription (Figure 2.8.2.

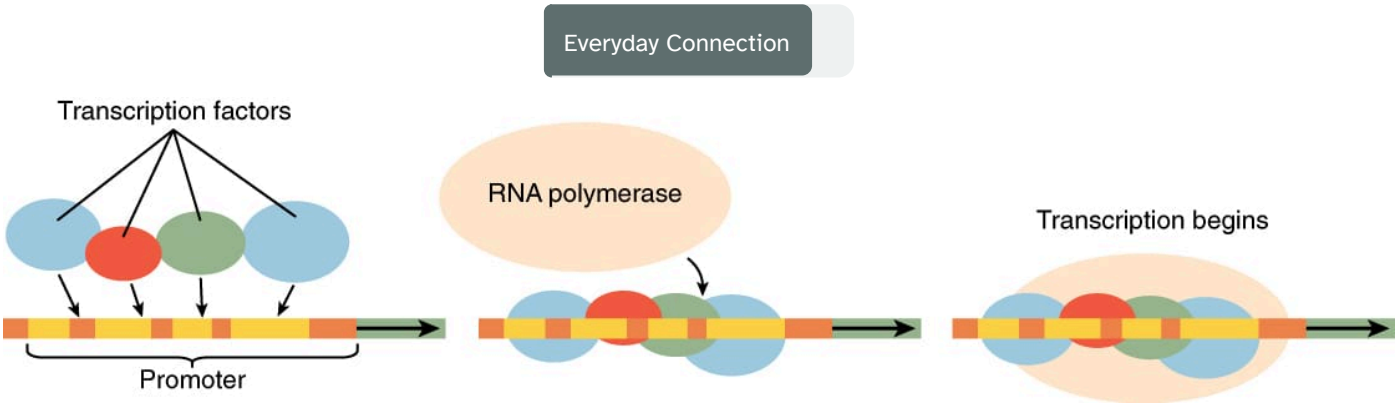


Figure 2.8.2: : Transcription Factors Regulate Gene Expression While each body cell contains the organism's entire genome, different cells regulate gene expression with the use of various transcription factors. Transcription factors are proteins that affect the binding of RNA polymerase to a particular gene on the DNA molecules

Stem Cell Research

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

The mechanisms that induce a non-differentiated cell to become a specialized cell are poorly understood. In a laboratory setting, it is possible to induce stem cells to differentiate into specialized cells by changing the physical and chemical conditions of growth. Several sources of stem cells are used experimentally and are classified according to their origin and potential for differentiation. Human embryonic stem cells (hESCs) are extracted from embryos and are pluripotent. The adult stem cells that are present in many organs and differentiated tissues, such as bone marrow and skin, are multipotent, being limited in differentiation to the types of cells found in those tissues. The stem cells isolated from umbilical cord blood are also multipotent, as are cells from deciduous teeth (baby teeth). Researchers have recently developed induced pluripotent stem cells (iPSCs) from mouse and human adult stem cells. These cells are genetically reprogrammed multipotent adult cells that function like embryonic stem cells; they are capable of generating cells characteristic of all three germ layers.

Because of their capacity to divide and differentiate into specialized cells, stem cells offer a potential treatment for diseases such as diabetes and heart disease (Figure 2.8.3). Cell-based therapy refers to treatment in which stem cells induced to differentiate in a growth dish are injected into a patient to repair damaged or destroyed cells or tissues. Many obstacles must be overcome for the application of cell-based therapy. Although embryonic stem cells have a nearly unlimited range of differentiation potential, they are seen as foreign by the patient's immune system and may trigger rejection. Also, the destruction of embryos to isolate embryonic stem cells raises considerable ethical and legal questions.

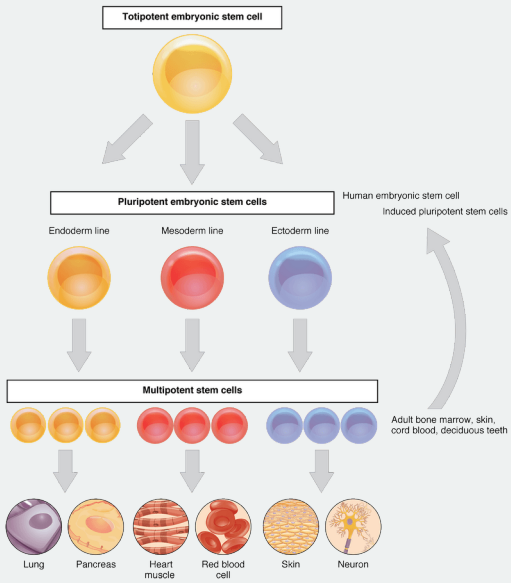


Figure 2.8.3: **Stem Cells.** The capacity of stem cells to differentiate into specialized cells make them potentially valuable in therapeutic applications designed to replace damaged cells of different body tissues.

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

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2.9: Cell Physiology — Body Fluids and Fluid Compartment

Cell physiology focuses on how cells maintain balance and carry out essential functions that keep the body alive and functioning.

Master this section and you'll be able to

- Explain the importance of water in the body
- Contrast the composition of the intracellular fluid with that of the extracellular fluid
- Explain the importance of protein channels in the movement of solutes
- Identify the causes and symptoms of edema

Cell physiology is the study of how cells **function**. This field of biology looks at the everyday activities that keep cells alive and working, like taking in nutrients, making energy, building proteins, and getting rid of waste.

Think of it as understanding how each tiny cell acts like a **mini factory**:

- It has systems for **communication**,
- machinery for **making products**,
- and pathways for **transporting materials** in and out.

In A&P, learning about cell physiology helps you understand how the body works at its most basic level — and how all those small cellular processes add up to keep tissues, organs, and organ systems running smoothly.

The chemical reactions of life take place in **aqueous solutions**. The **dissolved substances** in a solution are called **solutes**. In the human body, solutes vary in different parts of the body, but may include proteins—including those that transport lipids, carbohydrates, and, very importantly, electrolytes. Often in medicine, a mineral dissociated from a salt that carries an electrical charge (an **ion**) is called an **electrolyte**. For instance, sodium ions (Na^+) and chloride ions (Cl^-) are often referred to as electrolytes.

In the body, water moves through **selectively-permeable cell membranes** and from one compartment of the body to another by a process called **osmosis**. Osmosis is basically the **diffusion of water** from regions of higher water concentration to regions of lower water concentration, along an osmotic gradient across a selectively-permeable membrane. As a result, water will move into and out of cells and tissues, depending on the relative concentrations of the water and solutes found there. An appropriate balance of solutes inside and outside of cells must be maintained to ensure normal function.

Body Water Content

The human body is made mostly of **water**. In fact, water makes up about **75% of an infant's body**, and around **50–60% of an adult's body**. As we get older, that percentage can drop to about **45%**. Why does it change? Because as we grow, the amount of muscle, fat, bone, and other tissues in our body changes too.

Some parts of the body have **more water than others**. For example, the **brain and kidneys** are about **80–85% water,** they are basically water-packed! On the other hand, your **teeth** are mostly solid, with only about **8–10% water**. (See figure below).

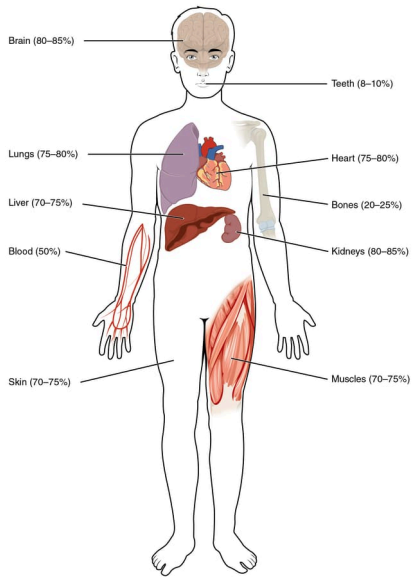


Figure 2.9.1: **Water Content of the Body's Organs and Tissues.** Water content varies in different body organs and tissues, from as little as 8 percent in the teeth to as much as 85 percent in the brain.

Fluid Compartments

Body fluids can be discussed in terms of their specific **fluid compartment**, a location that is largely separate from another compartment by some form of a physical barrier. The **intracellular fluid (ICF)** compartment is the system that includes all fluid enclosed in cells by their plasma membranes.

Extracellular fluid (ECF) surrounds all cells in the body. Extracellular fluid has two primary constituents: the fluid component of the blood — called **plasma** — and the **interstitial fluid (IF)** that surrounds all cells not in the blood (See figure below).

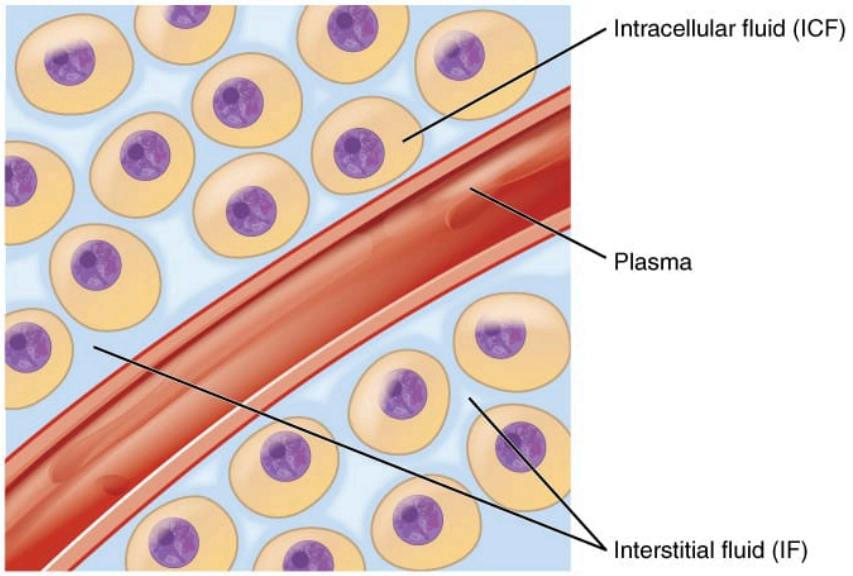


Figure 2.9.2: **Fluid Compartments in the Human Body.** The intracellular fluid (ICF) is the fluid within cells. The interstitial fluid (IF) is part of the extracellular fluid (ECF) between the cells. Blood plasma is the second part of the ECF. Materials travel between cells and the plasma in capillaries through the IF.

Intracellular Fluid

The **ICF** lies within cells and is the **principal component of the cytosol/cytoplasm**. The ICF makes up about 60 percent of the total water in the human body, and in an average-size adult male, the ICF accounts for about 25 liters (seven gallons) of fluid (Figure 2.9.3). This fluid volume tends to be very stable, because the amount of water in living cells is closely **regulated**. If the amount of water inside a cell falls to a value that is too low, the cytosol becomes too concentrated with solutes to carry on normal cellular activities; if too much water enters a cell, the cell may burst and be destroyed.

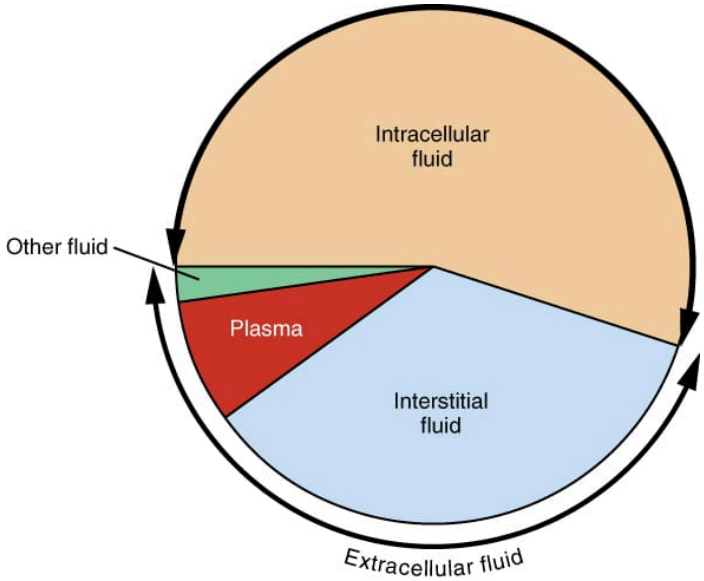


Figure 2.9.3: **Pie Chart Showing the Proportion of Total Body Fluid in Each of the Body's Fluid Compartments.** Most of the water in the body is intracellular fluid. The second largest volume is the interstitial fluid, which surrounds cells that are not blood cells. Next is plasma, then a small proportion of "other fluid."

Extracellular Fluid

The **ECF** accounts for the other one-third of the body's water content. **Approximately 20 percent of the ECF is found in plasma**. Plasma travels through the body in blood vessels and transports a range of materials, including blood cells, proteins (including clotting factors and antibodies), electrolytes, nutrients, gases, and wastes. Gases, nutrients, and waste materials travel between capillaries and cells through the IF. Cells are separated from the IF by a selectively permeable cell membrane that helps regulate the passage of materials between the IF and the interior of the cell.

The body has **other water-based ECF.** These include the **cerebrospinal fluid** (CSF) that bathes the brain and spinal cord, **lymph**, the **synovial fluid** in joints, the **pleural fluid** in the pleural cavities, the **pericardial fluid** in the cardiac sac, the **peritoneal fluid** in the peritoneal cavity, and the **aqueous humor of the eye**. Because these fluids are outside of cells, these fluids are also considered components of the ECF compartment.

Composition of Body Fluids

The compositions of the two components of the ECF — plasma and IF — are more similar to each other than either is to the ICF (Figure 2.9.4). Blood plasma has high concentrations of sodium, chloride, bicarbonate, and protein. The IF has high concentrations of sodium, chloride, and bicarbonate, but a relatively lower concentration of protein. In contrast, the ICF has elevated amounts of potassium, phosphate, magnesium, and protein. Overall, the ICF contains high concentrations of potassium and phosphate (HPO_4^{2-}), whereas both plasma and the ECF contain high concentrations of sodium and chloride.

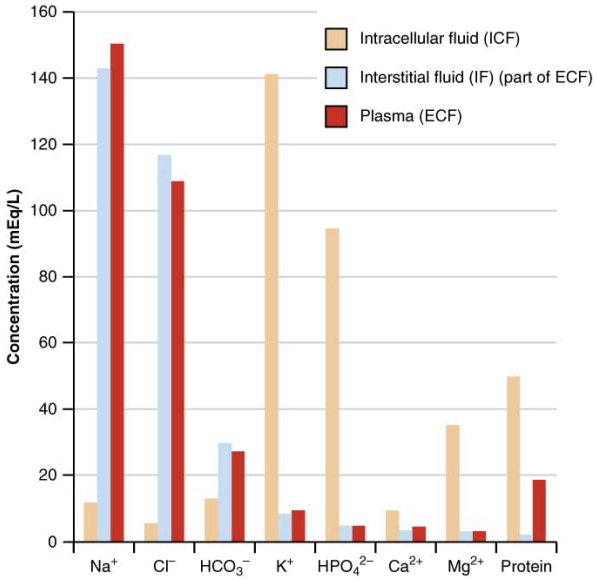


Figure 2.9.4: **Concentrations of elements in key bodily fluids.** The graph shows the composition of the ICF, IF, and plasma. The compositions of plasma and IF are similar to one another but are quite different from the composition of the ICF.

Most **body fluids** have a **neutral charge**, meaning they contain a balanced number of **positive ions (cations)** and **negative ions (anions)**. Two of the most important ions are **sodium (Na⊕)** and **chloride (Cl⊖)**, which are found mostly **outside** your cells (in the IF, the fluid between cells; and in your blood plasma). Another important ion, **potassium (K⊕)**, is found mostly **inside** your cells (in the ICF).

Even though sodium and potassium can slowly **leak** in and out of cells through tiny pores, your body works hard to keep their levels in the right places. To do this, cells use **sodium-potassium pumps** — special proteins in the cell membrane that use **energy from ATP** to move sodium **out** of the cell and potassium **in**. This pump helps maintain the proper balance of ions, which is important for things like nerve signals and muscle contractions. (See image below).

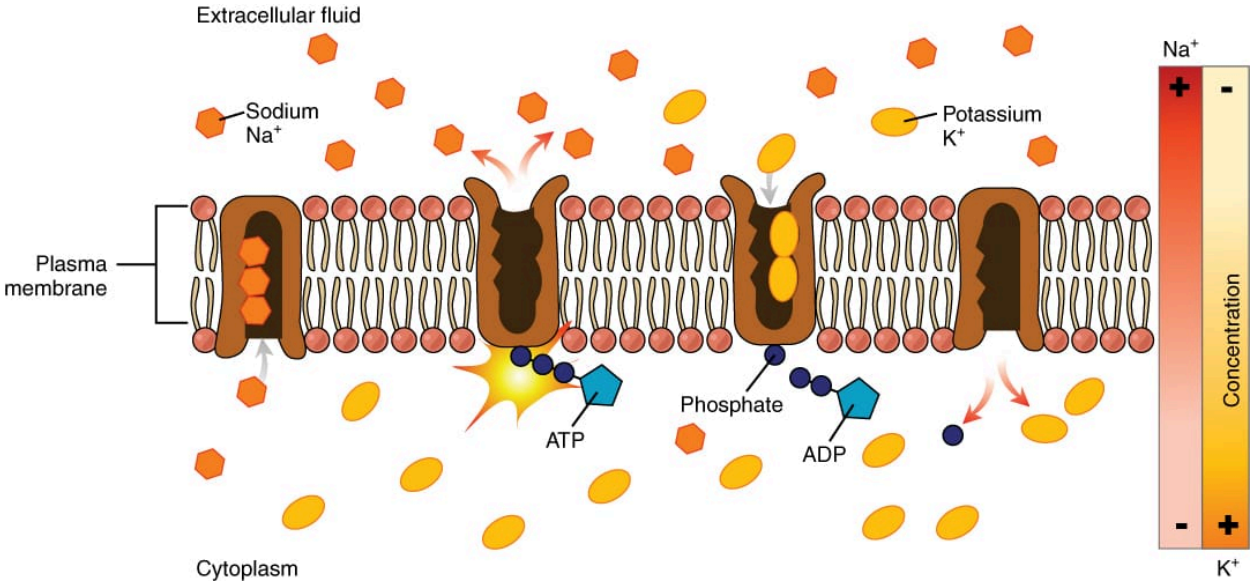


Figure 2.9.5: **The sodium-potassium pump.** The sodium-potassium pump is powered by ATP to transfer sodium out of the cytoplasm and into the ECF. The pump also transfers potassium out of the ECF and into the cytoplasm. (credit: modification of work by Mariana Ruiz Villarreal)

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2.10: Passive Movements across the Cell Membrane — Simple Diffusion

Diffusion is a process of passive transport in which molecules move from an area of higher concentration to one of lower concentration.

Master this section and you'll be able to

- Explain the principles of passive transport and describe how molecules move in relation to a concentration gradient, including what happens when dynamic equilibrium is reached.
- Identify the key factors that influence the movement of substances across the cell membrane.
- Explain the process of simple diffusion.
- Apply diffusion principles to real-life physiological scenarios, such as gas exchange in the lungs, dehydration, and filtration in the kidneys.

What is Diffusion?

Diffusion is the **passive movement** of molecules from an area of **high concentration** to an area of **low concentration**. In other words: diffusion happens **down a concentration gradient.** It continues until the substance is evenly spread out.

Once equilibrium is reached, molecules still move, but there is **no net movement** in any one direction. This is called a **dynamic equilibrium**.

Each type of particle will diffuse at its own rate, depending on the steepness of its individual concentration gradient.

After a substance has finished diffusing and is evenly spread throughout a space, its concentration gradient disappears. But that does not mean the molecules stop moving! In fact, molecules are always in motion because of their **inherent kinetic energy** — they constantly jiggle, bump, and slide past one another. Even without a concentration gradient, they keep moving randomly in all directions.

What changes is that there is **no longer a net movement** of molecules from one area to another. This balance is called **dynamic equilibrium**: molecules continue to move, but because their concentrations are equal everywhere, the number of molecules moving in one direction is matched by the number moving the opposite way. So the overall distribution stays the same, even though individual molecules are still active.

A classic example of diffusion is a drop of food coloring spreading through a glass of water. The coloring moves from where it is highly concentrated to where it is not, until it is evenly distributed (see image below).

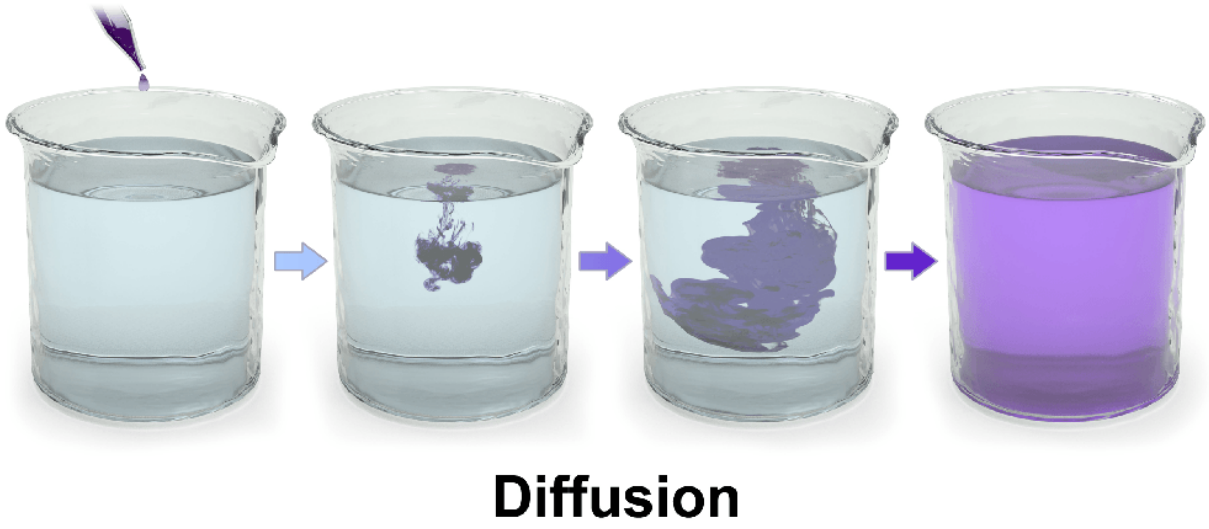


Figure 2.10.1: **Diffusion in a water glass —** One very easy **diffusion demonstration** is to pour a few drops of food colorir a glass of water and watch as the color spreads through the glass.

When someone is cooking food in a kitchen, the smell begins to waft through the house, and eventually everyone can tell what's for dinner! This is due to the diffusion of odor molecules through the air, from an area of high concentration (the kitchen) to areas of low concentration (your upstairs bedroom).

Diffusion is a **passive process of transport**. A single substance tends to move from an area of high concentration to an area of low concentration until the concentration is equal across a space. You are familiar with diffusion of substances through the air. For example, think about someone opening a bottle of ammonia in a room filled with people. The ammonia gas is at its highest concentration in the bottle; its lowest concentration is at the edges of the room. The ammonia vapor will diffuse, or spread away, from the bottle; gradually, more and more people will smell the ammonia as it spreads. Materials move within the cell 's cytosol by diffusion, and certain materials move through the plasma membrane by diffusion. Diffusion expends no energy. On the contrary, concentration gradients are a form of potential energy, dissipated as the gradient is eliminated.

Diffusion across Cell Membranes

At this point, you know that diffusion means molecules move from where they are more concentrated to where they are less concentrated.

In the cells of our body, this process allows **small molecules**, like **oxygen**, **carbon dioxide**, **ions**, and some **nutrients,** to **pass through the cell membrane** without using energy. It is therefore a **passive process**, meaning it does **not require energy** — the particles move naturally, just by bouncing around due to their inherent kinetic energy. It is one of the main ways cells exchange materials with their environment to maintain balance and stay healthy.

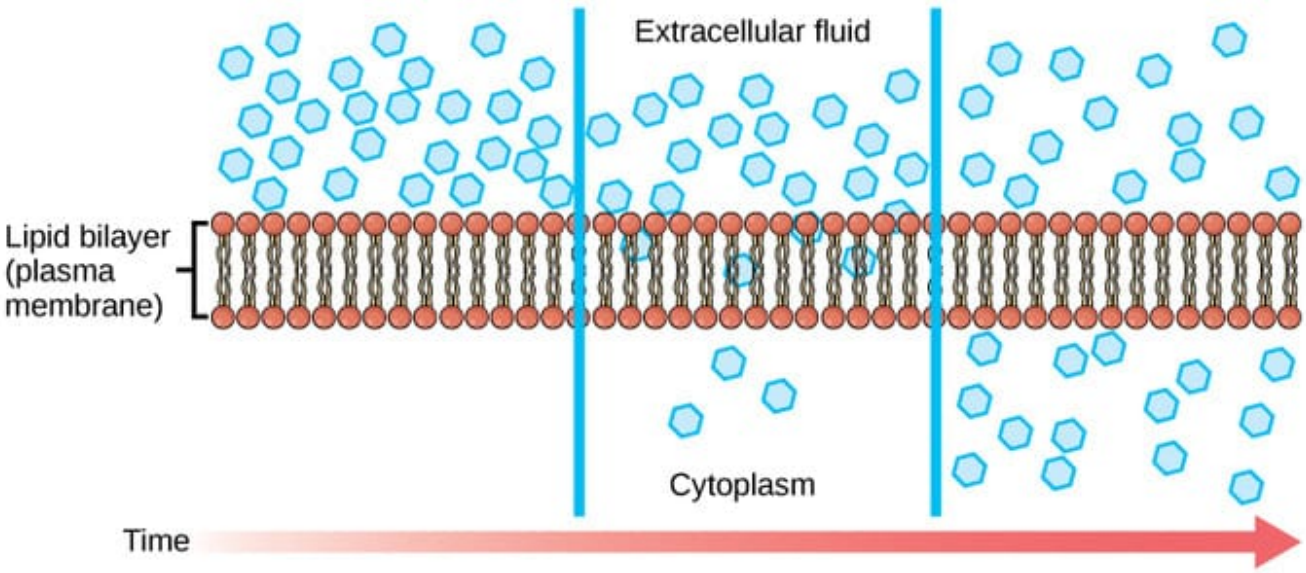


Figure 2.10.2: **Diffusion through a membrane.** Diffusion through a permeable membrane moves a substance from an area of high concentration (extracellular fluid, in this case) down its concentration gradient (into the cytoplasm).

What Affects the Rate of Diffusion?

Within a system, there will be different rates of diffusion of the different substances in the medium:

- **Concentration Gradient**
  The bigger the difference in concentration, the faster diffusion happens. As the gradient evens out, diffusion slows down.
- **Mass of Molecules**
  Heavier molecules move more slowly and therefore diffuse more slowly. Lighter molecules zip around faster and diffuse quicker.
- **Temperature**
  Heat = energy! Higher temperatures give molecules more energy, so they move (and diffuse) faster. Colder temps slow things down.
- **Solvent Density**
  A thick or crowded medium slows diffusion. Imagine trying to run through honey vs. water. For example, in dehydration, cells lose water and their cytoplasm becomes more dense, slowing diffusion inside the cell. That is one reason why dehydration can make you feel foggy or even faint—your neurons struggle to function when internal diffusion slows down.
- **Solubility**
  Molecules that are nonpolar or lipid-soluble, like oxygen (O_2) or carbon dioxide (CO_2), move easily through the cell membrane and diffuse quickly. Polar or charged molecules have a harder time crossing.
- **Membrane Surface Area & Thickness**
  A larger surface area = more diffusion! A thicker membrane = slower diffusion.
- **Distance Traveled**
  The farther molecules have to go, the slower they move. This is one big reason cells are so small. If a cell gets too big, it takes too long for nutrients to get to the center—and the cell could die.

Factors Affecting Diffusion

Factor	How It Affects Diffusion
Concentration Gradient	Bigger differences cause faster diffusion; smaller differences slow it down as equilibrium is approached.
Molecule Size (Mass)	Larger molecules move more slowly; smaller ones diffuse faster.
Temperature	Higher temps = more energy = faster diffusion. Cold slows it down.
Solvent Density	A thick medium (like syrup) slows diffusion. Water is easier to move through.
Solubility	Lipid-soluble (nonpolar) molecules diffuse more easily across membranes.
Membrane Surface Area	More area = more places to cross = faster diffusion.
Membrane Thickness	Thicker membranes slow down diffusion.
Distance to Travel	The farther the distance, the slower the diffusion — this limits how big cells can grow.

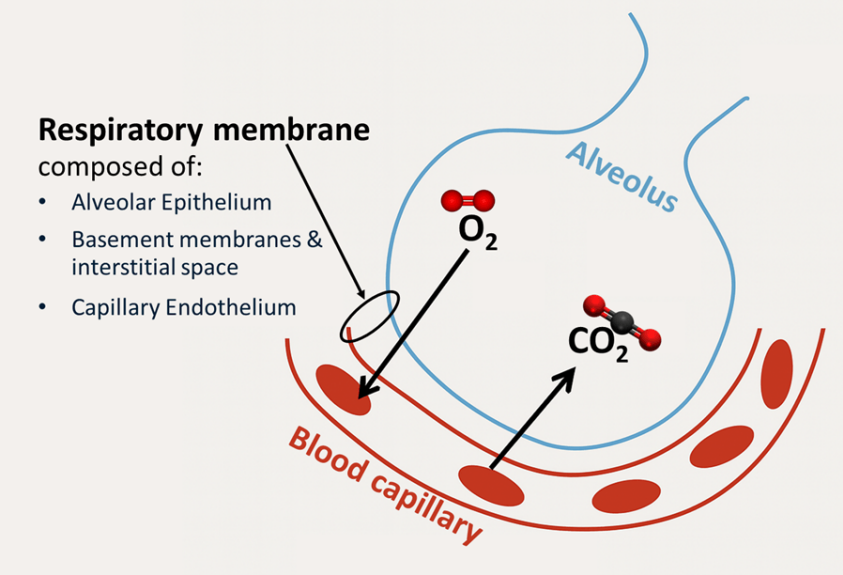


Figure 2.10.3: **Real life example of diffusion through a membrane.** During external respiration, oxygen (O_2) is inhaled into the lungs and diffuses from the alveolus into the surrounding blood capillaries, while carbon dioxide (CO_2) diffuses in the opposite direction—from the blood into the alveolus—to be exhaled.

A healthy **respiratory membrane** is thin and moist, allowing gases to diffuse efficiently. **Oxygen (O_2)** moves from the alveoli into the bloodstream, while **carbon dioxide (CO_2)** moves from the blood into the alveoli to be exhaled.

However, in certain medical conditions, this vital diffusion process is disrupted:

- In **emphysema**, the alveolar walls are damaged and break down. This reduces the total surface area available for gas exchange and makes the membrane less efficient. As a result, less oxygen gets into the blood, and carbon dioxide removal is impaired.

- In **pneumonia**, the alveoli fill with fluid and inflammatory cells. This creates a physical barrier that thickens the respiratory membrane and blocks gas exchange. Oxygen cannot diffuse into the blood effectively, and carbon dioxide becomes trapped.

Both conditions make it **difficult for oxygen to reach body tissues** and for waste gases to be cleared. This can lead to **shortness of breath, rapid breathing, fatigue**, and dangerously **low blood oxygen levels**. These examples emphasize how critical diffusion across the respiratory membrane is to survival. We will get back to this when we cover the respiratory system.

Yet another example of how important diffusion is to **homeostasis** occurs during **dehydration**. When cells lose water, their **cytoplasm becomes denser and more crowded**, making it harder for molecules like ions, nutrients, and waste to move around. This **slows diffusion** and disrupts vital cell functions. The dehydration effect is especially dangerous in **neurons**, which depend on rapid molecular movement for communication and survival. When diffusion slows, brain function suffers, leading to symptoms like **dizziness, confusion, and even coma** in severe cases.

What About Filtration?

Filtration is like a turbocharged version of diffusion. Instead of just relying on concentration gradients, it also uses **pressure** to push materials through a membrane. This happens in your kidneys, where high blood pressure forces water and solutes out of the blood and into the tubules that make urine.

This makes the diffusion more efficient, but the downside is that **too much pressure** can push large proteins through the filter and into the urine. Proteins are normally not supposed to pass. That is why protein in the urine can be a warning sign of high blood pressure damaging your kidneys.

Simple Diffusion:

This is the most basic type of diffusion. It happens when **small, lipid-soluble molecules** move **directly through the cell membrane** from an area of higher concentration to an area of lower concentration. Because this process does **not require any energy**, it is called a form of **passive transport**.

As you have learned in this module, the **plasma membrane is made of a lipid bilayer**. That means only molecules that can mix with lipids can pass through easily. To do that, a molecule must be **small and nonpolar (uncharged)** — like **oxygen and carbon dioxide**. These molecules simply drift through the membrane until the concentration is equal on both sides, a state called **equilibrium**.

On the other hand, molecules that are **not lipid-soluble** — like **polar, charged, or hydrophilic molecules** — **cannot** pass through the membrane this way. They need help in the form of **protein channels or carriers** to cross the barrier.

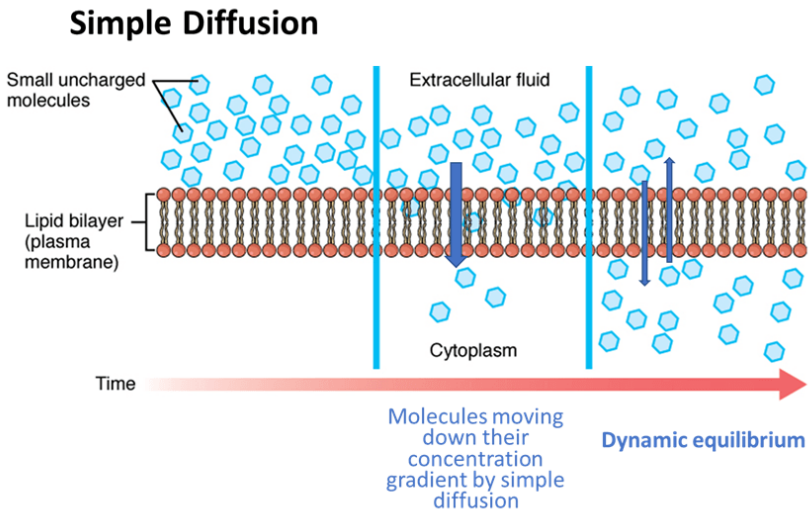


Figure 2.10.4: **Simple Diffusion.** The structure of the lipid bilayer allows small, uncharged substances such as oxygen and carbon dioxide, and hydrophobic molecules such as lipids, to pass through the cell membrane, down their concentration gradient, by simple diffusion.

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2.11: Passive Movements across the Cell Membrane — Facilitated Diffusion and Osmosis

Facilitated diffusion is a process by which molecules are transported across the plasma membrane with the help of membrane proteins.

Master this section and you'll be able to

- Describe the differences between simple diffusion, facilitated diffusion, and osmosis.
- Explain the roles of channel proteins and carrier proteins in facilitated diffusion.
- Predict the direction of water movement during osmosis based on solute concentration.

Facilitated Diffusion: When Simple Diffusion Needs a Sidekick

In the last section, you learned about **simple diffusion** — the simplest form of passive transport, where small, nonpolar molecules like oxygen and carbon dioxide slip right through the lipid bilayer and move down their concentration gradient all by themselves.

But not all molecules are so lucky.

Some are simply too big — or not lipophilic enough (because they are polar or carry a charge) — to sneak through the lipophilic center of the phospholipid bilayer. These molecules cannot pass directly through the cell membrane, no matter how steep the concentration gradient is. They need a little help.

That is where **facilitated diffusion** comes in. Like simple diffusion, it is still **passive** (no ATP required) and still moves molecules **down their concentration gradient:** from high to low concentration. The key difference? These molecules need a **transport protein** to get across the membrane. The transport proteins are integral membrane proteins, meaning they span the whole cell membrane — they are transmembrane proteins — and they function as **either channels** for the material **or carriers**.

You can think of it like this:

- **Simple diffusion** is like walking through an open doorway.
- **Facilitated diffusion** is like being let in by a doorman — someone (a protein!) opens the way for you when you cannot do it alone.
  This process allows essential molecules like **glucose, amino acids, and ions** to enter or leave cells safely and efficiently.
  By the way, for those of you who have not had any chemistry: **Ions are atoms (or molecules) that carry an electric charge** because they have either gained or lost one or more electrons.

As mentioned above, these "doorman" proteins come in two forms:

1) Channels

Channel proteins create water-filled (hydrophilic) passageways through which polar and charged substances can pass. Channel proteins can be **open at all times**, constantly allowing a particular substance into or out of the cell, depending on the concentration gradient; **or** they can be **gated** and can only be opened by a particular biological signal.

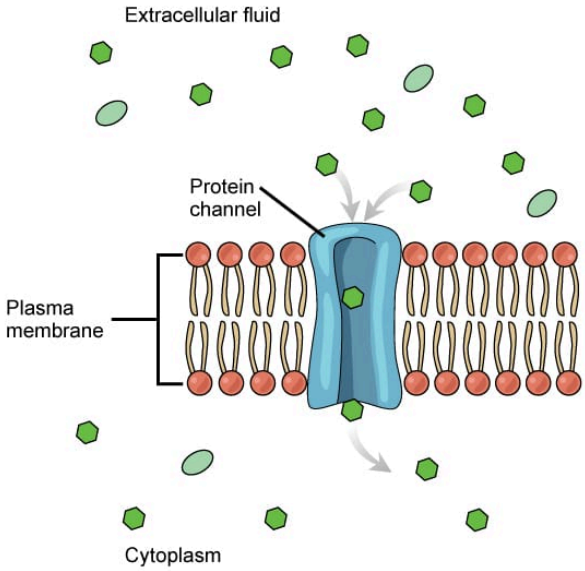


Figure 2.11.1: **Channel Proteins in Facilitated Diffusion.** Facilitated transport moves substances down their concentration gradients. They may cross the plasma membrane with the aid of channel proteins.

Channels are specific for the substance that is being transported. Channel proteins have hydrophilic domains exposed to the intracellular and extracellular fluids; they additionally have a hydrophilic channel through their core that provides a hydrated opening through the membrane layers. Passage through the channel allows polar compounds to avoid the nonpolar central layer of the plasma membrane that would otherwise slow or prevent their entry into the cell. **Aquaporins** are channel proteins that allow water molecules (which are polar) to pass through the membrane at a very high rate.

Channel proteins are either open at all times or they are “gated,” which controls the opening of the channel. The attachment of a particular ion to the channel protein may control the opening or other mechanisms or substances may be involved. In some tissues, sodium and chloride ions pass freely through open channels, whereas in other tissues, a gate must be opened to allow passage. An example of this occurs in the kidney, where both forms of channels are found in different parts of the renal tubules. Cells involved in the transmission of electrical impulses, such as nerve and muscle cells, have gated channels for sodium, potassium, and calcium in their membranes. Opening and closing of these channels changes the relative concentrations on opposing sides of the membrane of these ions, resulting in the facilitation of electrical transmission along membranes (in the case of nerve cells) or in muscle contraction (in the case of muscle cells).

2) Carriers

Carrier proteins bind to a particular substance, then alter their shape to bring that substance into or out of the cell.

Carrier proteins are typically specific for a single substance. This adds to the overall selectivity of the plasma membrane. The exact mechanism for the change of shape is poorly understood. Proteins can change shape when their hydrogen bonds are affected, but this may not fully explain this mechanism. Each carrier protein is specific to one substance, and there are a finite number of these proteins in any membrane. This can cause problems in transporting enough of the material for the cell to function properly.

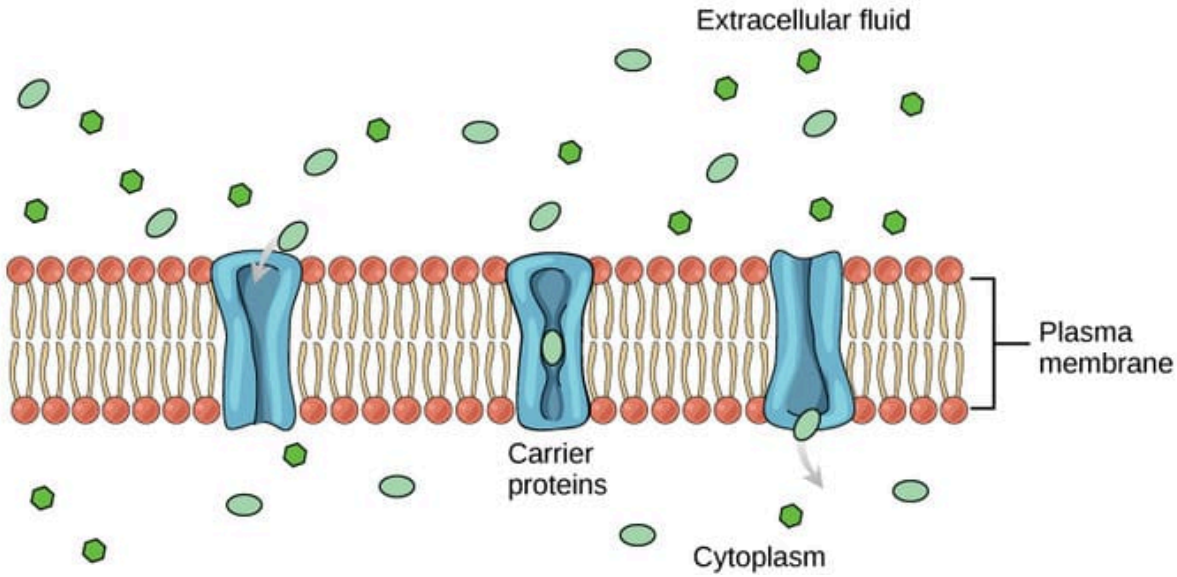


Figure 2.11.2: **Carrier Proteins in Facilitated Diffusion**. Some substances are able to move down their concentration gradient across the plasma membrane with the aid of carrier proteins. Carrier proteins change shape as they move molecules across the membrane.

A great example of **facilitated diffusion** happens in the **kidneys**.

When your blood is filtered in the kidneys, useful substances like **glucose, water, salts, ions, and amino acids** are removed temporarily from the blood into a fluid called **filtrate**. But your body does not want to lose all those valuable nutrients — so in another part of the kidney, these substances are **reabsorbed back into the blood.**

For glucose, this reabsorption depends on **carrier proteins** in the kidney tubule cells. These proteins help glucose move **back into the bloodstream by facilitated diffusion**. But here is the catch: there are only **so many glucose carrier proteins** available. If **too much glucose** is present—like in **uncontrolled diabetes**—the carrier proteins cannot keep up. Once they reach their maximum capacity, **any extra glucose stays in the filtrate and is excreted in the urine**.

This is why people with high blood sugar are sometimes said to be **"spilling glucose into the urine."**

Elsewhere in the body, another set of specialized carrier proteins — called **GLUTs (glucose transporters)** — are responsible for moving glucose and similar sugars across the membranes of different cells. These transporters help regulate where glucose goes, depending on the needs of each tissue.

Channel and carrier proteins transport material at different rates. Channel proteins transport much more quickly than do carrier proteins. Channel proteins facilitate diffusion at a rate of tens of millions of molecules per second, whereas carrier proteins work at a rate of a thousand to a million molecules per second.

Osmosis: When Water Takes the Lead

By now, you have seen how molecules can move across membranes without using energy — as long as they go from an area of high concentration to an area of low concentration.

- With **simple diffusion**, small nonpolar molecules pass right through the membrane.
- With **facilitated diffusion**, larger or charged molecules get help from protein channels or carriers.

Now let us talk about a **special case of passive transport** that involves **water** — and only water. This process is called **osmosis**.

So What Is Osmosis?

Osmosis is the **passive movement of water across a selectively permeable membrane** according to the concentration

gradient of water across the membrane. Osmosis occurs until the concentration gradient of water goes to zero or until the hydrostatic pressure of the water balances the osmotic pressure.

The amount of water present is inversely proportional to the concentration of solutes. Remember: **solutes** are the substances (like salts, sugars, or ions) that are **dissolved in a liquid solvent**, usually water, to create a solution

While diffusion transports materials across membranes and within cells, osmosis transports only water across a membrane.

Here is the rule of thumb:
👉 **Water moves toward the side with more solutes — because that side has less "free" water.**
In simpler terms: **water follows the crowd (of solutes)** in an effort to even things out.

Osmosis vs. Facilitated Diffusion

While facilitated diffusion helps **molecules** like glucose or ions move across the membrane using transport proteins, **osmosis moves the water** that surrounds those solutes. In most cases, water cannot diffuse directly through the membrane, but rather it needs to use **special water channels called aquaporins**.

Why Osmosis Matters in Real Life

- In your **red blood cells**, osmosis helps keep the right amount of water inside. If too much water enters, the cell can swell and burst. If too much leaves, the cell shrivels up.
- In your **kidneys**, osmosis helps control how much water is retained or lost in the urine, depending on how salty the surrounding environment is.

Mechanism of Osmosis

Imagine two full glasses of water. One has a single teaspoon of sugar in it, whereas the second one contains one-quarter cup of sugar. If the total volume of the solutions in both cups is the same, which cup contains more water?

Answer: Because the large amount of sugar in the second cup takes up much more space than the teaspoon of sugar in the first cup, the first cup has more water in it.

Now, imagine a beaker with a selectively permeable membrane separating the two sides or halves. On both sides of the membrane the water level is the same, but there are different concentrations of a dissolved substance, or solute, that cannot cross the membrane (otherwise the concentrations on each side would be balanced by the solute crossing the membrane).

If the volume of the solution on both sides of the membrane is the same but the concentrations of solute are different, then there are different amounts of water (the solvent) on either side of the membrane. If there is more solute in one area, then there is less water; if there is less solute in one area, then there must be more water.

A principle of diffusion is that the molecules move around due to their inherent kinetic energy. The molecules will therefore spread evenly throughout the medium if they can. However, only the material capable of passing through the membrane will diffuse through it. In this example, the solute cannot diffuse through the membrane, but the water can. Water has a concentration gradient in this system. Thus, water will diffuse down its concentration gradient, crossing the membrane to the side where it is less concentrated. This diffusion of water through the membrane — osmosis! — will continue until the concentration gradient of water goes to zero or until the hydrostatic pressure of the water balances the osmotic pressure. In the beaker example, this means that the level of fluid in the side with a higher solute concentration will go up. See the image below.

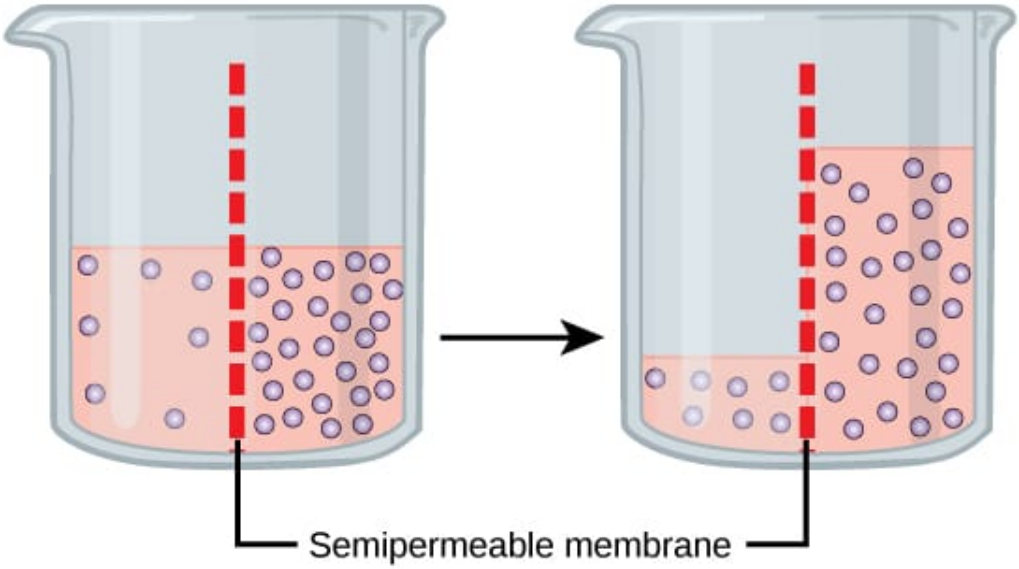


Figure 2.11.3: **Osmosis**. In osmosis, water always moves from an area of higher water concentration to one of lower concentration. In the diagram shown, the solute cannot pass through the selectively permeable membrane, but the water can.

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2.12: Tonicity

Tonicity, which is directly related to the osmolarity of a solution, affects osmosis by determining the direction of water flow.

Master this section and you'll be able to

- Define tonicity and describe its relevance to osmosis.
- Compare hypotonic, isotonic, and hypertonic solutions, and predict how each affects the volume and shape of a cell.

💧 Introduction to Tonicity

Tonicity describes how a solution outside the cell (the *extracellular fluid*) affects the movement of water into or out of the cell — and as a result, how it can change the cell's volume.💡 Remember: The solutes cannot cross the membrane, but the water can. So the water moves to even things out.

Tonicity is closely tied to **osmolarity**, which is the total concentration of solutes in a solution:

- A solution with **low solute concentration** has **low osmolarity**, which means there are **fewer dissolved particles (solute) and more water** in the mixture.
- A solution with **high solute concentration** has **high osmolarity**, which means there are **more dissolved particles (solute) and less free water** (because there is less room for water molecules available).

If two solutions with different osmolarities are separated by a selectively permeable membrane (like a cell membrane) that **lets water through but not the solutes**, water will move from the side with more water (low osmolarity) to the side with less water (high osmolarity). This is osmosis in action!

🐟 Why Can Saltwater Fish Not Live in Freshwater?

Tonicity explains why some fish can only survive in either salt water or fresh water — not both. For example, a saltwater fish has cells that are used to living in a salty environment. Its cells are packed with solutes to match the **high osmolarity** of the ocean water.

But if you suddenly move that saltwater fish into freshwater (which has **low osmolarity**, or fewer solutes and more water), the water will rush into the fish's cells. Why? Because water moves toward areas with more solutes, trying to "balance things out." The fish's cells swell, and eventually, they can burst. That is why saltwater fish cannot survive in fresh water — and vice versa.

Osmolarity and Cell Survival: The Tonicity Trio

Three key terms — **hypotonic**, **isotonic**, and **hypertonic** — describe how the osmolarity of the fluid surrounding a cell compares to the osmolarity inside the cell. Let's break down how each type of solution affects the movement of water and the shape of the cell.

1) Hypotonic Solutions: Water Moves Into the Cell

In a **hypotonic** solution, the fluid *outside* the cell has a **lower osmolarity** than the fluid *inside* the cell. That means:

- The extracellular fluid has **fewer solutes** and **more water** compared to the inside of the cell.
- Water moves **into** the cell, following its concentration gradient.

Since living systems always use the **cytoplasm** (the fluid inside the cell) as the reference point, the prefix **“hypo-”** tells us that the **extracellular fluid** has a lower solute concentration (and thus a higher water concentration) than the cell.

As water enters the cell, the cell swells. If too much water enters, it may **burst** (a process called **lysis**).

2) Hypertonic Solutions: Water Moves Out of The Cell

In a **hypertonic** solution, the word **“hyper-”** tells us the extracellular fluid has **more solutes** than the fluid inside the cell — meaning it has **less water**.

Because the **cell has more water** than the surrounding fluid, water starts to **leave the cell** in an attempt to balance things out.

As the water exits, the cell begins to **shrink and shrivel.** The outcome is akin to a grape turning into a raisin. Not exactly ideal for cell survival!

3) Isotonic Solutions: No NET Water Movement

An **isotonic** solution is the **Goldilocks** zone for cells: **not too salty, not too watery, but just right**. ⚖️

In this case, the **osmolarity of the extracellular fluid is exactly the same** as the fluid inside the cell. That means the concentration of solutes (and water) is balanced on both sides of the membrane.

Water molecules still move in and out of the cell, but they do so **at equal rates**, so there is **no net gain or loss of water**. The cell stays the same size—happy and stable!

Review the image below: red blood cells are great visual examples of how tonicity affects cell shape.

- In a **hypertonic solution**, water leaves the cell, causing it to **shrink and shrivel**.
- In an **isotonic solution**, they keep their normal, round shape — everything is in balance.
- In a **hypotonic solution**, water rushes in, making the cell **swell** — and if the difference is too extreme, the cell can **burst** (a process called **hemolysis**).

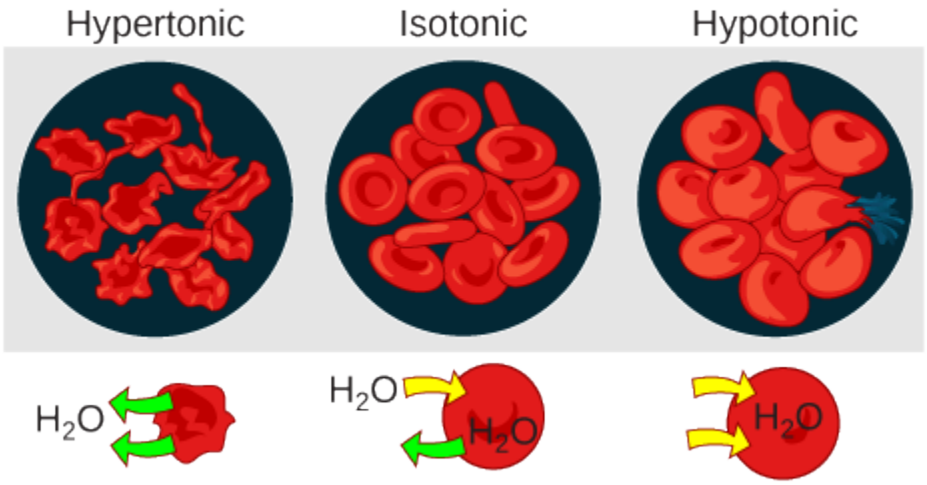


Figure 2.12.1: **Changes in Cell Shape Due to Dissolved Solutes**. Osmotic pressure changes the shape of red blood cells in hypertonic, isotonic, and hypotonic solutions.

⚠️ One Final Note

Just because a solution looks “clear” or “cloudy” does not tell you how concentrated it is. Osmolarity depends on the **number of dissolved particles**, not how the solution looks. You could have a crystal-clear solution that has tons of dissolved solutes—and therefore a very high osmolarity!

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2.13: Primary Active Transport — Pumps

The sodium-potassium pump maintains the electrochemical gradient of living cells by moving sodium in and potassium out of the cell.

Master this section and you'll be able to

- Describe the role of primary active transport in maintaining ion gradients across the cell membrane.
- Break down how the sodium-potassium pump works step by step to create an electrochemical gradient across the cell membrane.

Primary Active Transport: Powering the Cell's Ion Highways ⚡

One of the most important jobs in your body's cells is keeping the right ions on the right side of the membrane. To make that happen, cells use a process called **primary active transport**, which uses energy (from ATP) to move ions **against** their concentration gradients. That means from areas of low concentration to high — exactly the opposite of diffusion.

The superstar of this process? The **sodium-potassium pump** (also known as **Na⁺/K⁺ ATPase**). This primary active transporter is embedded in the plasma membrane of all animal cells and uses energy from ATP to move ions against their concentration gradients. Specifically, it pumps three sodium ions (Na^+) out of the cell and two potassium ions (K^+) into the cell with each cycle. This unequal exchange helps maintain the proper intracellular and extracellular concentrations of Na^+ and K^+, which is essential for cell volume regulation, electrical excitability, and secondary active transport.

Why Does This Matter?

The Na^+/K^+ ATPase is described as an **electrogenic pump** because it generates a net movement of electrical charge. As you learned in the previous paragraph: three positively charged Na^+ ions are pumped out for every two K^+ ions pumped in. This creates an **electrochemical gradient** across the membrane, meaning there is both a **difference in charge (electrical gradient)** and a **difference in ion concentration (chemical gradient)**.

This gradient is not just helpful — it is critical for key physiological processes like secondary active transport, nerve impulse transmission, and muscle contraction. Stay tuned: we will explore these applications in more detail later in the semester!

How the Sodium-Potassium Pump Works: 4 Quick Steps

While you work through each step, use **Figure 2.13.1** as your sidekick — it is there to help make the whole process click. For many of us, pictures really *do* say a thousand words. 😊

1. **Three sodium ions (Na^+)** from inside the cell bind to the pump protein.
2. **ATP is hydrolyzed**, and a phosphate group is attached to the pump, providing the energy needed for it to change shape.
3. As the **Na^+/K^+ pump** changes shape, it reorients itself towards the outside of the cell, and the three **sodium ions are released.**
4. The pump's new shape allows **two potassium ins (K^+) to bind** and the phosphate group to detach. Without the phosphate group, the protein changes shape again, flipping back its opening towards the inside of the cell (the cytoplasm) and r**eleasing the potassium ions into the cell.**

After the K^+ ions are released into the cell, the the pump is ready to start all over again.

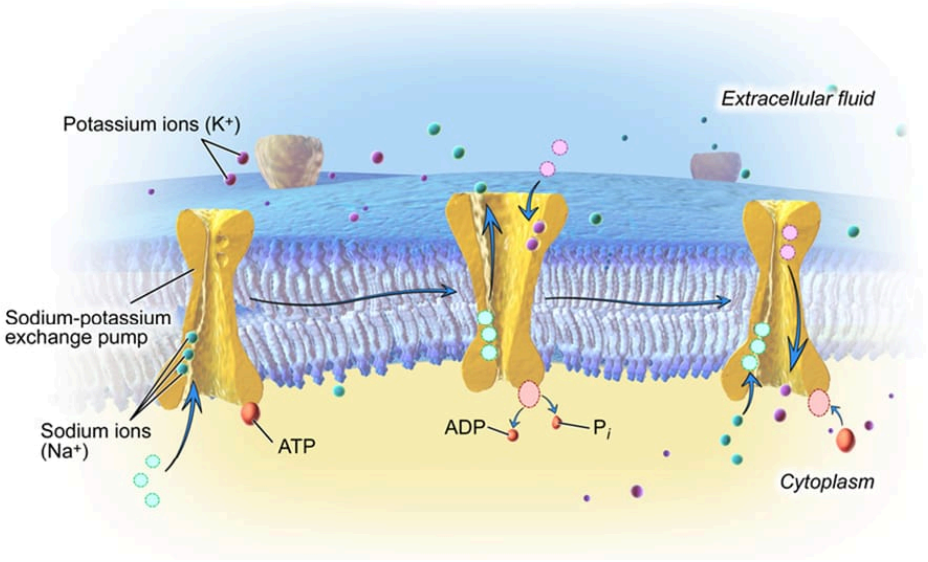


Figure 2.13.1: The **Sodium-Potassium Exchange Pump.** Primary active transport moves ions across a membrane, creating an electrochemical gradient (electrogenic transport).

The Result: A Charged Imbalance

For every **three sodium ions kicked out**, only **two potassium ions come in**. That creates a tiny electrical imbalance, making the inside of the cell slightly **more negative** than the outside. This difference in charge is called the **membrane potential**, and it is critical for all sorts of physiological processes.

This is why the sodium-potassium pump is considered an **electrogenic pump.** It literally helps generate electricity in your cells. And by maintaining that ion gradient, it also sets the stage for **secondary active transport** (which borrows the Na⁺ gradient to move other substances like glucose).

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2.14: Vesicular Transport — Endocytosis and Exocytosis

Vesicular transport is also a form of active transport that moves substances into or out of the cell using membrane-bound vesicles.

Master this section and you'll be able to

- Describe the role of vesicular transport as a form of active transport.
- Outline the similarities and differences of endocytosis and exocytosis.
- Compare the different types of endocytosis, specifically phagocytosis, pinocytosis, and receptor-mediated endocytosis.

Vesicular transport is another type of **active transport** in which materials are moved into or out of the cell using small, membrane-bound sacs called **vesicles**. The process requires energy (usually from ATP) and allows the cell to transport large molecules, fluids, or even particles that cannot cross the membrane directly. It includes both **endocytosis** (bringing substances into the cell) and **exocytosis** (releasing substances out of the cell). Endocytosis takes up particles into the cell by invaginating the cell membrane, resulting in the release of the material inside of the cell.

Endocytosis: Bringing Stuff into the Cell

This type of active transport moves **liquids and large substances** — including **big molecules, cell fragments, or even entire cells** — **into** a cell.

There are several variations of **endocytosis**, but they all share one key feature:
the **plasma membrane folds inward** (invaginates) to form a pocket around the material to be transported.

This pocket then **pinches off from the membrane**, forming a **vesicle** inside the cell that contains the material. The vesicle is made from the very same plasma membrane that surrounded the cell to begin with — a clever bit of cellular recycling!

There are three main types of endocytosis:

1) Phagocytosis: Cell Eating

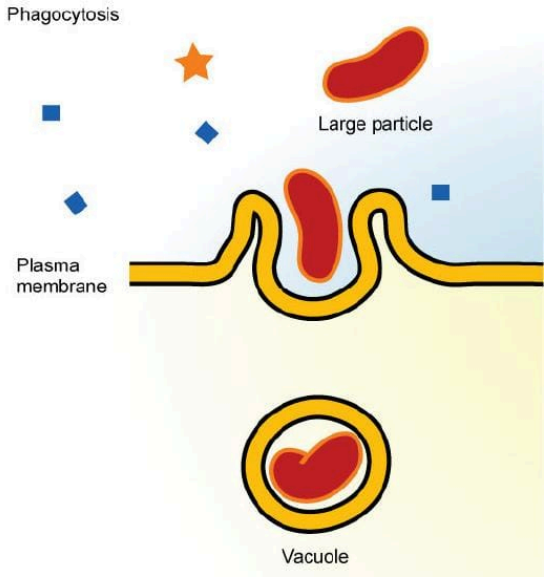


Figure 2.14.1: **Phagocytosis.** In phagocytosis, the cell membrane surrounds the particle and engulfs it.

Phagocytosis is a form of endocytosis often described as **“cell eating.”** It is how special cells — **Phagocytes** — take in **very large particles**, such as cell debris, foreign invaders, or even entire cells.

For example, when harmful microorganisms enter the body, **neutrophils and macrophages** (both phagocytic cells or phagocytes) respond by **surrounding and engulfing** the invader. The engulfed material is then destroyed inside the phagocyte. This process is a critical part of your immune defense system.

How Does Phagocytosis Work?

Before phagocytosis begins, a section of the **inner surface of the plasma membrane** becomes coated with a special protein called **clathrin**. This protein helps stabilize and shape the forming vesicle.

The clathrin-coated membrane **reaches out** around the target particle and eventually **encloses** it, forming a **vesicle** inside the cell. Once the vesicle is fully inside:

- **Clathrin is released**, and
- The vesicle fuses with a **lysosome and is now called a "phagolysosme".** Remember, lysosomes are organelles filled with digestive enzymes. The engulfed material is then broken down.

Once useful nutrients are absorbed, the remaining waste is expelled when the phagolysosome releases its contents by fusing with the plasma membrane. The vesicle membrane is then recycled, becoming part of the cell’s surface once again.

2) Pinocytosis: Cell Drinking 🥛

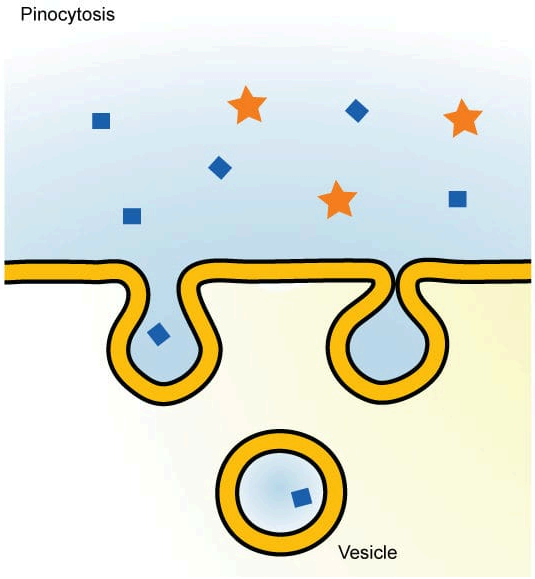


Figure 2.14.2: **Pinocytosis.** In pinocytosis, **the cell membrane invaginates,** surrounding a small volume of fluid and pinching it off.

"Pino-" = Greek for "drink". So, pinocytosis literally means “cell drinking.” It got this name when scientists first thought that cells were purposefully sipping extracellular fluid.

What is actually happening? The cell is **bringing in small amounts of fluid** from its surroundings, along with any **dissolved nutrients or molecules** it might need.

Unlike phagocytosis (which brings in big particles), **pinocytosis creates smaller vesicles**, and these **do not fuse with lysosomes**. Instead, they help the cell absorb useful substances directly from the fluid outside.

3) Receptor-mediated Endocytosis

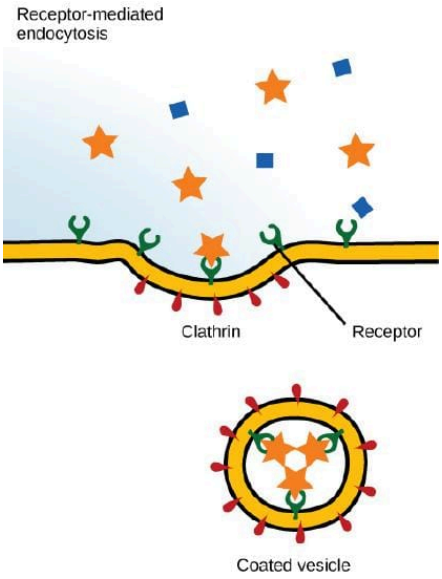


Figure 2.14.3: **Receptor-Mediated Endocytosis.** In receptor-mediated endocytosis, uptake of substances by the cell is targeted to a single type of substance that binds to the receptor on the external surface of the cell membrane.

Sometimes a cell wants to take in something *very specific* — like a VIP guest at a party. That is where **receptor-mediated endocytosis** comes in. This is a special form of **vesicular transport** where the cell uses **receptor proteins** on its surface to "catch" and bring in particular molecules from the extracellular fluid. Once the right **ligand** (molecule) binds to the receptor, a **clathrin-coated pit** forms on the inside of the membrane, creating a vesicle that pulls the desired molecules inside the cell.

This process is highly selective — and very important. If receptor-mediated endocytosis does not work properly, the cell cannot remove certain substances from the blood or tissues, and their levels can rise to dangerous levels. A real-life example? **LDL**, or "bad" cholesterol, is normally cleared from the blood this way. But in people with a genetic disorder called **familial hypercholesterolemia**, the LDL receptors are faulty or missing. That means the LDL cannot be removed, leading to dangerously high cholesterol levels and an increased risk of heart disease.

Even though this system is designed to be selective and secure, some crafty invaders have figured out how to exploit it. Certain viruses and bacterial toxins — like the flu virus, diphtheria toxin, and cholera toxin — can **mimic the shape** of the molecules normally taken in, **tricking the receptors into letting them inside.** It is like a sneaky intruder slipping past security by pretending to be on the guest list.

Exocytosis: Sending Stuff Out of the Cell

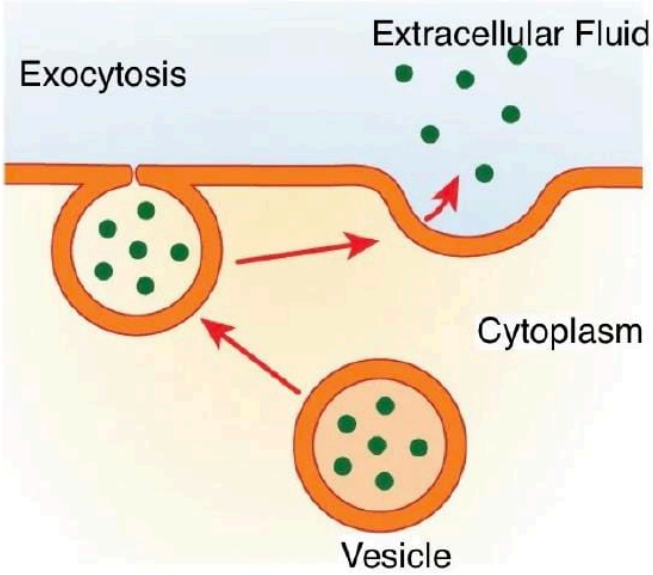


Figure 2.14.4: **Exocytosis.** Exocytosis is a form of active transport that releases materials from the cell by fusing an internal vesicle with the cell membrane, allowing its contents to exit into the extracellular space.

This form of **active transport** is how cells get rid of materials — or send important products like enzymes and hormones to other parts of the body.

In exocytosis, substances are packaged inside **membrane-bound vesicles** within the cell. These vesicles travel to the cell's outer membrane, where they **fuse with the plasma membrane**.

Once the vesicle fuses, its contents are **released into the extracellular fluid**, and the vesicle's membrane becomes part of the cell membrane — a perfect example of biological upcycling!

Cells use exocytosis for all sorts of critical tasks:

- **Digestive cells** in the stomach and pancreas release enzymes this way.
- **Endocrine cells** secrete hormones like insulin using exocytosis.
- **Immune cells** release histamine to help trigger inflammation and immune responses.

Without exocytosis, your body could not digest food, regulate blood sugar, or fight off infections.

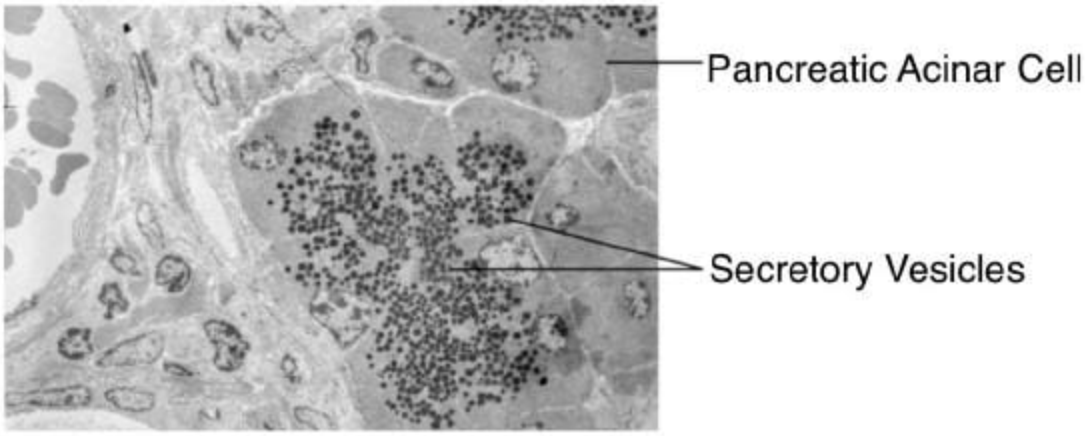


Figure 2.14.5: **Enzyme Products of Pancreatic Cells.** Pancreatic acinar cells play a crucial role in producing and secreting numerous enzymes responsible for digesting food. The small black granules in the figure represent secretory vesicles filled with enzymes. These enzymes are destined for export from the cells through the process of exocytosis. LM × 2900. (Micrograph provided by the Regents of University of Michigan Medical School ©

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3: TISSUES AND THE INTEGUMENTARY SYSTEM

3.1: Introduction to Tissues

3.2: Epithelial Tissue — Covers and Communicates

3.3: Connective Tissue — Supports and Protects

3.4: Muscle Tissue — Built to Move

3.5: Nervous Tissue — Perceives and Responds

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3.1: Introduction to Tissues

Tissues are groups of similar cells working together to perform a specific function in the body.

Master this section and you'll be able to

- Explain what a tissue is.
- Identify the four main tissue types.

From One Cell to Many: How Our Tissues Take Shape 🔬

Although your body is made up of at least 200 different types of cells — ranging from squishy fat cells to long, skinny nerve cells — every single one of them starts from a single fertilized egg (a so-called zygote). That one cell divides and multiplies into trillions of others, all carrying the same DNA blueprint, yet each destined to take on a unique role.

So how do we go from a handful of identical cells to the complex, beautifully organized structures that make up your skin, heart, brain, and more?

The answer lies in ***tissues*** — groups of similar cells that work together to perform specific functions. Cells do not float randomly around the body. Instead, they organize into well-defined layers and structures, forming the tissues that build every organ and system in your body. This level of organization is not just efficient, it is essential for life.

🔍 A cervical tissue micrograph (see image below), for example, shows just how orderly and purposeful this arrangement can be. Cells are neatly layered, performing their duties with precision. But when cancer disrupts normal cell division, that neat structure breaks down, and the tissue loses its organized function. This is exactly what **histologists** — scientists who study tissues under the microscope — look for when diagnosing disease.

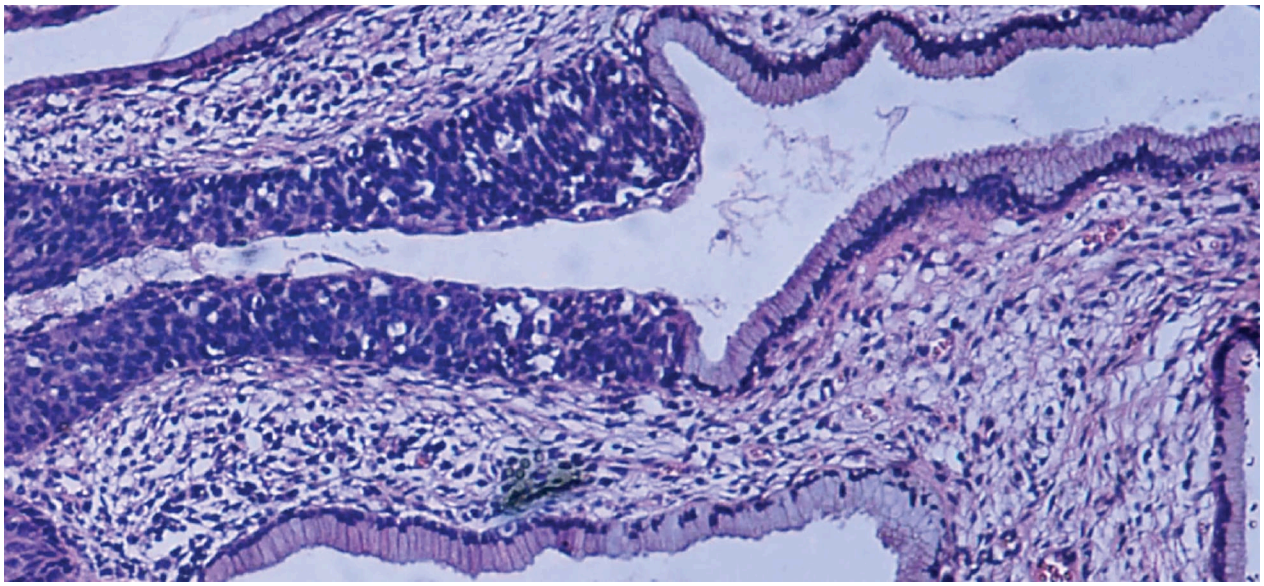


Figure 3.1.1: **Micrograph of Cervical Tissue.** This figure is a view of the regular architecture of normal tissue (right side) contrasted with the irregular arrangement of cancerous cells on the left. (credit: “Haymanj”/Wikimedia Commons)

Despite the incredible variety in cell shape and function, all human tissues fall into four main categories:

- **Epithelial tissue** (lining and covering surfaces),
- **Connective tissue** (supporting and binding),

- **Muscle tissue** (movement), and
- **Nervous tissue** (communication and control).

Complex multicellular organisms have tissues as a basic level of organization, where cells perform coordinated tasks. In animals and plants, tissues further organize into organs and systems. However, the presence of true tissues is not universal among all multicellular life. For example, sponges (Phylum Porifera), though multicellular, do not have organized tissue layers.

In the next few pages, let us take a closer look at how cells join forces to form tissues — and how tissues, in turn, build you.

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3.2: Epithelial Tissue — Covers and Communicates

Epithelial tissue covers the body, lines all cavities, and makes up the glands.

Master this section and you'll be able to

- Describe the major functions of epithelial tissue.
- Differentiate between the various types of epithelial tissue based on the number of cell layers and cell shape.
- Explain the structural characteristics of epithelial tissue: such as polarity, avascularity, specialized cell junctions, and attachment to a basement membrane.

Epithelial Tissue Functions

Epithelial tissue serves as a critical boundary between different environments in the body. Almost all substances, whether entering or exiting the body, must pass through some type of epithelium. In fulfilling this role as an interface, epithelial tissue supports a wide array of vital functions:

1. **Protection**
   - Shields underlying tissues from physical trauma, harmful radiation, toxins, and dehydration (desiccation).
2. **Absorption**
   - Specialized epithelial cells in the digestive tract absorb nutrients and other substances, often exhibiting unique adaptations to enhance this process.
3. **Regulation and Excretion**
   - Controls the movement of chemicals between underlying tissues and body cavities, playing a key role in excretion and maintaining internal balance.
4. **Secretion**
   - Responsible for releasing hormones directly into the bloodstream (via **endocrine glands**).
   - Produces sweat, mucus, digestive enzymes, and various other substances that are transported to body surfaces or cavities via **ducts** coming from **exocrine glands**.

     Now you know that **glands** are always composed of epithelial tissue and **classified** based on how their secretions are released:

     - **Exocrine glands** use ducts to send their products to a targeted surface or cavity.
     - **Endocrine glands** (by contrast) release hormones directly into the bloodstream, not through ducts
5. **Sensation**
   - Contributes to sensation by housing specialized sensory receptors that detect stimuli such as touch, pressure, temperature, pain, and chemical changes and by working closely with nervous tissue to convert these stimuli into interpretable nerve signals.

Epithelial tissue, through all these functions, is essential for the protection, maintenance, and communication of the body's internal and external environments.

Characteristics of Epithelial Layers

Epithelial tissue is far from ordinary — it's like nature's living cellophane wrap, covering and protecting almost every surface in your body, inside and out. Picture **sheets of cells** packed so tightly together that nothing can sneak through except what's allowed. These cells are not held together just by chance; **strong protein connections** lock them into a sturdy, continuous layer, making the tissue both resilient and flexible.

What makes epithelial layers unique? First, they're **avascular**, meaning they don't have their own blood vessels. Instead, they cleverly **absorb nutrients by diffusion** from the connective tissue just below them. And they are not cut off from the world — they are **innervated**, allowing them to sense what's happening around them.

Epithelial cells have a distinct sense of direction, known as **polarity**: one side faces outwards — towards a body cavity, or the outside world — while the other side anchors firmly to the non-cellular **basement membrane**. Think of this basement membrane as biological glue that secures the entire epithelial sheet in place.

Types of Epithelial Tissue

Epithelial tissue is not just a single, bland layer; its cells group together with a lot of personality! **Classification** is based on ***two key features:***

1. ### Number of layers:
    - **Simple** (one layer)
    - **Stratified** (multiple layers)
2. ### Shape of the topmost (apical) cells:
    - **Squamous** (flat and scale-like)
    - **Cuboidal** (cube-shaped)
    - **Columnar** (tall and column-like)

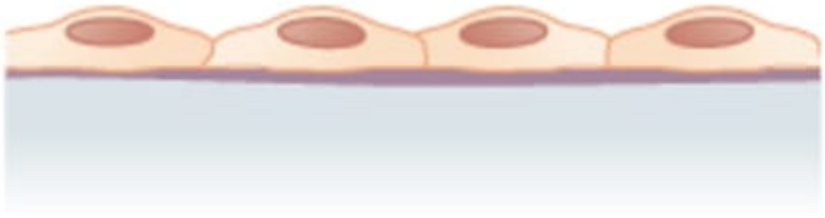
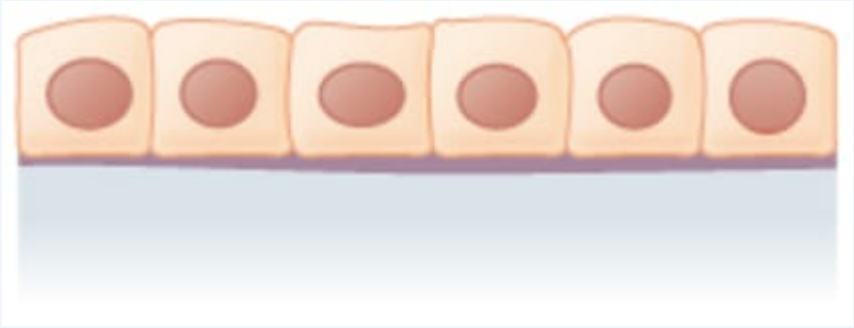
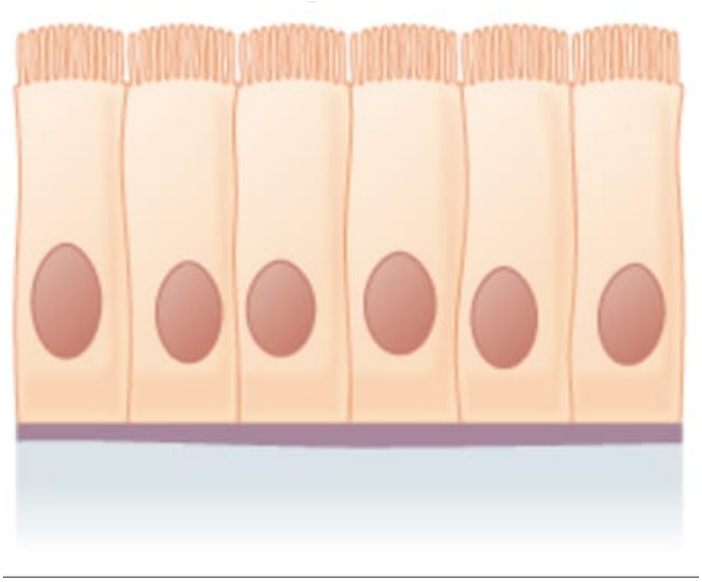
For example, your skin is shielded by several sturdy layers of squamous cells, making it tough and protective, while your small intestine uses a single layer of columnar cells, loaded with microscopic projections, to maximize the area for absorption.

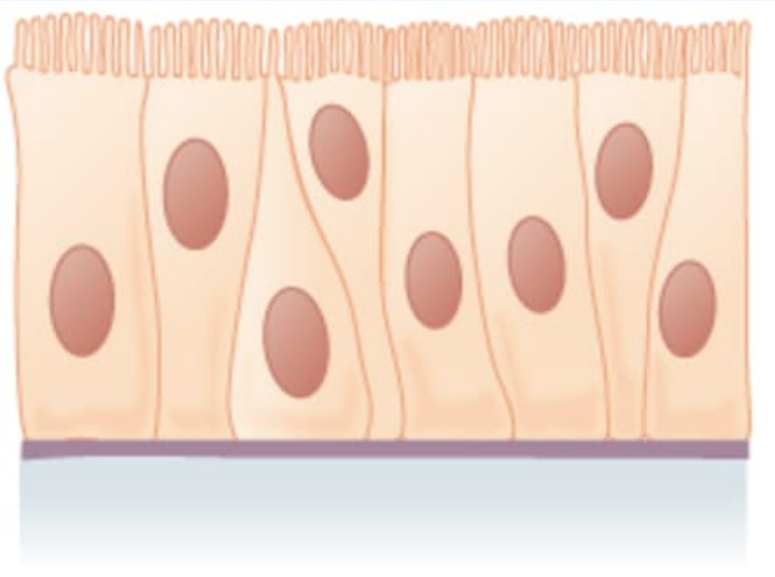
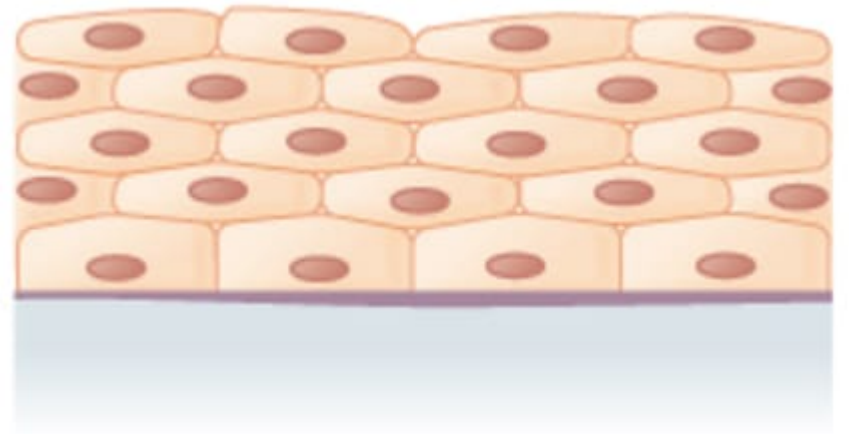
Epithelial tissue is also a master of specialization: some cells feature **microvilli** (to boost absorption, creating a 'brush border'), or **cilia** (to sweep away dust and pathogens in your airways). This adaptability helps epithelial tissue protect, absorb, filter, secrete — and even sense — what is happening in and around you.

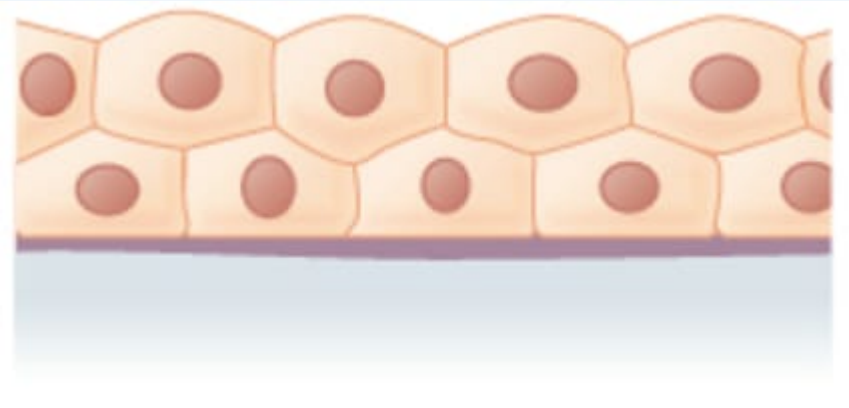
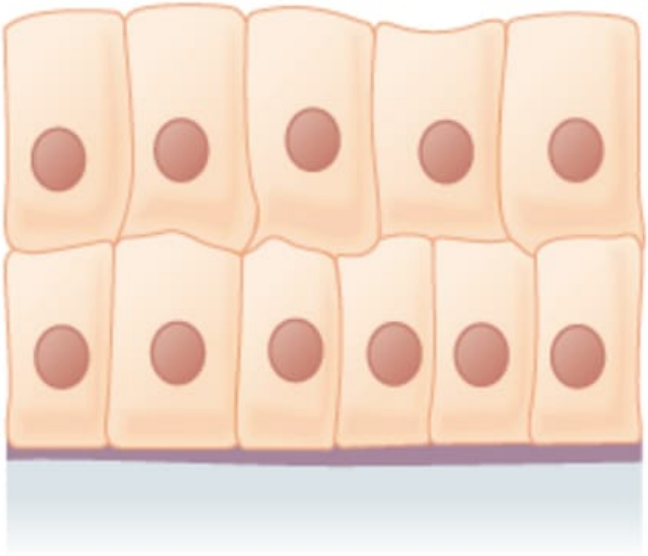
So next time you look at your skin, or think about the lining of your mouth or stomach, remember: you are looking at a superhero of the microscopic world, doing countless jobs to keep you healthy every single day!

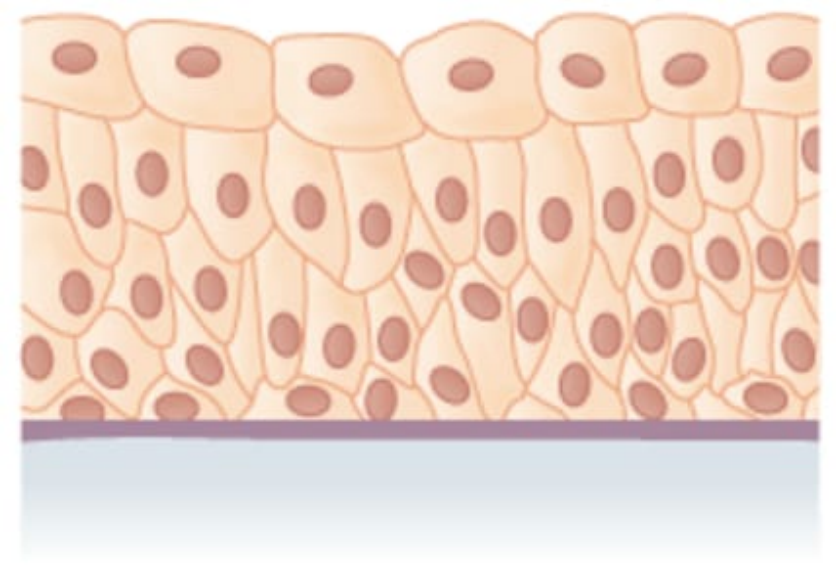
There are eight basic types of epithelium: six of them are identified based on both the number of cells and their shape; two of them are named by the type of cell (squamous) found in them. Epithelial tissue is classified based on the number of cells, the shape of those cells, and the types of those cells.

Epithelial Tissue Cells

Cells	Locations	Function
Simple squamous epithelium 	Air sacs of the lungs and the lining of the heart, blood vessels and lymphatic vessels	Allows materials to pass through by diffusion and filtration, and secretes lubricating substances
Simple cuboidal epithelium 	In ducts and secretory portions of small glands and in kidney tubules	Secretes and absorbs
Simple columnar epithelium 	Ciliated tissues including the bronchi, uterine tubes, and uterus; smooth (nonciliated tissues) are in the digestive tract bladder	Absorbs; it also secretes mucous and enzymes.

Cells	Locations	Function
Pseudostratified columnar epithelium 	Ciliated tissue lines the trachea and much of the upper respiratory tract	Secrete mucous; ciliated tissue moves mucous
Stratified squamous epithelium 	Lines the esophagus, mouth, and vagina	Protects against abrasion

Cells	Locations	Function
Stratified cuboidal epithelium 	Sweat glands, salivary glands, and mammary glands	Protective tissue
Stratified columnar epithelium 	The male urethra and the ducts of some glands.	Secretes and protects

Cells	Locations	Function
Transitional epithelium 	Lines the bladder, urethra and ureters	Allows the urinary organs to expand and stretch

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3.3: Connective Tissue — Supports and Protects

Connective tissue is very diverse, with many types of cells that help store energy, protect organs, and support the body's structure.

Master this section and you'll be able to

- Identify and distinguish between the types of connective tissue: proper, supportive, and fluid
- Explain the functions of connective tissues

Connective Tissue (CT): More Than Just "Glue"

As its name suggests, one of the primary jobs of connective tissue is to connect — linking tissues and organs together across the body. But it does far more than that. Unlike epithelial tissue, where cells are tightly packed together like tiles on a floor, connective tissue features cells that are more spread out, surrounded by a vast and varied ***extracellular matrix***. This matrix is produced by the cells themselves and is critical to the tissue's function.

The extracellular matrix consists of two key components: a ***ground substance*** (a fluid or gel-like material) and a **network of protein fibers** that crisscross through it. Depending on the type of connective tissue, this ground substance can range from watery (like in blood) to rubbery (like in cartilage) to solid and mineralized (like in bone). Despite the wide variety of connective tissue types, they usually share three basic ingredients: **cells**, **protein fibers**, and **ground substance**. The composition and proportions of these elements are finely tuned to the tissue's function — for example, the rigid matrix in bone supports the body, while phagocytic cells in loose connective tissue help clean up pathogens and cellular debris.

What Does Connective Tissue Do?

Connective tissue is the body's multi-tasking support crew. It provides structure and scaffolding for other tissues, from the flexible sheaths around muscle cells to the sturdy tendons that connect muscles to bones. The entire skeleton, in fact, is a specialized form of supportive connective tissue designed to hold the body upright and protect vital organs.

But that is not all. Connective tissues also play a protective role: fibrous capsules cushion delicate organs, and bone encases, and therefore protects, the brain and spinal cord. Specialized (immune) cells in loose connective tissue defend the body from microorganisms that invade it. Transport of fluid, nutrients, waste, and signaling molecules are ensured by specialized fluid connective tissues, such as blood and lymph. Adipose cells store surplus energy in the form of fat and contribute to the thermal insulation of the body.

Types of Connective Tissue

Connective tissues are broadly grouped into **three main categories**, based on what their matrix looks like and the types of fibers they contain:

1. **Connective Tissue Proper**
   This group includes **loose connective tissue** (like areolar and adipose tissue) and **dense connective tissue** (like tendons and ligaments). Both types contain a variety of cell types and protein fibers suspended in a thick, viscous ground substance.
   - *Loose connective tissue* has loosely arranged fibers with lots of open space, allowing flexibility and movement.
   - *Dense connective tissue* is packed with tightly bundled fibers, providing strength and resistance to stretching.
2. **Supportive Connective Tissue**
   This includes **cartilage** and **bone**, which give the body its framework and help protect soft tissues. These tissues feature

fewer cell types and more densely packed fibers. Bone has a hardened, calcified matrix due to calcium salt deposits, while cartilage remains more flexible.

3. **Fluid Connective Tissue**
   This group includes **blood** and **lymph**, in which specialized cells float in a watery matrix full of dissolved proteins, salts, and nutrients. These tissues are crucial for circulation, immune defense, and communication between distant parts of the body.

Different Types of Connective Tissues

Connective tissue proper	Supportive connective tissue	Fluid connective tissue
Loose connective tissue • Areolar • Adipose Dense connective tissue • Dense regular • Dense-irregular	Cartilage • Hyaline • Fibrocartilage • Elastic Bone	Blood Lymph

Connective Tissue Proper

Fibroblasts are present in all CT proper (Figure 3.3.1). A fibroblast is a young and active cell that produces and secretes the protein fibers and ground substance that make up the extracellular matrix in connective tissue. A **fibrocyte** is a less active, mature form of the fibroblast that helps maintain the tissue once the matrix has been formed. Fibroblasts, fibrocytes, adipocytes, and mesenchymal cells (= multipotent stem cells) are stationary cells, which means they always remain within the connective tissue. Other cells move in and out of the connective tissue in response to chemical signals. Macrophages, mast cells, lymphocytes, plasma cells, and phagocytic cells are found in connective tissue proper but are actually part of the immune system protecting the body.

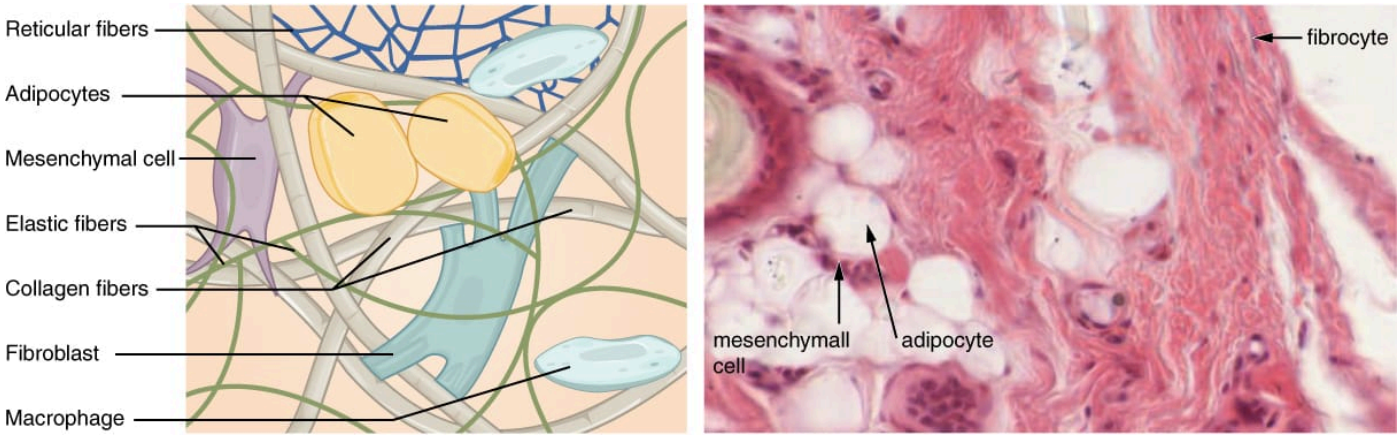


Figure 3.3.1: **Connective Tissue Proper.** Fibroblasts produce this fibrous tissue. Connective tissue proper includes the fixed cells fibrocytes, adipocytes, and mesenchymal cells. LM × 400. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Cell Types

The most abundant cell in connective tissue proper is the **fibroblast**. Polysaccharides and proteins secreted by fibroblasts combine with extra-cellular fluids to produce a viscous ground substance that, with embedded fibrous proteins, forms the extra-cellular matrix. As you might expect, a **fibrocyte**, the less active form of fibroblast, is the second most common cell type in

connective tissue proper.

Adipocytes are cells that store lipids as droplets that fill most of the cytoplasm.

The mesenchymal cell is a multipotent adult stem cell. These cells can differentiate into any type of connective tissue cells needed for repair and healing of damaged tissue.

The **macrophage** cell is a large cell derived from a monocyte, a type of white blood cell, which enters the connective tissue matrix from the blood vessels. The macrophages are an essential component of the immune system, which is the body's defense against potential pathogens and degraded host cells. When stimulated, macrophages release cytokines, small proteins that act as chemical messengers. Cytokines recruit other cells of the immune system to infected sites and stimulate their activities. Roaming, or free, macrophages move rapidly by amoeboid movement, engulfing infectious agents and cellular debris. In contrast, fixed macrophages are permanent residents of their tissues.

The mast cell, found in connective tissue proper, has many cytoplasmic granules. These granules contain the chemical signals histamine and heparin. When irritated or damaged, mast cells release histamine, an inflammatory mediator, which causes vasodilation and increased blood flow at a site of injury or infection, along with itching, swelling, and redness you recognize as an allergic response. Like blood cells, mast cells are derived from hematopoietic stem cells and are part of the immune system.

Connective Tissue Fibers and Ground Substance

Three main types of fibers are secreted by fibroblasts: collagen fibers, **elastic** fibers, and reticular fibers. Collagen fiber is made from fibrous protein subunits linked together to form a long and straight fiber. Collagen fibers, while flexible, have great tensile strength, resist stretching, and give ligaments and tendons their characteristic resilience and strength. These fibers hold connective tissues together, even during the movement of the body.

Elastic fiber contains the protein elastin along with lesser amounts of other proteins and glycoproteins. The main property of elastin is that after being stretched or compressed, it will return to its original shape. Elastic fibers are prominent in elastic tissues found in skin and the elastic ligaments of the vertebral column.

All fiber types are secreted by fibroblasts and embedded in ground substance.

Loose Connective Tissue

Loose connective tissue is found between many organs where it **acts both to absorb shock and bind tissues together.** It allows water, salts, and various nutrients to diffuse through to adjacent or imbedded cells and tissues.

Adipose tissue is a type of connective tissue made up mostly of **fat-storing cells.** There is very little space between the adipocytes. It contains many **capillaries**, which help the body quickly **store or release fat** depending on its needs.

This tissue plays several important roles: it **stores energy**, provides **insulation** to help maintain body temperature, and offers **cushioning** to protect organs from mechanical injury. You will find adipose tissue in places like around the **kidneys**, behind the **eyes**, and under the **skin**, where it helps protect and support the body.

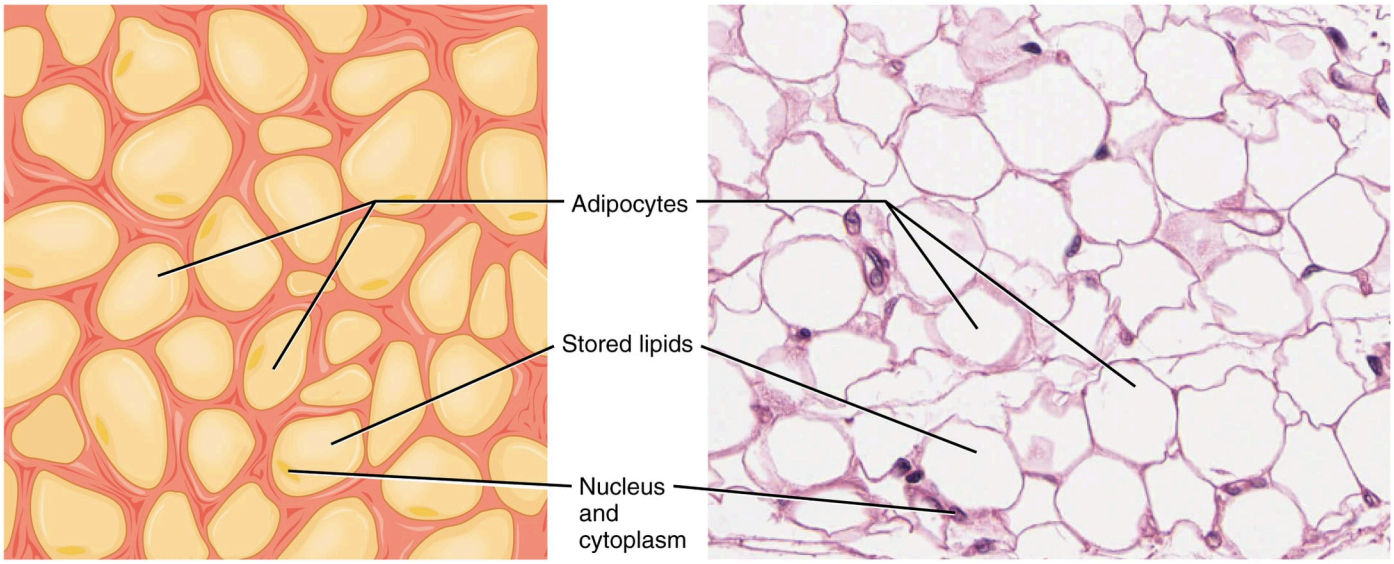


Figure 3.3.2: **Adipose Tissue.** This is a loose connective tissue that consists of fat cells with little extracellular matrix. It stores fat for energy and provides insulation. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Areolar tissue — the body's packing material — is a loose, flexible type of connective tissue with a **web-like structure**. It contains a mix of **cells and fibers** scattered in no particular pattern, which makes it great for **filling spaces** and **holding things in place**.

You can find it **between muscles**, **around blood and lymph vessels**, and **surrounding organs**—especially in the abdominal area. It also lies **just beneath most epithelial tissues**, providing support and helping form part of epithelial membranes.

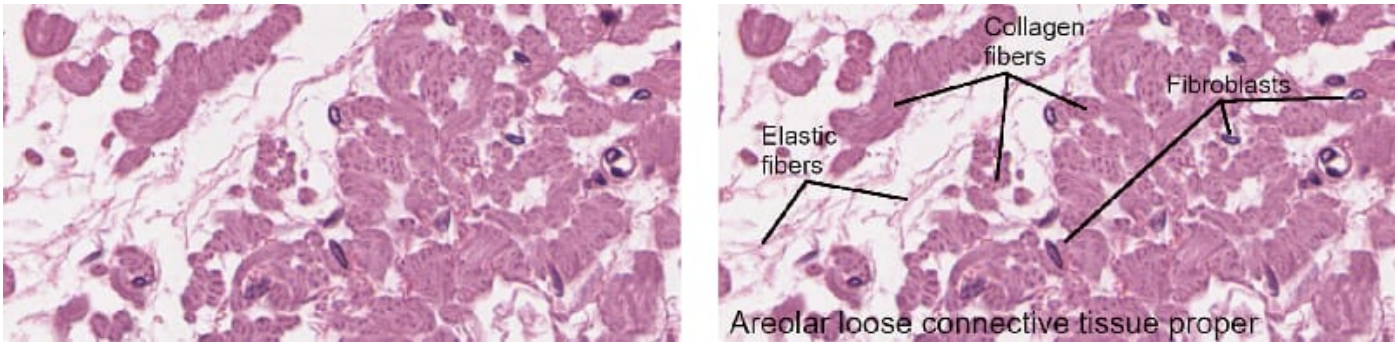


Figure 3.3.3: **Areolar (Loose) Connective Tissue.** Light micrographs showing loosely arranged collagen and elastic fibers with scattered fibroblasts in a gel-like matrix, allowing flexible support and diffusion.

Dense Connective Tissue

Dense connective tissue has **more collagen fibers** than loose connective tissue, which makes it **stronger and more resistant to stretching**. There are two main types: **dense regular** and **dense irregular**.

- **Dense regular connective tissue** has fibers that run **parallel to each other**, which makes it great at resisting pulling forces in **one direction**. This is the type of tissue found in **tendons** (which connect muscle to bone) and **ligaments** (which connect bone to bone). In most ligaments, the fibers are mostly parallel, but not perfectly aligned.
  Some ligaments are made of **dense regular elastic tissue**, which has stretchy **elastin fibers** along with collagen. This gives them the ability to **stretch and bounce back**—like the ligaments in your **vocal cords** or **between your vertebrae**.

- **Dense irregular connective tissue** has fibers arranged in a **random or crisscrossed pattern**. This layout gives the tissue strength in **many directions**, not just one. In some tissues, the fibers form a woven mesh; in others, they are layered in different directions like stacked sheets.
  A good example is the **dermis** (the tough layer of skin under the surface), which contains lots of collagen arranged irregularly. **Dense irregular elastic tissue**, found in **arterial walls**, combines strength with stretchiness—so arteries can **expand and**

snap back as blood pulses through them.

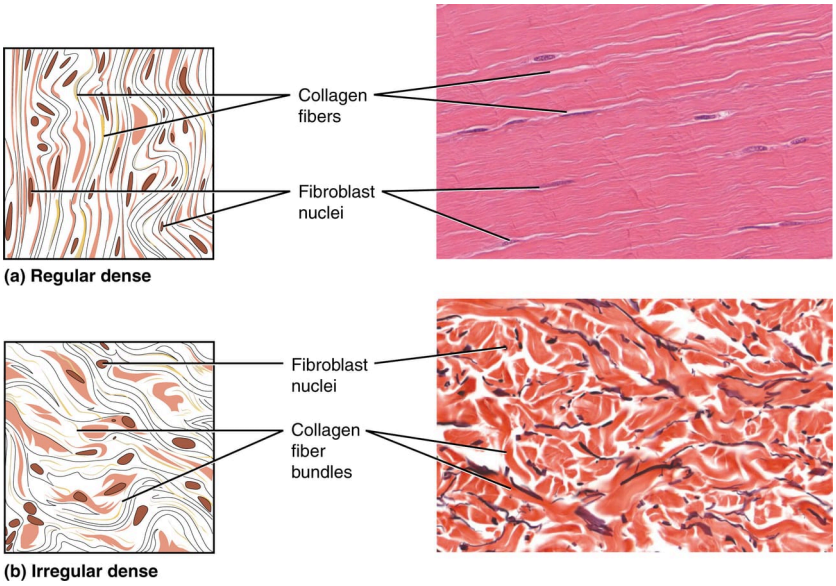


Figure 3.3.4: **Dense Connective Tissue.** (a) Dense regular connective tissue consists of collagenous fibers packed into parallel bundles. (b) Dense irregular connective tissue consists of collagenous fibers interwoven into a mesh-like network. From top, LM × 1000, LM × 200. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

Disorders of the...

Connective Tissue: Tendinitis

Your opponent stands ready as you prepare to hit the serve, but you are confident that you will smash the ball past your opponent. As you toss the ball high in the air, a burning pain shoots across your wrist and you drop the tennis racket. That dull ache in the wrist that you ignored through the summer is now an unbearable pain. The game is over for now.

After examining your swollen wrist, the doctor in the emergency room announces that you have developed wrist tendinitis. She recommends icing the tender area, taking non-steroidal anti-inflammatory medication to ease the pain and to reduce swelling, and complete rest for a few weeks. She interrupts your protests that you cannot stop playing. She issues a stern warning about the risk of aggravating the condition and the possibility of surgery. She consoles you by mentioning that well known tennis players such as Venus and Serena Williams and Rafael Nadal have also suffered from tendinitis related injuries.

What is tendinitis and how did it happen? Tendinitis is the inflammation of a tendon, the thick band of fibrous connective tissue that attaches a muscle to a bone. The condition causes pain and tenderness in the area around a joint. On rare occasions, a sudden serious injury will cause tendinitis. Most often, the condition results from repetitive motions over time that strain the tendons needed to perform the tasks.

Persons whose jobs and hobbies involve performing the same movements over and over again are often at the greatest risk of tendinitis. You hear of tennis and golfer's elbow, jumper's knee, and swimmer's shoulder. In all cases, overuse of the joint causes a microtrauma that initiates the inflammatory response. Tendinitis is routinely diagnosed through a clinical examination. In case of severe pain, X-rays can be examined to rule out the possibility of a bone injury. Severe cases of tendinitis can even tear loose a tendon. Surgical repair of a tendon is painful. Connective tissue in the tendon does not have abundant blood supply and heals slowly.

While older adults are at risk for tendinitis because the elasticity of tendon tissue decreases with age, active people of all ages can develop tendinitis. Young athletes, dancers, and computer operators; anyone who performs the same movements constantly is at risk for tendinitis. Although repetitive motions are unavoidable in many activities and may lead to tendinitis, precautions can be taken that can lessen the probability of developing tendinitis. For active individuals, stretches before

exercising and cross training or changing exercises are recommended. For the passionate athlete, it may be time to take some lessons to improve technique. All of the preventive measures aim to increase the strength of the tendon and decrease the stress put on it. With proper rest and managed care, you will be back on the court to hit that slice-spin serve over the net.

Interactive Link

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Watch this animation to learn more about tendonitis, a painful condition caused by swollen or injured tendons.

Supportive Connective Tissues

Two major forms of supportive connective tissue, cartilage and bone, allow the body to maintain its posture and protect internal organs.

Cartilage: Flexible, Tough, and Slow to Heal

Cartilage has a unique look and feel thanks to special sugar-based molecules called **chondroitin sulfates**. These combine with proteins in the ground substance to form **proteoglycans**, which give cartilage its firm-yet-flexible texture. The actual **cartilage cells**, called **chondrocytes**, live tucked inside little spaces in the matrix called **lacunae** (singular: *lacuna*).

Surrounding most cartilage is a protective outer layer of **dense irregular connective tissue** known as the **perichondrium**. Here's the catch: cartilage is **avascular**—it has no blood vessels. That means nutrients and oxygen have to **diffuse slowly** through the dense matrix to reach the chondrocytes. This is why cartilage injuries can take a long time to heal.

Types of Cartilage

There are **three main types** of cartilage, each with a different structure and role in the body:

- **Hyaline cartilage** is the most common type. It has lots of proteoglycans and short, scattered collagen fibers, making it appear **smooth and glassy** under a microscope. It is **strong yet flexible**, found in places like the **rib cage**, **nose**, and at the ends of bones in **moveable joints**. In embryos, hyaline cartilage forms a "template" for bones to develop. Growth plates at the ends of long bones are made of this tissue, allowing bones to grow during childhood.
- **Fibrocartilage** is **tougher** because it contains **thick bundles of collagen fibers**. It is built to handle pressure and stress—think **intervertebral discs** and **knee menisci**. It acts like a durable shock absorber.
- **Elastic cartilage** contains both **elastic fibers** and collagen, giving it a mix of **flexibility and strength**. Want an example? Gently tug your **earlobe**—that bounce-back comes from elastic cartilage! You will also find it in the **external ear** and parts of the **larynx**.

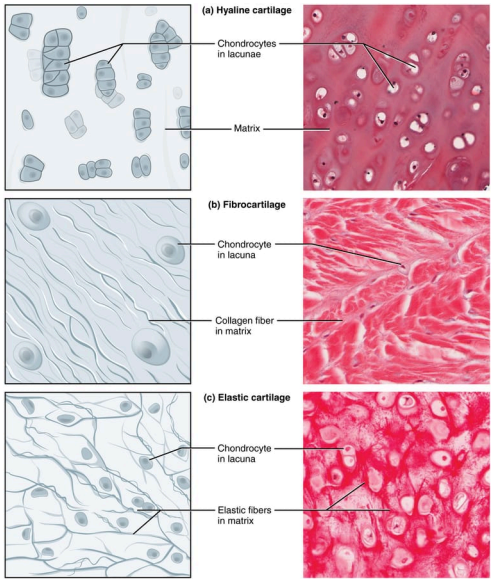


Figure 3.3.5: **Types of Cartilage.** Cartilage is a connective tissue consisting of collagenous fibers embedded in a firm matrix of chondroitin sulfates. (a) Hyaline cartilage provides support with some flexibility. The example is from dog tissue. (b) Fibrocartilage provides some compressibility and can absorb pressure. (c) Elastic cartilage provides firm but elastic support. From top, LM × 300, LM × 1200, LM × 1016. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

Bone: Strong, Solid, and Surprisingly Dynamic

Bone is the toughest of all connective tissues. It forms the body's framework, **supports your weight**, and **protects vital organs** like the brain, heart, and lungs. What makes bone so strong? Its **rigid matrix**, made of two powerful components:

- **Collagen fibers**, which give bone some **flexibility and resistance to shattering**
- **Mineral crystals** (mainly **hydroxyapatite**, a form of calcium phosphate), which provide **hardness and strength**

Together, these create a material that is **both sturdy and slightly flexible**—just the right combination to support your body without snapping under pressure.

The bone cells, called **osteocytes**, live in small spaces called **lacunae**, just like cartilage cells do. But unlike cartilage, bone is **rich in blood vessels**, which means it gets nutrients quickly and can **heal much faster** when injured.

If you look at a cross-section of a **long bone** under a microscope, you'll see the osteocytes arranged in **concentric rings** around a **central canal**—a beautifully organized pattern built for strength and nutrient flow.

For images on the bone tissue, see module 4, when we talk about the skeleton.

Two Types of Bone Tissue

There are **two forms** of bone tissue, each with its own structure and purpose:

- **Compact bone** is **dense and solid**, giving bones their **strength and durability**. It forms the outer layer of most bones.
- **Cancellous bone**, also called **spongy bone**, has a **lighter, lattice-like appearance**. It is full of open spaces between bony arches called **trabeculae**, which help **reduce bone weight** without sacrificing too much strength. You will find spongy bone in the **interior of bones** and at the **ends of long bones**, like your femur.

Fluid Connective Tissue: On the Move!

Blood and **lymph** are special types of **fluid connective tissue**—instead of having a solid or gel-like matrix, their **cells float in a liquid**. This setup makes them perfect for **transporting substances** all around the body.

In **blood**, the liquid matrix is called **plasma**, and it carries a mix of **cells** known as the **formed elements**, all of which originate from **stem cells in the bone marrow**:

- **Erythrocytes (red blood cells)** carry **oxygen** and a bit of **carbon dioxide**.
- **Leukocytes (white blood cells)** defend the body against **germs, toxins, and invaders**.
- **Platelets** are actually **cell fragments** that help with **blood clotting** when you get a cut.

White blood cells can even **leave the bloodstream** and move into nearby tissues to fight infection. Meanwhile, **nutrients, salts, hormones, and wastes** are dissolved in the plasma and delivered wherever the body needs them.

Lymph is another fluid connective tissue, made up of a **watery matrix** and **white blood cells**. It flows through a network of **lymphatic vessels**, which begin in tiny **lymphatic capillaries**. These vessels are **super permeable**, allowing **excess fluid** and even **large molecules** to drain out of tissues and into the lymph.

Eventually, lymph returns to the bloodstream, helping maintain fluid balance and delivering **important substances**—like **fats** absorbed from the digestive tract—that are too big to enter the blood directly. Think of the lymphatic system as a **recycling and delivery network** that supports both **immunity** and **nutrition**.

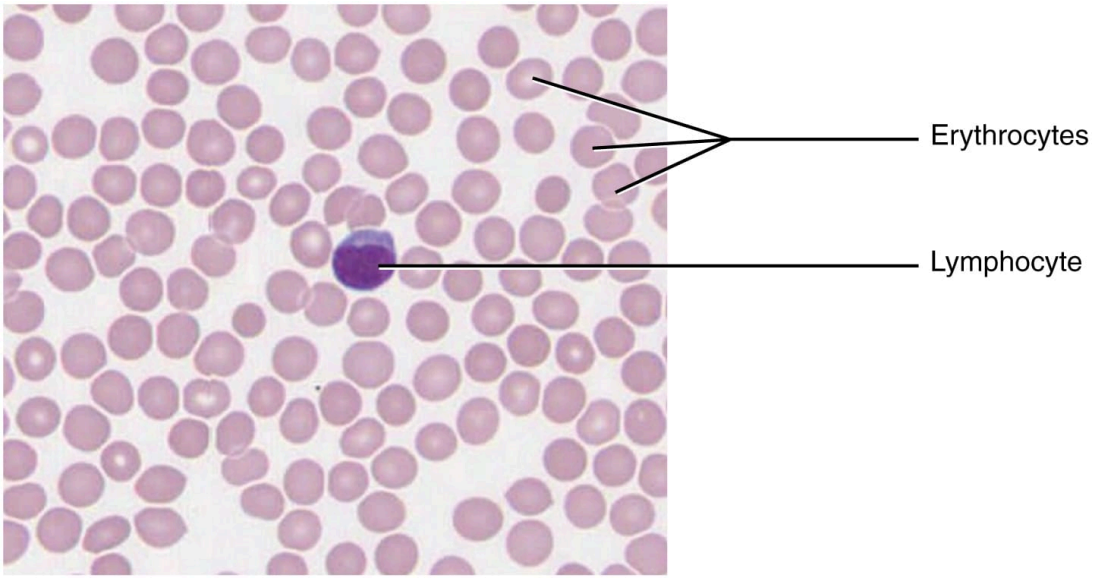


Figure 3.3.6: **Blood.** A Fluid Connective Tissue Blood is a fluid connective tissue containing erythrocytes and various types of leukocytes that circulate in a liquid extracellular matrix. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link

View the University of Michigan Webscope (opens in a new window) to explore a normal blood smear in greater detail.

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3.4: Muscle Tissue — Built to Move

The three types of muscle tissue are skeletal, smooth, and cardiac.

Master this section and you'll be able to

- Compare and contrast the structural and functional characteristics of the three muscle tissue types.
- Identify the location and primary role of each muscle type in the human body.
- Explain the differences between voluntary and involuntary muscle control and provide examples of each.

Muscle Tissue

Muscle tissue is another one of the four major types of tissues in the human body — and it is all about movement. Whether you are blinking, breathing, digesting, or sprinting for the bus, muscle tissue is at work.

What makes muscle tissue unique is its ability to **contract**, or shorten, which produces force. This force allows body parts to move, organs to function, and even blood to circulate. Muscle cells are sometimes called **muscle fibers** because of their long, thin shape. They are packed with specialized proteins that slide past one another to make contraction possible.

Muscle tissue also plays a role in:

- **Posture and support** – helping you stay upright
- **Heat production** – keeping your body temperature stable
- **Protection** – surrounding vital organs

Let's explore the **three different types of muscle tissue**, each with its own structure, function, and location in the body.

Classifying Muscle Tissue: Function Meets Form

Muscle tissue can be classified in two key ways:

- **Functionally**: Is it under conscious control? (Voluntary vs. Involuntary)
- **Morphologically**: Does it have visible bands? (Striated vs. Non-striated)

These two characteristics help us distinguish between the **three main types of muscle tissue**, which we will explore shortly.

Functional Classification

- **Voluntary**: You control the movement (e.g., raising your hand).
- **Involuntary**: The body controls it automatically (e.g., heartbeat or digestion).

Morphological Classification

- **Striated**: Muscle cells show visible stripes (bands) under the microscope due to the organized arrangement of protein filaments (myofibrils). This structure allows for strong, directional contractions.
- **Non-striated**: No visible stripes; the filaments are arranged less regularly, allowing for more versatile contraction

patterns.

Three Types of Muscle Tissue

• Skeletal Muscle

Skeletal muscle primarily attaches to bones of the skeletal system via **tendons**, allowing it to control body movements and maintain posture. For example, contraction of the **biceps brachii**, which connects the **scapula** to the **radius**, raises the forearm. Some skeletal muscles, especially in the face, attach directly to **other muscles or to the skin**, enabling facial expressions.

Skeletal muscle is typically under **voluntary control**, though some actions — like maintaining posture or balance — occur **subconsciously**. Structurally, skeletal muscle cells (**myocytes**) are **long, cylindrical**, and **multinucleated**, with nuclei located at the **periphery**. They also appear **striated** due to the organized arrangement of contractile proteins within the cell.

• Cardiac Muscle Tissue

Cardiac muscle tissue is found **only in the heart**, where its rhythmic contractions pump blood throughout the body and help maintain blood pressure.

Like skeletal muscle, cardiac muscle appears **striated** due to the organized arrangement of contractile proteins. However, unlike skeletal muscle, it is **involuntary**—it contracts without conscious control. One of the key features that distinguishes cardiac muscle is the presence of **intercalated discs**. These specialized structures allow cardiac cells to communicate and contract in a **coordinated, synchronized** manner.

Cardiac muscle cells (**cardiac myocytes**) are **shorter** than skeletal muscle cells and typically have **one or two centrally located nuclei**.

• Smooth Muscle Tissue

Smooth muscle tissue is found in association with many internal organs and body systems, including the **digestive**, **respiratory**, **urinary**, and **reproductive** systems. It plays a vital role in regulating the flow of substances through these systems, for example, by propelling food through the digestive tract via **peristalsis** (a wave-like contraction).

Unlike skeletal and cardiac muscle, smooth muscle is **non-striated**. Although it contains the same types of contractile proteins (**myofilaments**), they are arranged in a **different, less orderly** pattern. Smooth muscle is also **involuntary**, meaning it is not under conscious control.

Smooth muscle cells (**myocytes**) are **spindle-shaped** — wide in the middle and tapered at the ends — with a **single, centrally located nucleus**.

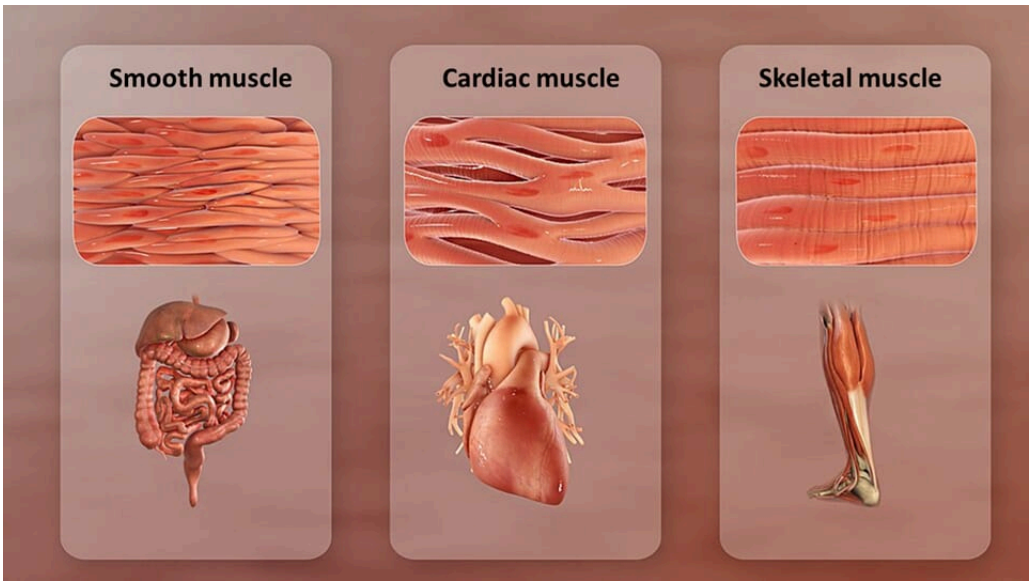


Figure 3.4.1: **Muscle Types. Cardiac** and **skeletal** muscle are both striated in appearance, while **smooth** muscle is not. Both cardiac and smooth muscle are involuntary while skeletal muscle is voluntary.

	Skeletal muscle	Cardiac muscle	Smooth muscle
Location	Attached to bones	Heart wall (myocardium)	Walls of hollow organs (e.g., digestive tract, blood vessels)
Function	Voluntary movement, posture	Pumps blood	Moves substances through organs
Control	Voluntary	Involuntary	Involuntary
Striations (banding)	Yes	Yes	No
Cell Shape	Long, cylindrical fibers	Usually one (sometimes two)	Spindle-shaped

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3.5: Nervous Tissue — Perceives and Responds

Nervous tissue, the final one of the four main tissue types, is composed of neurons and supporting cells called neuroglia.

Master this section and you'll be able to

- Identify the classes of cells that make up nervous tissue
- Describe the key structural features of a neuron.

Nervous tissue is what gives your body its “electric personality”. It is **excitable**, meaning it **can send and receive fast-moving electrochemical signals** that keep your brain, muscles, and organs in sync. This tissue is made up of two main types of cells: **neurons** and **neuroglia.**

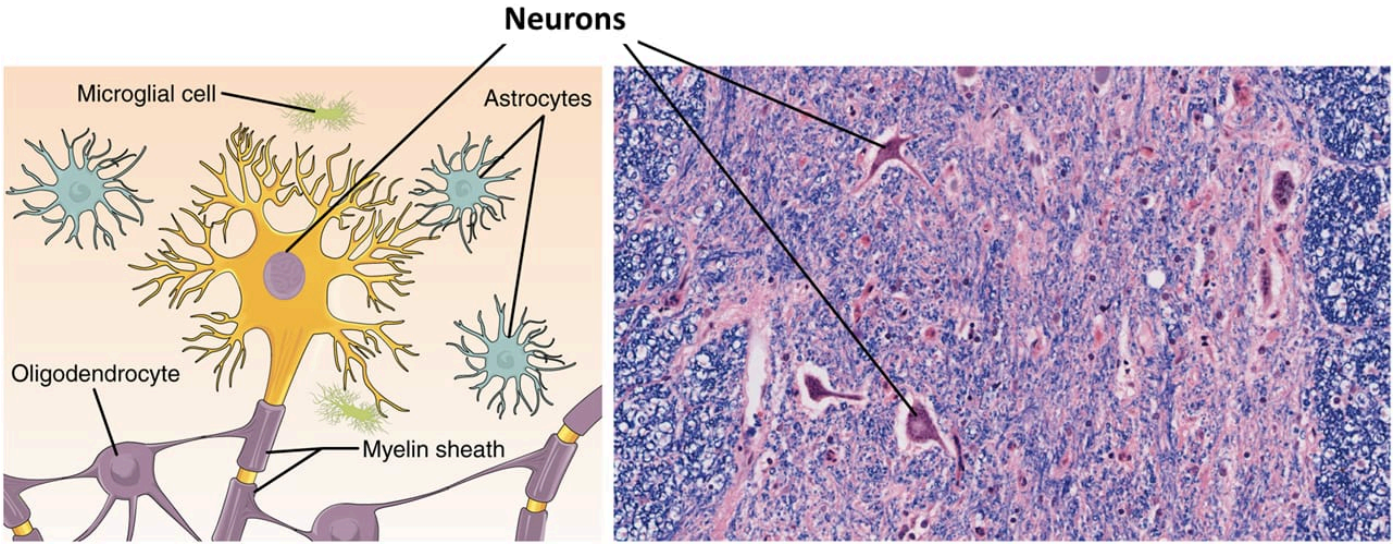


Figure 3.5.1: **Nervous Tissue.** The image on the top, shows a neuron cell body, also called the "soma". The soma contains the nucleus and all the other organelles an active cell needs. The dendrites transfer the nerve impulse to the soma. The axon carries the action potential away to another excitable cell. The bottom image shows a neuron surrounded by various glial cells, such as astrocytes, microglia, and oligodendrocytes with myelin, and on the right is a micrograph of a nervous tissue histology slide. LM × 872. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Meet the Neurons: The Nervous System’s Messengers

Neurons are the stars of the show — they send information along their length using **electrical signals** called **action potentials**, and then pass that info to other cells using **chemical messengers.** Neurons are the body’s information superhighway — designed to send and receive signals fast and efficiently. Each neuron has three main parts:

- **Cell Body (Soma):** This is the command center. It holds the nucleus and most of the cell’s machinery — like mitochondria and ribosomes — that keep the neuron alive and functioning.
- **Dendrites:** These are the neuron’s “antennae” — branching off the cell body to receive signals from other cells.
- **Axon:** A long, tail-like extension that carries signals away from the cell body. Many axons are wrapped in **myelin**, a protective, insulating sheath made by support cells. Myelin helps electrical impulses travel faster, like adding insulation to a wire.

When a neuron gets enough of a signal, it fires off an **action potential (AP).** An AP is an electrical impulse that zips down the axon to the **synapse**, a tiny gap between neurons (or between a neuron and a muscle or gland cell). At the synapse, chemicals called **neurotransmitters** carry the message across to the next cell. If the signal is strong enough, the next cell responds.

Neuron Shapes and Types:

Neurons come in different shapes depending on their job:

- **Multipolar neurons** have many dendrites and one axon (the most common type).
- **Bipolar neurons** have one dendrite and one axon, with the cell body in between.
- **Unipolar neurons** have a single process that splits into two branches—one acts like a dendrite, the other like an axon.

Neuroglia: The Unsung Heroes

On the sidelines but just as crucial are the **neuroglia** (**glia**, or **glial cells** for short), which act like the neuron's pit crew: they support, protect, and help regulate how those signals get sent. For a long time, **neuroglia** (or glial cells) were thought to just "hold things together" — hence the name "glia," which comes from the **Greek word for glue.** But modern research shows they do so much more!

Let's meet a few key players:

- ⭐ **Astrocytes** (star-shaped cells):
  These multitaskers help regulate ions in the fluid between neurons, clean up extra neurotransmitters, and help form the **blood-brain barrier**, which keeps harmful substances in the blood from entering the brain.
- 🧹 **Microglia:**
  Think of these as the brain's immune defense. Though not true neural cells (they're related to macrophages), microglia patrol the CNS and respond to injury or infection.
- 🧵 **Oligodendrocytes:**
  These cells create **myelin** in the **central nervous system** (CNS)—that's your brain and spinal cord.
- 🧵 **Schwann Cells:**
  Their cousins in the **peripheral nervous system** (PNS), Schwann cells wrap axons in myelin outside the brain and spinal cord.

Together, neurons and glial cells form the intricate web of communication that powers everything from your thoughts to your reflexes. Pretty amazing, right?

Feeling like this is a lot to take in? You are not wrong! We will return to this page and build on it when we dive into the Nervous System in Module 6.

Interactive Link

Follow this link(opens in new window) to learn more about nervous tissue. What are the main parts of a nerve cell?

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3.6: Epithelial Membranes

An epithelial membrane is a specific type of tissue membrane composed of a layer of epithelial tissue attached to an underlying layer of connective tissue.

Master this section and you'll be able to

- Differentiate among the three types of epithelial membranes (mucous, serous, and cutaneous membranes).
- Describe the layered structure of mucous and serous membranes.
- Outline the functions of mucous, serous, and cutaneous membranes.

Epithelial Membranes: Your Body's Protective Linings

Epithelial membranes are thin layers of tissue that cover surfaces, line cavities, and protect our organs. Each one is made of **epithelial tissue** (which acts like a barrier) and **connective tissue** (which gives support). Besides **protecting your body**, epithelial membranes also play critical roles in **secretion** and **absorption**, depending on where they are in the body.

There are **three main types:**

1) Mucous Membranes (Mucosae)

Mucous membranes, or **mucosae,** line body passageways and cavities that open to the outside, such as those in the **digestive, respiratory, and urogenital tracts**. They function primarily in **absorption** and **secretion**.

Structure

- **Epithelial Types:** The surface layer of mucous membranes is composed of **epithelial cells**. The type of epithelium varies by location:
    - **Stratified squamous epithelium** is common in areas subject to abrasion (e.g., mouth, esophagus).
    - **Simple columnar epithelium** predominates where absorption and secretion are important (e.g., stomach, intestines).
    - **Ciliated pseudostratified columnar epithelium** is a type of epithelial tissue that appears layered but is actually a single layer of cells, with cilia on the surface to help move mucus and trapped particles out of the airways (bronchi).
- **Layers:** Mucous membranes generally consist of three layers:
    - **Epithelium:** The outermost layer, responsible for protection, absorption, and secretion.
    - **Lamina propria:** A layer of loose connective tissue beneath the epithelium, containing blood vessels, nerves, lymphatics, and immune cells that support and nourish the overlying epithelium.
    - **Muscularis mucosae:** A thin layer of smooth muscle, present in many mucosae (especially in the digestive tract), that allows local movement of the mucosa.
- **Submucosa:** Beneath the mucosa (including the muscularis mucosae) is the **submucosa** — a separate layer of connective tissue that supports the mucosa and may contain glands. **Submucosal glands** (when present) secrete mucus or other fluids to help move particles along certain tracts, such as the esophagus and intestines. These glands work alongside **unicellular goblet cells** in the epithelium, which also produce mucus.

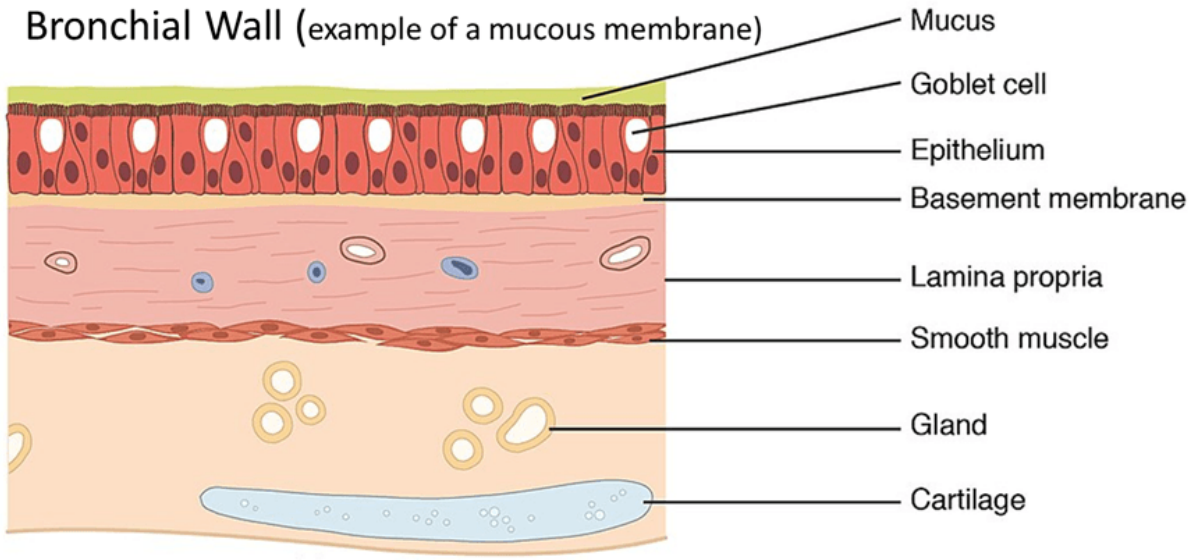


Figure 3.6.1: **Mucous Membrane Structure.** The bronchi leading to the lungs are lined with a **mucous membrane**. The epithelial layer is **pseudostratified columnar epithelium with cilia**. Scattered among the epithelial cells are **goblet cells**, which secrete mucus to trap inhaled dust particles and potential pathogens lilke the COVID or the flu viruses.

Function

- Mucus Secretion: Most, but not all, mucous membranes secrete mucus. Mucus helps trap particles — including pathogens — which helps prevent them from penetrating deeper tissues or progressing further in the body. Mucus also maintains tissue moisture and aids in lubrication.
- **Protective and Immune Function:** Mucous membranes are integral to the body's protection and its immune system, serving as a physical barrier and hosting immune cells in the lamina propria.
- **Location-specific variation:** The exact composition (cell types, thickness, presence of glands) of varies according to the region's function and exposure to stress or pathogens.

2) Serous Membranes (Serosae)

Serous membranes, also called serosae or serosas, are thin, double-layered tissue membranes that line internal **closed body cavities which do not open to the exterior** and cover the organs within these cavities.

Structure

- **Thin, double-layered membranes** with
  - A single layer of specialized **simple squamous epithelial cells** (called **mesothelial cells**). They rest on a **basement membrane** and are responsible for the **secretion of serous fluid**. Some serous fluid is also **passively transferred** through this **thin** cell layer as an ultrafiltrate. However, the majority of serous fluid is actively produced and secreted by the mesothelial cells. **Both mechanisms — active secretion and selective permeability — contribute to the precise composition and volume of serous fluid.**
  - A **loose connective tissue layer** underneath, which is rich in blood vessels, lymphatics, nerves, and provides structural support for the membrane.

  Each serous membrane has two distinct layers:

  - **Parietal layer**: Lines the body cavity wall.
  - **Visceral layer**: Covers and adheres directly to the organs (viscera) within the cavity.

Between these two layers is a narrow **serous cavity** filled with a small amount of watery **serous fluid**. This fluid is secreted by the mesothelial cells.

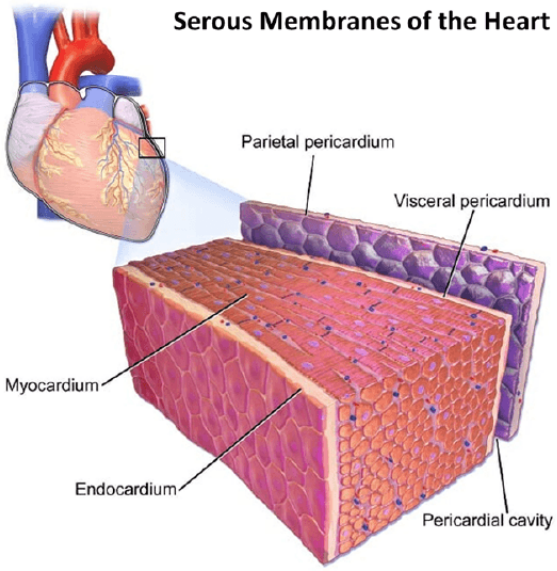


Figure 3.6.2: **Serous Membranes in Action.** The **pericardium** is the protective sac that surrounds the heart. Its inner surface is lined by a **serous membrane** called the **serous pericardium**, which is a **double-layered** membrane. The **parietal layer** lines the inner surface of the pericardial sac, while the **visceral layer** (also called the **epicardium**) is tightly attached to the surface of the heart. Between these two layers is the **pericardial cavity**, filled with **serous fluid** that cushions the heart and reduces friction with each heartbeat.

Function

- The main function of serous membranes is to **reduce friction** between moving organs (such as the heart and lungs) and surrounding body walls by producing and maintaining a thin lubricating serous fluid.
- This arrangement allows internal organs to move smoothly against both body walls and each other, facilitating movements such as breathing, heartbeat, and peristalsis in the digestive tract.
- The serosa also acts as a **protective barrier** and supplies organs with blood and lymphatic vessels through its connective tissue layer.

Types and Locations

Three principal serous membranes, each lining a major body cavity and enveloping the organs inside:

Name	Cavity Lined	Organs Covered	Visceral Layer Name	Parietal Layer Name
Pleura	Thoracic	Lungs	Visceral pleura	Parietal pleura
Pericardium	Pericardial	Heart	Visceral pericardium	Parietal pericardium
Peritoneum	Abdominal	Abdominal organs	Visceral peritoneum	Parietal peritoneum

3) Cutaneous Membrane

- Also known as your **skin**
- Protects against dehydration, infection, and mechanical damage

The second part of this module will explore the cutaneous membrane in greater detail, so we will save further discussion of that topic for later.

👉 All epithelial membranes play critical roles in **protection**, **secretion**, and **absorption**, depending on where they are in the body.

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3.7: Tissue Repair and Wound Healing

Wound healing is divided into four overlapping states: 1) hemostasis, 2) inflammation, 3) proliferation, and 4) remodeling.

Master this section and you'll be able to

- Describe the overlapping phases of tissue repair and wound healing.
- Differentiate between epidermal and deep (full-thickness) wounds.
- Identify the signs of inflammation.

Wound healing is a complex physiological process by which the skin, or any injured organ, repairs itself after injury. The main aim of wound healing is to prevent or limit further damage, to clean and seal the wound against infection, to restore tissue strength, and, if possible, tissue function.

Wounds in the skin can either be classified as **epidermal** (shallow, in which the dermis remains intact) or **deep** (in which the dermis is damaged; this is sometimes referred to as a full thickness wound).

The Four Phases of the Wound Healing Process

The wound healing process occurs in **four overlapping phases**: hemostasis, inflammation, proliferation, and remodeling (also known as maturation). Each phase has distinctive cellular and biochemical activities:

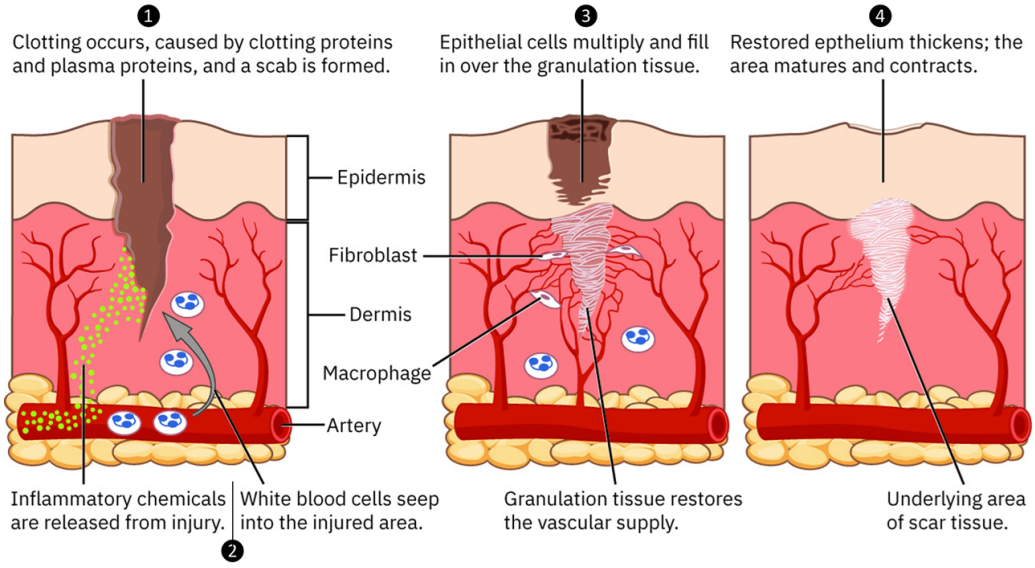


Figure 3.7.1: **The phases of wound healing are inflammation, proliferation, and maturation.** This process begins immediately after an injury and varies in length. (CC BY 4.0; Rice University & OpenStax)

1) Hemostasis: Stop the Bleeding!

The moment an injury occurs, your body acts fast to **stop the bleeding** and maintain *homeostasis*. Even a small cut can damage blood vessels, so the body kicks off the **hemostasis phase** — the first step in wound healing.

Here is what happens:

- **Blood vessels constrict** (*vasoconstriction*) to reduce blood flow

- **Platelets rush in** and stick together at the injury site
- **Fibrin forms a sticky mesh** that strengthens the clot and seals the wound

This clot acts like a temporary plug, preventing both blood loss and germs (bacteria and viruses) from getting in. The process is called **coagulation**, and it usually wraps up within **minutes to hours**, though it can last up to two days in some cases.

2) Inflammation: Calling in the Clean-Up Crew

Once bleeding is under control, your body shifts into clean-up mode. The blood vessels near the wound **dilate** (widen). This process is called **vasodilation** and allows more blood to reach the area, bringing in **white blood cells** — especially ***neutrophils*** and ***macrophages*** — which are drawn to the site by chemical signals released from the damaged tissue.

These **immune cells** are your body's first responders. Their **jobs**?

- **Fight off invading microbes**
- **Break down and remove dead cells and debris**
- **Release growth factors** that kickstart tissue repair

The inflammation phase is easy to spot because it causes these **four classic signs**:🔥 **Redness,** 🌡️ **Heat,** 💥 **Swelling, and** 😣 **Pain**

This phase lasts from a couple of days up to about a week or more in acute, healthy, healing wounds.

3) Proliferation: Rebuilding the Neighborhood

Once the wound is clean and the bleeding has stopped, it is time to rebuild. During the **proliferative phase**, the body works to **repair and fill in** the injured area.

Here is what is happening under the surface:

- **Granulation tissue** forms — a soft, pink scaffold of new connective tissue
- **Fibroblasts** move in and produce **collagen** and **extracellular matrix** to support healing
- **New blood vessels grow** (***angiogenesis***) to supply nutrients and oxygen
- **Wound edges contract** to reduce the wound size
- **New epithelial cells** spread across the surface (***reepithelialization***) to restore the skin barrier

The wound may look **pink or red**, slightly raised, and moist during this stage—this is a good sign! Depending on the wound's depth and extent, this phase can last from **several days to three weeks or more**.

4) Remodeling (Maturation): Strengthening the Repairs

In the **final phase** of wound healing, the body focuses on **long-term repair**. The goal now is not just to fill in the wound, but to **restore strength and function** to the newly formed tissue.

Here is what happens during remodeling or maturation:

- **Collagen fibers reorganize and tighten**, making the tissue stronger.
- **Unneeded cells are removed** through ***apoptosis*** (cell suicide — a kind of cellular self-destruct for the greater good).
- **Scar tissue** forms — it is tough but only has about **80% of the strength** of the original tissue, and it is **less elastic.**

This **remodeling phase** can take **months to a year or longer**, especially for larger or deeper wounds.

⏳ *Important note*: Wound healing is not a tidy step-by-step process — **these phases often overlap**. Factors like the wound's size, depth, location, and the overall health of the person can greatly affect how quickly (and how well) the wound heals.

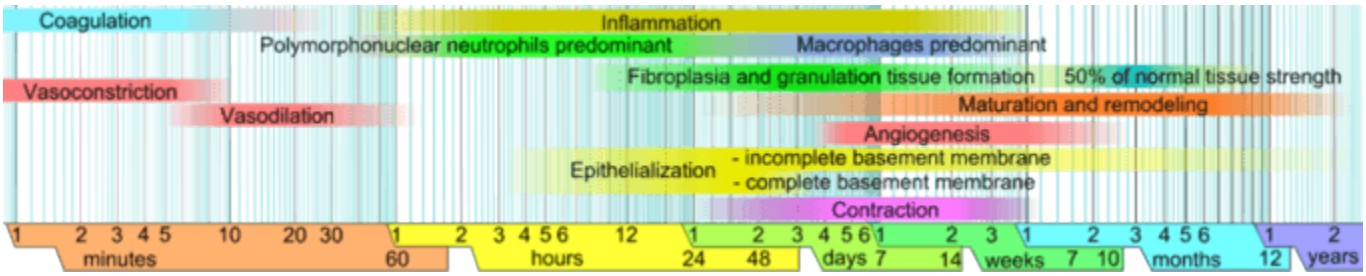


Figure 3.7.2: **Phases of Wound Healing.** This graph shows the length of time for various responses to occur during a wound healing process. Limits vary within faded intervals, mainly by wound size and healing conditions. The image does not include major impairments that cause chronic wounds.

When Healing Does Not Go According to Plan...

The wound healing process described above represents a **best-case scenario**, where both the **epidermis and dermis** are fully restored. But in real life, things do not always go perfectly.

Early on, the body's **top priority** is to protect against blood loss and infection — not necessarily to make the skin look perfect afterward. As a result, especially in **larger or deeper wounds**, the outcome may be **less than perfect**, leading to the formation of **scar tissue** instead of fully regenerated skin.

Additionally, sometimes, healing goes off course:

🛑 The process might stall, leading to **chronic wounds** like pressure ulcers or diabetic foot sores.

⚠️ If the **proliferative phase drags on**, it can result in **fibrosis,** an overgrowth of scar tissue that interferes with normal function

In short, wound healing is a complex and delicate process—and when disrupted, it can lead to long-term consequences.

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3.8: Overview of Cancer

Cancer, known medically as a malignant neoplasm, is a broad group of various diseases, all involving unregulated cell growth.

Master this section and you'll be able to

- Explain the biological basis of cancer.
- Identify and describe key environmental, lifestyle, and genetic risk factors that increase the likelihood of cancer development.
- Compare major cancer treatment strategies.

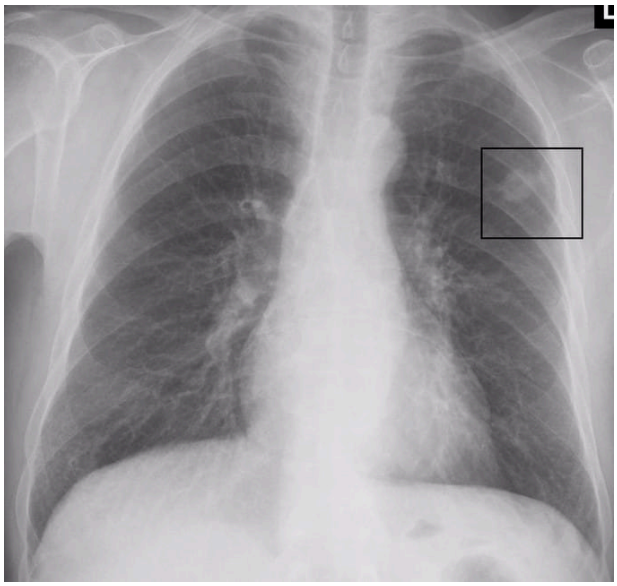
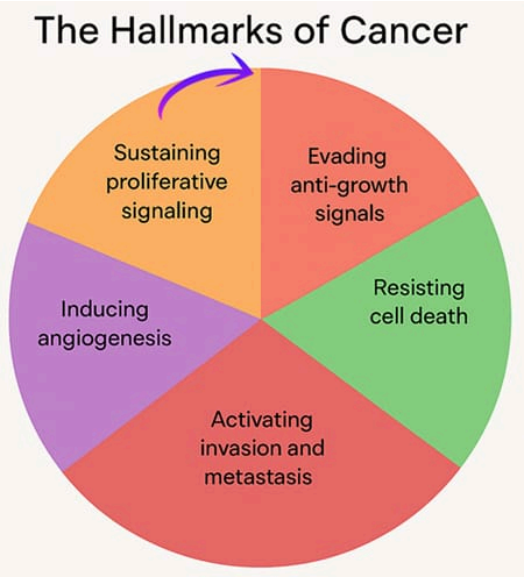


Figure 3.8.1: **Chest x-ray showing lung cancer in the left lung.** A tumor present in the lung is marked via the black box.

What Is Cancer?

Cancer is a broad group of diseases characterized by the uncontrolled growth and division of abnormal cells, typically driven by genetic mutations and other cellular changes. Cancers are **malignant neoplasms** — a neoplasm being an abnormal mass of tissue resulting from excessive cell proliferation. Unlike **benign neoplasms**, malignant tumors have the potential to invade surrounding tissues and, in many cases, spread (**metastasize**) to distant organs through the blood or lymphatic system. Metastasis is a major hallmark of cancer and significantly contributes to its severity and the challenge of effective treatment.



Hallmarks of Cancer

The six original hallmarks of cancer, as proposed by Hanahan and Weinberg in 2000, outline the fundamental capabilities that allow cancer cells to grow uncontrollably, survive longer than normal cells, and spread throughout the body. They are:

1. **Sustaining proliferative signaling:** Unregulated cell growth and division.
2. **Evading anti-growth signals:** Continuous growth and division even given contrary signals.
3. **Resisting cell death:** Avoidance of programmed cell death (evading apoptosis).
4. **Enabling replicative immortality:** Unlimited cell division.
5. **Inducing angiogenesis:** Stimulation of new blood vessel growth to supply nutrients and oxygen to the tumor.
6. **Activating invasion and metastasis:** Invasion of tissue and formation of metastases.

Signs and Symptoms

Cancer is often asymptomatic in its early stages; symptoms typically emerge as the tumor grows and begins to invade surrounding tissues. Early symptoms usually reflect a loss of function in the affected organ.

For example, individuals with lung cancer may experience breathlessness and a persistent cough, although symptoms can vary significantly between patients. Because many cancer-related symptoms overlap with those of other conditions, early diagnosis is frequently challenging.

As the disease progresses, systemic symptoms such as unexplained weight loss, fatigue, and fever may develop. Signs of metastasis — such as swollen lymph nodes, or enlargement of the liver or spleen — can also appear.

Classification

Cancers are classified based on the type of cell from which they originate, with the assumption that tumor cells resemble their tissue of origin. The main categories include:

- **Carcinoma**: Cancers that arise from **epithelial cells**, which line the inner and outer surfaces of the body. Carcinomas are the most common type of cancer, particularly in older adults, and include most cancers of the **breast, prostate, lung, pancreas, and colon**.

- **Sarcoma**: Cancers originating from **connective tissues** such as **bone, cartilage, fat, muscle, and blood vessels**. These tissues develop from **mesenchymal cells**. Mesenchymal cells, often referred to as **mesenchymal stem cells (MSCs)**, are **multipotent** stem cells that can differentiate into various types of connective tissue cells, including fibroblasts, osteoblasts (bone cells), chondroblasts (cartilage cells), adipocytes (fat cells), and myoblasts (muscle cells)
- **Lymphoma and leukemia**: Both arise from **hematopoietic (blood-forming) cells**. **Leukemias** typically originate in the bone marrow and circulate in the blood, while **lymphomas** originate in lymphatic tissues (such as lymph nodes).
- **Germ cell tumor**: Cancers derived from **pluripotent germ cells**. These most often occur in the **testes** (e.g., seminoma) or **ovaries** (e.g., dysgerminoma), but can occasionally appear in other sites.
- **Blastoma**: Cancers that arise from **immature or embryonic precursor cells**. Blastomas are most commonly diagnosed in children.

This classification by cell or tissue of origin provides a foundation for understanding the biology, prognosis, and treatment of different cancer types.

Causes of Cancer

Cancer develops when cells acquire genetic mutations that disrupt normal control of cell growth and division, allowing cells to grow uncontrollably. **These mutations may be inherited or acquired over a lifetime due to environmental exposures and lifestyle choices.**

Environmental and Lifestyle Factors

Research suggests that 80–90% of cancers are linked to environmental and lifestyle factors that increase cancer risk, including:

Chemical Carcinogens:

- **Smoking**, the leading preventable cause of cancer, especially lung and several other cancers.
- **Obesity**, which increases the risk of cancers such as breast, colon, and endometrial cancer.
- **High alcohol consumption,** associated with cancers of the mouth, throat, liver, and breast.
- **Environmental pollutants,** including asbestos, arsenic, and certain chemicals in polluted air, water, or food.

Physical Carcinogens:

- Damage to DNA caused by exposure to ionizing radiation, such as **X-rays**, and
- **ultraviolet (UV) radiation** from sunlight.

Biological Carcinogens:

- Chronic infections with certain **viruses**, including human papillomavirus (HPV) and hepatitis B and C viruses, as well as some
- **bacteria**, such as Helicobacter pylori, and
- **parasites** can increase cancer risk.

Aging:

- The risk of developing cancer increases with age, due to both accumulated genetic damage and decreased effectiveness of cellular repair mechanisms.

It is important to understand that being exposed to these factors does **not guarantee** that someone will get cancer. It simply **raises the risk** compared to people not exposed to them. Cancer usually results from a combination of genetic susceptibility and prolonged exposure to one or more risk factors.

Genetic Risk Factors

While most cancers are linked to environmental and lifestyle factors, **genetics also play a role**:

- Some people **inherit mutations** in specific genes that significantly increase their cancer risk.
    - A classic example: people with inherited mutations in the **BRCA1** or **BRCA2 genes** face a much higher risk of developing breast and ovarian cancers.
- Other genetic syndromes and mutations exist, but strong inherited risks account for only a minority of all cancer cases.

Most cancers result from a **complex interaction** of these factors, and the presence of multiple risks over time raises the likelihood of cancer developing.

Genetics of Cancer

Cancer is a disease characterized by dysregulated cell proliferation. At the genetic level, this proliferation is normally controlled by the balanced expression of genes that either promote or inhibit cell growth. Mutations — often triggered by environmental or lifestyle factors — can alter the expression or function of these regulatory genes, leading to uncontrolled cell division.

These genes fall into two major categories:

- **Oncogenes**: Genes that promote cell growth and division, such as *MYC*. When abnormally activated or overexpressed, they can drive excessive proliferation.
- **Tumor suppressor genes**: Genes that inhibit cell division or promote cell death, such as *TP53*. When inactivated or underexpressed, they fail to restrain cell growth.

Malignant transformation can result from the formation of abnormal oncogenes, the inappropriate activation of normal oncogenes, or the loss of function in tumor suppressor genes. In most cases, multiple genetic alterations are required to convert a normal cell into a cancerous one.

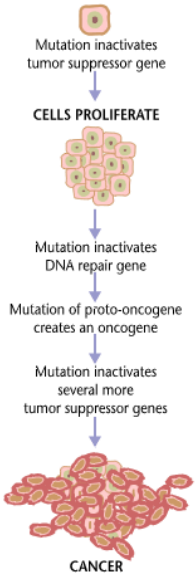


Figure 3.8.2: **Pathway of cancer development.** Cancer develops due to mutations in several key genes that control cell proliferation and survival.

Cancer Therapy: A Personalized Approach

Cancer treatment is not one-size-fits-all. It depends on the type of cancer, where it is in the body, and the needs of the individual patient.

The most common treatment options include:

🩻 Surgery

Surgery is often the first line of treatment for solid, localized tumors. In addition to removing as much of the tumor as possible, surgery allows doctors to collect tissue samples (biopsies) that help determine the exact type and characteristics of the cancer.

💊 Chemotherapy

Chemotherapy uses drugs that kill rapidly dividing cells—like cancer cells. However, it does not specifically target only tumor cells. Other healthy cells that divide quickly, like those in the hair follicles, digestive tract, and bone marrow, are also affected. This explains the common side effects such as hair loss, nausea, and fatigue.

☢️ Radiation Therapy (Radiotherapy)

Radiotherapy uses high-energy ionizing radiation to destroy cancer cells. It is usually aimed directly at the tumor site to minimize damage to surrounding healthy tissue. Radiation may be used alone (for example, in some early-stage head and neck cancers), but is more commonly combined with surgery or chemotherapy.

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3.9: Introduction to the Integumentary System

The integumentary system covers the entire body and functions in protection, temperature regulation, sensation, and vitamin D production.

Master this section and you'll be able to

- Identify the main components of the integumentary system.
- Outline its various functions.

When you look at your skin in the mirror, what comes to mind? Maybe you think about covering it with makeup, adding a new tattoo, or getting a piercing. But have you ever paused to consider that your skin is part of one of the body's **most essential and dynamic systems** — the **integumentary system**?

The integumentary system includes your **skin and its accessory structures**, such as **hair, nails, sweat glands, and oil glands**. And it does *way* more than influence your appearance. This system is your body's first line of defense and helps you **regulate temperature**, **sense your surroundings**, and even **make vitamin D** from sunlight.

Fun fact: Your skin alone accounts for about **16% of your body weight** and covers **1.5 to 2 square meters.** This makes the integumentary system **the largest organ system** in the human body!

Because it shields your delicate internal organs from harm, the skin deserves daily **care and protection** — just like your heart, lungs, and brain. After all, it is not just a surface... it is a living, responsive barrier that helps keep you healthy and safe.

In part 2 of Module 3 you will learn about the structure and function of the integumentary system, as well as some of the diseases, disorders, and injuries that can affect this system.

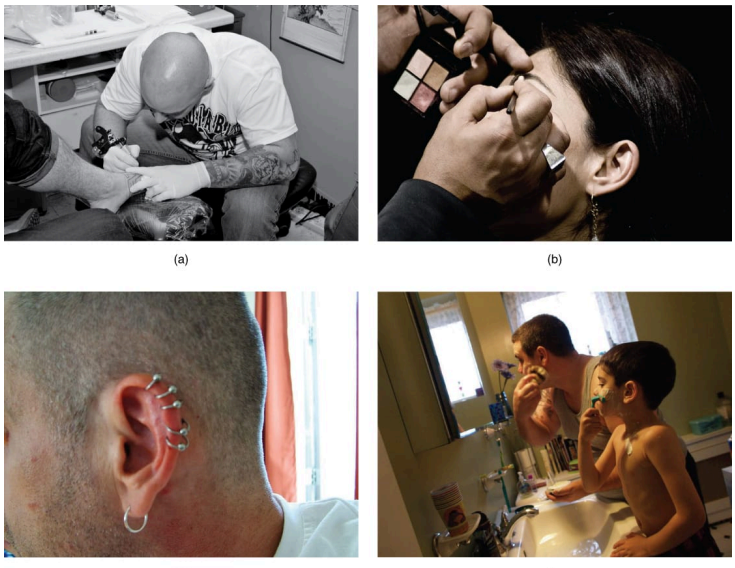


Figure 3.9.1: **Your Skin is a Vital Part of Your Life and Appearance** (a–d). Some people choose to embellish it with tattoos (a), makeup (b), and even piercings (c). (credit a: Steve Teo; credit b: "spaceodissey"/flickr; credit c: Mark/flickr; credit d: Lisa Schaffer)

🌟 More Than Skin Deep: Meet the Integumentary System

Let's make sure everybody understands right away: **your skin and your integumentary system are *not* the same thing**!

- The **skin** is one **organ** that covers the outside of the body and is made of layers (**epidermis**, **dermis**, and underlying

hypodermis).

- The **integumentary system** is the skin **and** everything that grows out of or works with it: hair, nails, sweat glands, oil (sebaceous) glands, and related nerves and tissues.

Students often use the terms interchangeably, but while the skin is the most visible part, it is just **one** piece of a much larger and more impressive puzzle.

The Integumentary system includes:

- 🧍 **Skin** – your body's largest organ and a multilayered marvel of protection.
- 💇 **Hair** – helps regulate heat and provides sensory input.
- 💅 **Nails** – protect your fingertips and help with fine motor tasks.
- 💦 **Sweat glands** – regulate body temperature through perspiration.
- 🛢️ **Sebaceous (oil) glands** – help waterproof and soften the skin.
- 🖐️ **Sensory receptors —** allow you to sense light touch, vibration, pain and more.

In summary, the **integumentary system** is your body's outermost line of defense — a high-functioning team that protects you, helps regulate your temperature, keeps you in touch with your surroundings, and even plays a role in **vitamin D synthesis** (a.k.a. the sunshine vitamin ☀️).

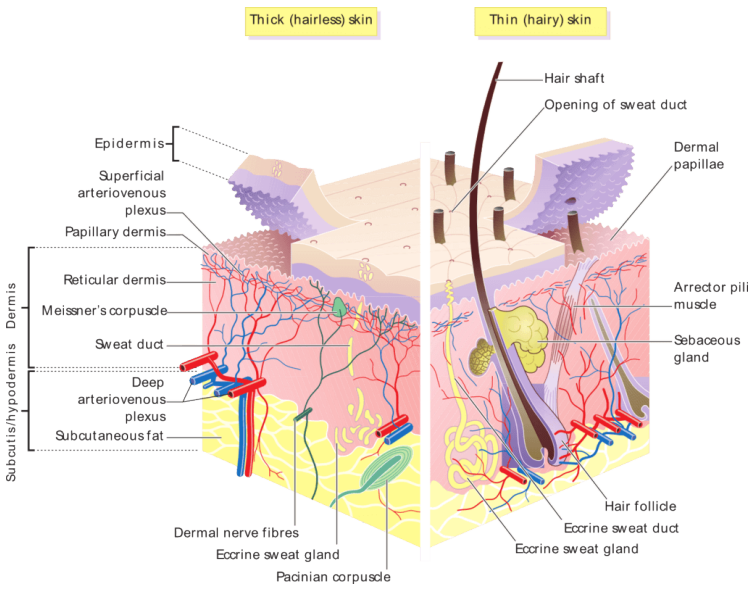


Figure 3.9.2: **Integumentary System Overview —** Cross-section comparing thick (hairless) and thin (hairy) skin with labeled structures like glands, nerves, vessels, and follicles.

Together, these components of the integumentary system work as a team to keep your body functioning smoothly. The **skin and its accessory structures** form a **barrier that protects** deeper tissues from injury, dehydration, and invading pathogens. They also help **regulate body temperature** through processes like sweating and blood vessel dilation or constriction. Specialized sensory receptors embedded in the skin constantly **monitor your environment** — detecting touch, pressure, temperature, and pain — so your body can react quickly and appropriately. In addition, the skin plays a crucial role in **vitamin D synthesis** when exposed to sunlight.

Altogether, these functions support one of the most important jobs of the integumentary system: helping the body maintain **homeostasis**, or internal balance, in the face of changing external conditions.

Understanding that the **skin is just one player** in this system will help you appreciate the complex teamwork involved in keeping your body safe, responsive, and functioning smoothly.

🧠 Want to Remember All the Parts of the Integumentary System?

Try this memory aid:
S.H.A.N.G. = **Skin**, **Hair**, **Accessory glands**, **Nails**, **Glands** (sweat and oil)
Together, they make up your body's "SHANG"ri-La of protection and regulation!

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3.10: Structure of the Skin — Epidermis

The epidermis is the outer, avascular layer of the skin, made of strata where keratinocytes are produced and mature into a tough, water-resistant barrier that protects the body.

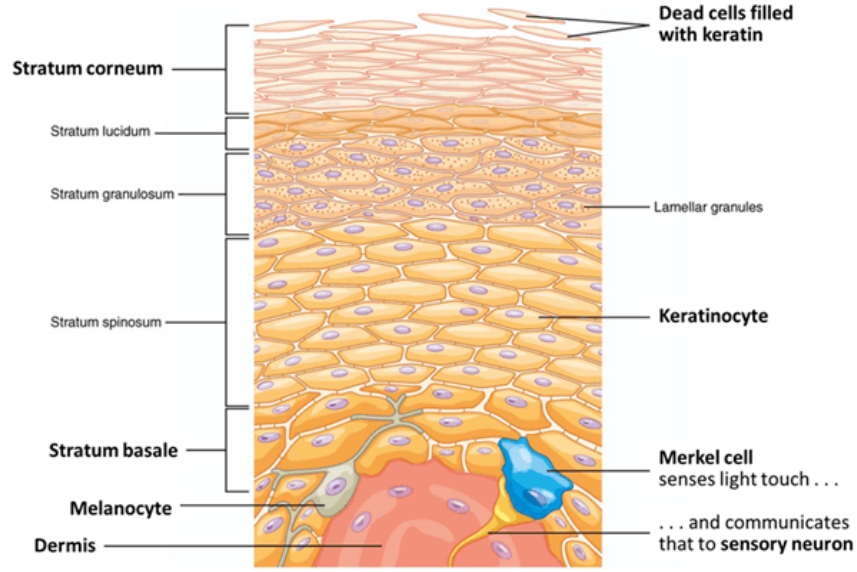
Master this section and you'll be able to

- Identify and describe the layers of the epidermis (focusing on the stratum basale and stratum corneum)
- Explain the process of keratinocyte maturation and how structural changes support skin function.

The epidermis provides a protective waterproof barrier that also keeps pathogens at bay and regulates body temperature.

Layers of the Epidermis

The **epidermis** is the outermost layer of your skin — the part you can see and touch. Unlike deeper layers, it has **no blood vessels of its own**. That is why shaving usually does not cause bleeding, even though it removes countless skin cells. Bleeding only happens if you cut deep enough to reach the layers below, where the blood supply is located.



The **epidermis** is made up of **four distinct layers**, or **strata**.

In areas subject to frequent friction — like the **palms of your hands** and the **soles of your feet** — a **fifth layer** — the stratum lucidum — is present to provide extra protection.

Memory tip: 💡 "**Lucy** is only found in **thick** skin"

From **the most superficial to the deepest**, the layers of the epidermis are:

- **Stratum corneum** (basal layer)
- Stratum lucidum *(only in thick skin)*
- Stratum granulosum
- Stratum spinosum
- **Stratum basale or stratum germinativum** (horny layer).
  The term **stratum germinativum** reflects the layer's key role in **cell division** or "germination." Derived from the Latin

germinare, meaning “to sprout” or “to grow,” the name highlights its function as the **regenerative base** of the epidermis. This layer contains **mitotically active basal cells** that continually divide to produce new **keratinocytes**, which migrate upward through the epidermis. These basal cells act as **epidermal stem cells**, essential for maintaining and replenishing the skin.

The Stratum Basale: Your Skin’s Cellular Birthplace

The **stratum basale** (also called the **stratum germinativum**) is the **deepest layer of the epidermis** — the one closest to the blood vessels in the **dermis** just below.

This layer is a big deal. Why? Because **it is the only part of the epidermis where cells divide** (through mitosis). That is why it gets the name *germinativum* — think “germinate” or “grow.”

The main cells made here are called **keratinocytes**, and they are the most common cells in the entire epidermis. In fact, while the epidermis also contains melanocytes, Merkel cells, and immune cells, the epidermis is made up of 95% keratinocytes. The stratum basale is primarily made up of **basal keratinocyte cells**, which can be considered the **stem cells of the epidermis**. They divide to form the keratinocytes of the stratum spinosum, which migrate superficially. Keratinocytes produce **keratin**, a tough, protective protein that helps shield us from microbes, chemicals, and physical injury.

🧪 **Fun Fact**: Your body makes **millions** of new keratinocytes every single day in the stratum basale!

As new cells form, they start to **push older cells upward** through the layers of the epidermis. While traveling toward the surface, these older cells **change in shape, structure, and chemistry.** That is what gives each layer (or *stratum*) of the epidermis its unique look and function.

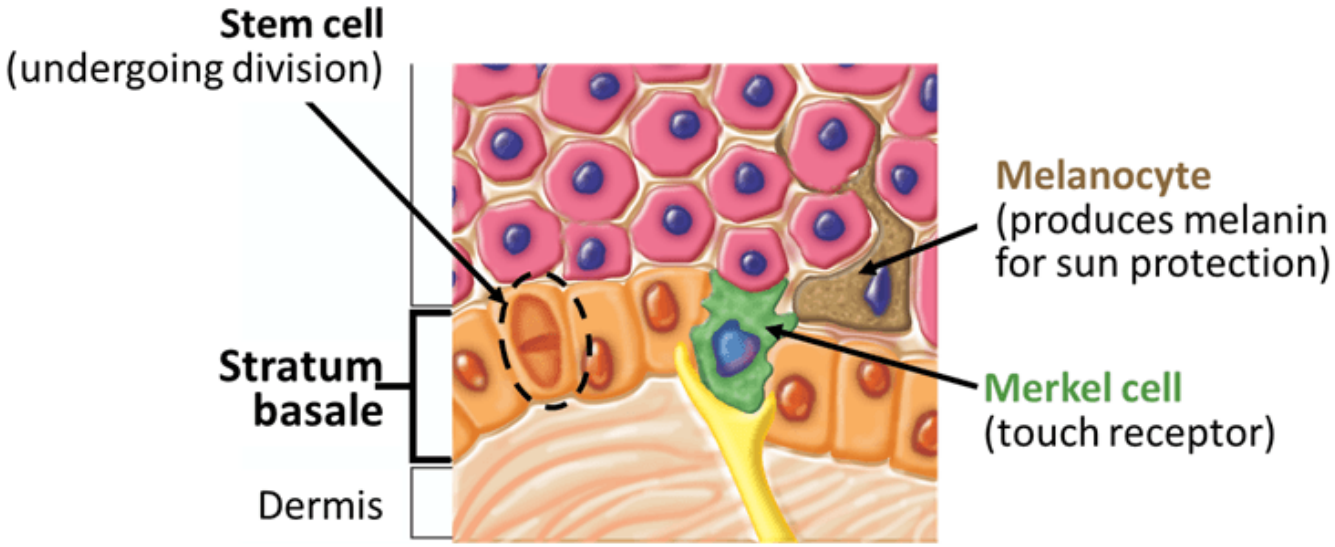
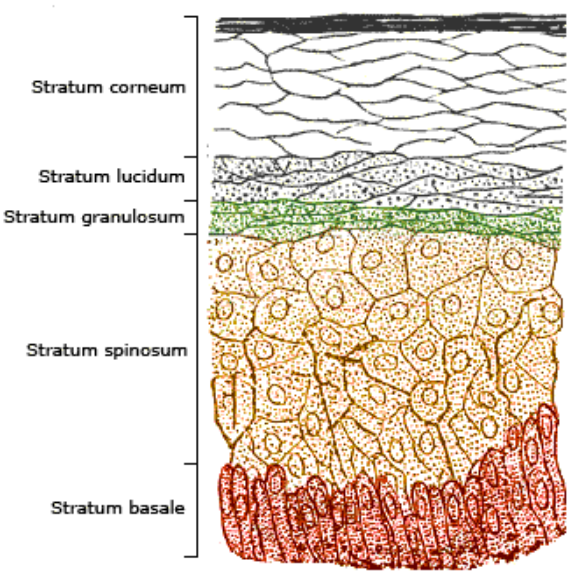


Figure 3.10.1: **Stratum basale.** Section of epidermis showing stem cells, melanocyte, and Merkel cell in the stratum basale.

Stratum Spinosum, Granulosum, and Lucidum: What Happens to Your Skin Cells



When a **keratinocyte stem cell** divides in the **stratum basale**, one daughter cell remains behind as a stem cell, while the other becomes a regular **keratinocyte** and begins its journey upward, starting to produce **keratin**.

The first layer it enters is the **stratum spinosum**, named for the **spiny shape** of its cells.

Next, the keratinocyte moves into the **stratum granulosum**, which gets its name from the **granules** found in its cells. Here, the keratinocyte produces large amounts of **keratin** and becomes increasingly filled with it — a process called **keratinization**. As this happens, the cells become **flatter, more brittle**, and eventually **lose their nuclei**. Deprived of nutrients and oxygen from the blood supply below (in the dermis), the keratinocytes **die** as they continue moving upward.

📌 In **thick skin** (such as the palms of your hands and soles of your feet), there is one extra layer to pass through: the **stratum lucidum**. This layer is named for its **clear (lucid)** appearance under the microscope and is found only in these **hairless, high-friction areas** where the skin is thickest.

By the time the keratinocytes reach the **stratum corneum** — the **outermost layer** — they are **dead, flat cells packed with keratin**. This top layer acts like a **protective shield**, keeping out microbes and helping to prevent water loss.

Stratum Corneum

The **stratum corneum** (also called the **horny layer**) is the **outermost layer of the epidermis** — the part you can see and touch. It contains 15 - 30 layers of dead cells.

The keratinocytes in this layer are called **corneocytes**. These cells are **filled with keratin** and **no longer have a nucleus or organelles**. They are the **final stage** of **keratinocyte differentiation**, which starts in the stratum basale, continues as the cells move upward, and finally ends in the stratum corneum.

In short, **corneocytes function as your skin's shield.** They form a **tough barrier,** shielding the deeper layers from many manners of environmental harm. The stratum corneum is also **resistant to water penetration**, preventing you from drowning in the rain

Eventually, corneocytes are **shed into the environment** and become the **dandruff in our hair**, and a part of the **dust in our homes.** Dust mites, microscopic, insect-like creatures — actually tiny arachnids, related to spiders and ticks — love to feed on flakes of dead skin shed by humans and pets.🪰 Though you cannot see them with the naked eye, they are present in nearly every household, thriving particularly in warm and humid environments 😱.

The entire journey — from a brand-new keratinocyte in the stratum basale to a flaked-off corneocyte in the stratum corneum —

takes about **15 to 45 days**.

Exfoliation is the process of removing this outermost layer of dead skin cells. Cosmetic treatments like **microdermabrasion** or **chemical peels** help slough off some of the dry, dull surface, aiming to make the skin appear **fresher and healthier**. Fun fact: the **ancient Egyptians** were among the first to recognize the beauty benefits of exfoliation!

⚠️ However, **overdoing exfoliation** can harm the living tissue underneath and lead to irritation or damage. Moderation is key.

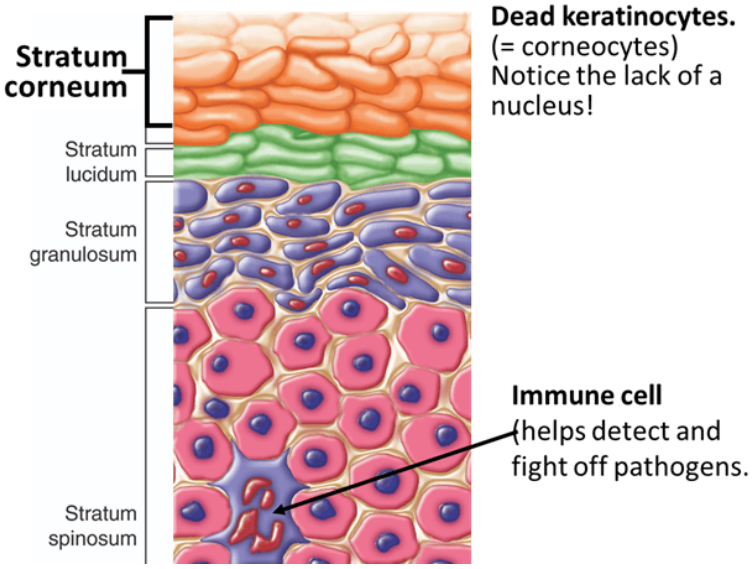


Figure 3.10.2: **Stratum corneum.** Layers of the epidermis showing keratinocytes from stratum spinosum to stratum corneum.

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3.11: Melanin and Skin Color

Skin color is determined largely by the amount of melanin pigment produced by melanocytes in the skin.

Master this section and you'll be able to

- Explain how differing degrees of skin color are produced.
- Outline how melanin helps shield the skin from UV rays.
- Describe how genes and sunlight affect skin color.
- Identify the cause and effects of albinism.

Melanin

Melanin is a natural pigment primarily responsible for the color of human skin, hair, and eyes. It is produced by specialized cells known as **melanocytes**, irregularly shaped cells located in the basal layer (stratum basale) of the epidermis. Their name is derived from two parts: **melano-**, which means **black** or darkness, and **-cyte**, which means **cell**.
The synthesis of melanin, called **melanogenesis**, takes place within the melanocytes in organelles called **melanosomes**. There are two main types of melanin:

- **Eumelanin**, which is brown to black and most abundant, and
- **Pheomelanin**, which is yellow to red.

Interestingly, most people have about the same number of melanocytes. What makes the difference is ***how much*** melanin these cells produce and what type.

🧬 Your genes largely control how much melanin your body makes, but environmental factors — especially exposure to sunlight — also play a big role. When your skin is exposed to ultraviolet (UV) rays, melanocytes respond by producing more melanin. This extra melanin acts like a natural sunscreen by absorbing and scattering harmful UV rays, protecting your skin cells' DNA from damage that could lead to mutations or skin cancer.

☀️ However, there is a trade-off. High levels of melanin can make it harder for your skin to produce vitamin D from sunlight. This highlights the delicate balancing act between UV protection and keeping your metabolism healthy.

In summary, melanin is critical not only for determining skin color but also for protecting the body from environmental hazards such as UV radiation. Its production is intricately controlled by genetic, hormonal, and environmental factors, making skin color a complex trait influenced by both biology and external conditions.

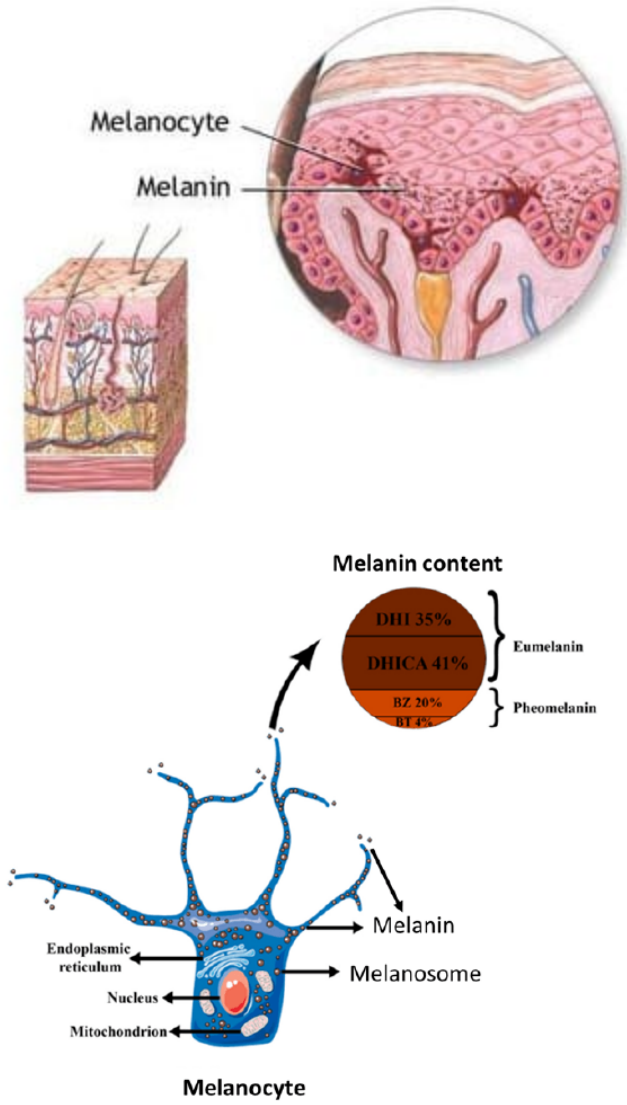


Figure 3.11.1: **Melanocytes.** On the left is a cross-section of skin showing melanocytes in the stratum basale. On the right is a schematic illustration of a melanocyte releasing melanin from its melanosomes.

How Skin Color is Determined

Human skin color is primarily determined by the **amount, type, and distribution of melanin**. Since nearly all people — regardless of background — have about the same number of melanocytes in their skin, the diversity in skin color arises from genetic differences that control how active these melanocytes are, how much melanin they produce, and the types (such as **eumelanin** and **pheomelanin**) that are synthesized. The **genetics** of each individual play a key role: multiple genes influence melanin production and the characteristics of melanosomes (the organelles where melanin is made and stored).

In addition to genetics, **environmental factors** — especially exposure to ultraviolet (UV) radiation from sunlight — also significantly influence skin color. UV exposure triggers increased melanin production in the skin, resulting in what we commonly call a tan. This **facultative pigmentation** (as opposed to the **constitutive** or genetically determined baseline color) serves a protective function: **melanin absorbs and disperses UV rays,** reducing the risk of DNA damage, sunburn, and skin cancers. Some areas of the body, such as nipples, moles, and the palms, can have a different shade than the surrounding skin due to local variations in melanocyte activity and melanin type. For example, dark-skinned individuals often have lighter palms and soles, while lighter-skinned individuals may have darker nipples and moles, reflecting these local differences in melanin distribution and type.

In summary, both genetics and environmental exposure work together to determine a person's skin color, with melanin acting as

the key pigment in this process.

The system is complex: **over 100 genes** have been found to influence pigmentation, and the process can be modified by sun exposure over a person's lifetime.

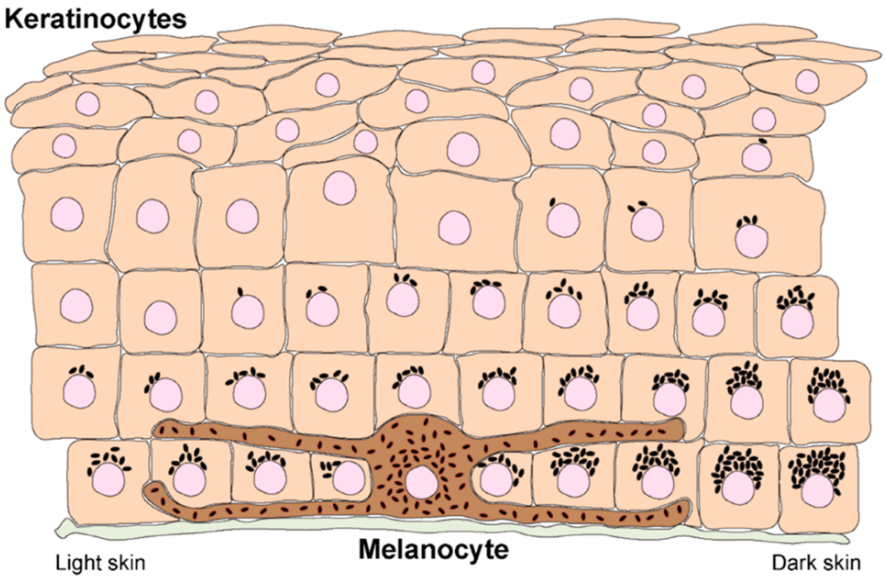


Figure 3.11.2: **Melanocyte Activity.** In individuals with dark skin, melanocytes transfer more melanin to keratinocytes than in those with light skin. Within keratinocytes, this melanin forms protective supranuclear caps — positioned just above the nuclei — where it absorbs and scatters ultraviolet (UV) radiation. These caps serve as physical shields, helping to protect the DNA from UV-induced damage and mutations.

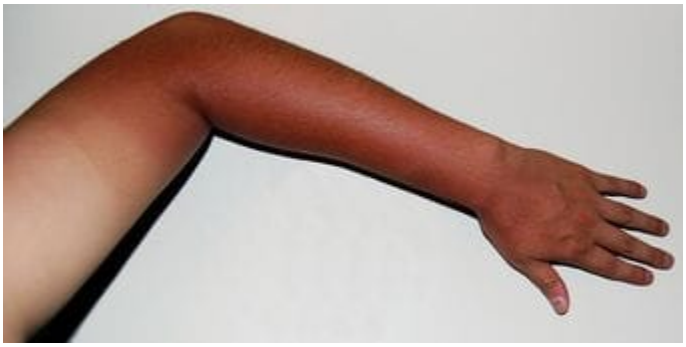


Figure 3.11.3: **Tanned Skin.** Exposure to UV radiation through tanning causes changes in the pigmentation of the skin by increasing melanin production.

The Role of Keratinocytes

Although people with darker skin have more active melanocytes than those with lighter skin, the visible tone of our skin also depends on keratinocytes (the most abundant cells in the epidermis). Keratinocytes receive melanin from neighboring melanocytes. Each melanocyte extends multiple dendritic processes, or "arms," allowing it to contact and transfer melanin to **up to 40 surrounding keratinocytes**, establishing what is known as the **epidermal-melanin unit**.

Melanin is packaged within organelles called melanosomes, which are transported from the body of the melanocyte out to the tips of these dendrites. From there, melanin is transferred to keratinocytes through several possible mechanisms, including phagocytosis (where keratinocytes engulf pieces of melanocyte dendrite containing melanin), membrane fusion, or transfer of vesicles loaded with melanin. Once inside the keratinocytes, the melanin forms protective "**caps**" above the cell nucleus, shielding the cell's DNA from ultraviolet (UV) radiation. This process is crucial for **photoprotection**, as DNA damage from UV light can lead to mutations and skin cancer.

Albinism

A lack of melanin production results in a condition called albinism, which is marked by **extremely light skin**, **hair, and eye color** due to the **absence or dysfunction of the enzymes necessary for melanin synthesis**. These individuals receive very little or no melanin in their keratinocytes, making them especially sensitive to the sun and at higher risk for UV-induced skin damage.



Figure 3.11.4: **Albinism.** Albinism is more common in Africa than in most other regions, with prevalence estimates ranging from about 1 in 5,000 to 1 in 15,000 people, and even higher in some Southern African populations, such as the Tonga tribe in Zimbabwe (up to 1 in 1,000). Regional and ethnic variations are influenced by genetics and social factors like consanguinity. Because albinism is more visually apparent in darker-skinned populations, it is more widely recognized in Africa. This, combined with limited access to sun protection and healthcare, makes albinism a notable public health concern due to increased risks such as skin cancer and social stigma.

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3.12: Structure of the Skin — Dermis and Hypodermis

The dermis consists of a papillary and a reticular layer that serve to protect and cushion the body from stress and strain.

Master this section and you'll be able to

- Differentiate among the regions of the dermis.
- Describe the structure and function of the hypodermis.

🧁 Layers of the Skin: Think of It as a Three-Layered Cake

Your skin is made up of three main layers, each with its own unique structure and function:

- **Epidermis (Top Layer):** A thin, protective barrier — the part you see and touch.
- **Dermis (Middle Layer):** The supportive core where most of the important action happens.
- **Hypodermis (Bottom Layer):** A cushiony base made mostly of fat and connective tissue — great for insulation and padding.

💪 Meet the Dermis

As you now know, lying just beneath the epidermis is the dermis — a much thicker and sturdier layer that quietly handles most of the heavy lifting. It is often described as the “tough” layer of the skin because much of it is built from **dense irregular connective tissue** packed with **collagen** and **elastin fibers**. These fibers give your skin its **strength, elasticity, and resilience**, making it far more resistant to tearing and stretching than the fragile epidermis above.

The dermis itself is subdivided into two layers:

- **Papillary region** (upper layer): **Loose areolar connective tissue** with **blood vessels and sensory receptors**. The papillary region helps form your fingerprints! This layer provides nutrients to the epidermis and helps with temperature regulation.
- **Reticular region** (deeper layer): Because it is composed of **dense irregular connective tissue rich in collagen and elastin fibers**, the reticular region is where most of the dermis’s strength resides, and why it is well-suited for durability and stretch.

The dermis is also where the following important structures can be found:

- **Blood vessels** 🩸: Keep your skin nourished and help with body temperature control.
- **Nerve endings** 🧠: Let you feel pressure, pain, heat, cold, and touch.
- **Hair follicles** 💇: Anchors for your hair.
- **Sweat and oil glands** 💦: Help regulate temperature and keep your skin moisturized.
- **Immune cells** 🛡️: First responders to germs or injury.

The primary function of the dermis is to cushion the body from stress and strain. Thanks to the dermis, your skin is strong and flexible, heals after injuries, senses touch, temperature, and pain, and even helps to maintain proper body temperature. Without the dermis, we would be fragile, numb, and poorly protected from the outside world.

Did You Know Leather Comes from the Dermis?

Yep — that leather jacket, wallet, or belt you own? It started as **animal skin**, and not just any part — it is made from the **dermis**, the thick collagen-packed middle layer. Most leather comes from cows, but goats, pigs, and sheep also donate their dermis to fashion and function.

The process of transforming skin into leather is called **tanning**, and it is all about turning soft, biological tissue into something **tough, flexible, and rot-resistant**. Let's look at the **Steps of Leather Processing:**

1. **Preparation:** The hide is soaked to remove dirt and rehydrate the tissue. The **epidermis and hair are removed** (typically through a chemical process called *liming*), leaving behind the **collagen-rich dermis**.
2. **Fleshing & Splitting:** Any remaining **fat, muscle, or subcutaneous tissue** is scraped away. The dermis may then be **split into thinner layers**, depending on the desired leather type (e.g., **top-grain** vs. **split leather**).
3. **Tanning:** The cleaned dermis is soaked in **tanning agents** (such as chromium salts or plant-based tannins). These chemicals **stabilize collagen fibers**, preventing rot and making the leather **durable and flexible**.
4. **Drying & Finishing:** The tanned leather is **dried, dyed, softened**, and **treated with oils, waxes, or protective coatings** — tailored to its final use, whether for **footwear, upholstery, bags, or belts**.

So the next time you see a leather item, remember: **you are looking at preserved dermis** — the same layer of skin that gives *your* body strength, elasticity, and sensory power!

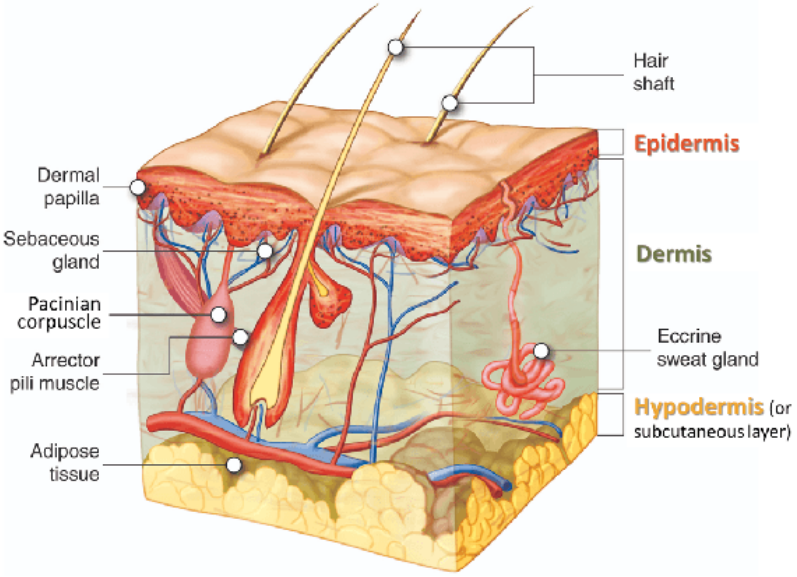


Figure 3.12.1: **Human Skin.** Cross-section of human skin showing epidermis, dermis, and hypodermis with labeled structures.

The Papillary Layer

The **papillary layer** of the dermis plays a vital role in supporting the **epidermis**, the skin's outer layer. It **delivers nutrients** to the epidermis, which lacks its own blood supply, allowing it to produce new keratinocytes. This layer also helps **regulate skin temperature**, contributing to overall body temperature balance.

Both nutrient delivery and temperature regulation are made possible by the **dense network of capillaries** within the papillary layer. These blood vessels also carry away **waste products** from the surrounding cells — a crucial job, since waste buildup could otherwise damage or kill skin cells.

In **light-skinned individuals**, the **pinkish hue** of the skin is due to these blood vessels. When you **blush**, it is the dilation of vessels in this layer that causes the reddening of your skin.

This layer gets its name from the **dermal papillae** — uneven, finger-like projections that interlock with the epidermis above. (Check the image above.) The papillae not only **strengthen the connection between the two skin layers** but also **form the patterns that make up your fingerprints**.

The Reticular Layer

The **reticular layer** is the deeper portion of the dermis, and it plays a key role in **strengthening the skin** and giving it **elasticity** — the ability to stretch and return to its original shape (like after a pinch or pull). This layer is densely packed with **collagen and elastin fibers**, which provide the skin with both durability and flexibility.

It also houses many important **structures**, including:

- **Hair follicles**
- **Sweat glands** — of two types:
    - **Apocrine glands**, found in the armpits and groin, contribute to **body odor** when their secretions mix with skin bacteria.
    - **Eccrine glands**, found all over the body, help **cool us down** by releasing sweat that **evaporates** from the skin surface.
- **Sebaceous glands**, which secrete **sebum** — an oily substance that **moisturizes and protects** the skin and hair from drying out.

In addition, the reticular layer contains:

- **Nerve endings** that detect sensations such as **pain, pressure, temperature, and itch**
- **Lymphatic vessels**, which help transport **immune cells** that defend against pathogens entering through breaks in the skin

Together, the fibers and structures in this layer make the reticular dermis essential for **skin resilience, sensory input, immune defense**, and **temperature regulation**.

The Hypodermis: Your Skin's Supportive Underside

Beneath the dermis lies the **hypodermis**, also known as the **subcutis** or **subcutaneous tissue**. Though not technically part of the skin proper, it plays an essential supporting role. This layer is made up of **loose connective tissue** rich in **collagen fibers** and **fat cells** (adipocytes).

The **fat** in the hypodermis serves several key functions:

- It **insulates** the body, helping to retain heat in cold environments.
- It acts as a **shock absorber**, cushioning internal structures like muscles and organs from physical impacts.
- It also serves as a **backup energy source**, storing calories the body can use in times of need.

Because this layer is soft, vascular, and easy to access, it is also the target site for **subcutaneous injections** — which is where the **"hypodermic" needle** gets its name.

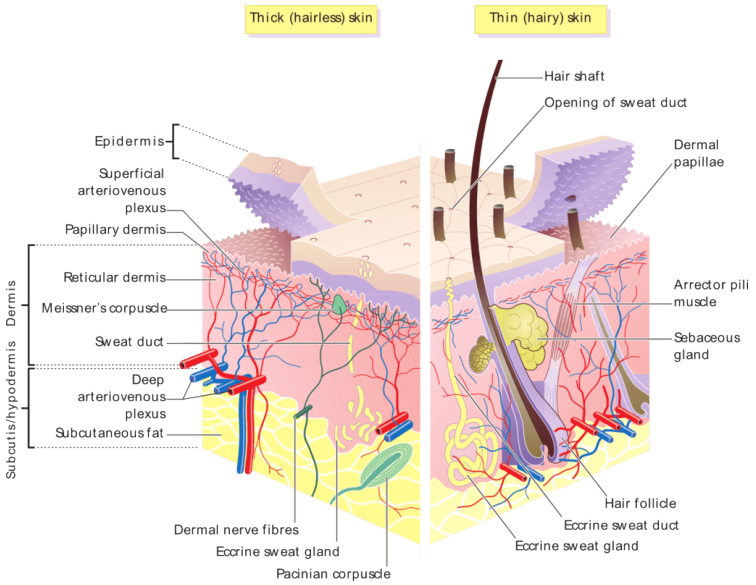


Figure 3.12.2: **Skin and its structures.** Cross-sectional diagram comparing thick (hairless) and thin (hairy) skin. Shows labeled layers: epidermis, dermis (papillary and reticular), and hypodermis. Highlighted are also eccrine sweat glands, hair follicles, nerve fibers, blood vessels, and sensory receptors.

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3.13: Sweat and Sebaceous Glands

Your skin contains two main types of glands: sweat glands, which help cool the body, and sebaceous (oil) glands, which keep the skin and hair moisturized.

Master this section and you'll be able to

- Compare and contrast eccrine and apocrine sweat glands.
- Explain the function of sweat.
- Describe the location and function of sebaceous glands.

Sweat Glands: Your Skin's Built-In Cooling System

Sweat glands, also known as **sudoriferous glands**, are simple tubular structures found almost everywhere on the body. Their primary function is to regulate temperature.

Each sweat gland is made up of two parts:

- A **secretory portion**, where sweat is produced.
- An **excretory duct**, which carries the sweat to the body surface to be excreted.

Sweat is produced in the coiled secretory portion of the sweat gland. This portion is typically located in the dermis, but in some cases, it may extend into the hypodermis. From there, the excretory duct carries the sweat upward through the dermis and into the epidermis, where it opens at a **pore** on the surface.

Humans have two main types of sweat glands: **eccrine** and **apocrine glands**. Eccrine glands are distributed across most of the body and are primarily responsible for regulating body temperature by producing a watery, odorless sweat. In contrast, apocrine glands are concentrated in specific areas such as the armpits and groin. They produce a thicker, milky fluid that, when broken down by skin bacteria, can lead to body odor. Together, these sweat glands play essential roles in thermoregulation and the body's response to stress.

Eccrine Glands

The **most numerous** types of sweat glands in our skin, found almost everywhere on the body, are called **eccrine sweat glands**. These are the true sweat glands in the sense of helping to regulate body temperature. Sweating cools the body through the process of **evaporative cooling**.

When your internal temperature rises, sweat glands release a clear, odorless substance (sweat) consisting primarily of **water and NaCl** onto the surface of your skin. The key to cooling is not just the presence of sweat, but its evaporation. As sweat evaporates, it absorbs heat from your skin because the process of turning water (sweat) into vapor requires energy — specifically, the "heat of vaporization." This energy comes from your body's heat, which is carried away with the vapor, lowering your skin and body temperature. This mechanism is especially important when environmental temperatures are high, since evaporation can still remove heat even if the air temperature is close to or above body temperature.

Apocrine Glands

Apocrine sweat glands are large, specialized glands mainly found in **areas with hair follicles** such as the armpits (axillae), groin, around the nipples (areola), and the perianal region. Unlike eccrine glands, which open directly onto the skin, apocrine glands release their secretions into hair follicles just below the skin surface. While apocrine glands exist at birth, their significant

activity starts during puberty, likely due to hormonal influences.

Apocrine glands produce a thick, oily, and initially odorless secretion containing water, lipids, proteins, and steroids. Their excretions are converted by skin bacteria into various chemicals we associated with **body odor**. Apocrine sweat glands play virtually no role in body temperature regulation; their primary function in humans is thought to be related to scent release rather than cooling.

Structurally, these glands share some basic features with the eccrine glands — they both consist of a **secretory coil** (where sweat is produced) and a **duct** (which transports sweat). However, they differ in several key aspects: apocrine glands are larger and their secretory portion is bigger, with a larger lumen. Additionally their ducts open into hair follicles rather than the skin surface.

Modified apocrine glands include **mammary glands** (which produce milk), **ceruminous glands** (which produce earwax), and **ciliary glands** (on the eyelids).

While the exact function of apocrine glands is still not fully understood, we do know they become active during times of stress, pain, and sexual arousal — though the reasons behind this are not yet clear. Similarly, the purpose of body oder in humans is not completely known, but research suggests it may play an important role in communication. Body odor may act as a **chemical signal**, helping to share information about a person's identity, emotional state, or even genetic compatibility when choosing a mate.

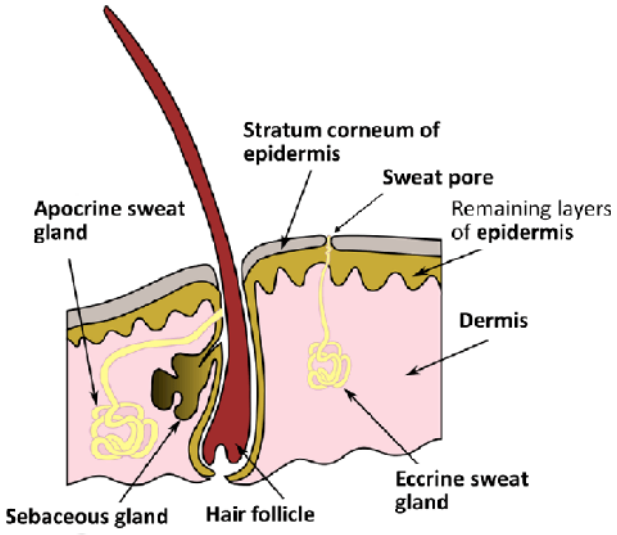


Figure 3.13.1: **Human Skin.** Cross sectional image of skin showing the two types of sweat glands and a sebaceous gland.

Sebaceous Glands

Sebaceous glands (also known as **oil glands**) are the **sebum** producing glands of the dermis. Sebum is an oily substance, composed mostly of lipids mixed with epithelial cell debris. It plays a key role in lubricating and waterproofing the skin and hair, helping to keep them soft, supple, and protected against drying and external damage.

Sebaceous glands develop from the epithelial cells of the hair follicle itself (specifically the external root sheath of the hair follicle). Their ducts thus usually open up into the upper part of a hair follicle, called the infundibulum. However, some sebaceous gland ducts open directly onto our skin surface such as at the corner of the mouth and the glans penis.

They function through a **holocrine secretion process**, meaning the entire gland cell fills with sebum and then ruptures to release its oily content. The cells are continuously regenerated from the gland's periphery.

Sebaceous glands are active from birth, producing a waxy coating that protects newborn skin. They become particularly active

during puberty under hormonal influence. Their secretions also have antimicrobial properties, contributing to skin defense.

While the sebaceous glands are present just about all over the skin, they are notably absent on the palms of the hands and the soles of the feet. The sebum being excreted by your body today began production around 8 days ago.

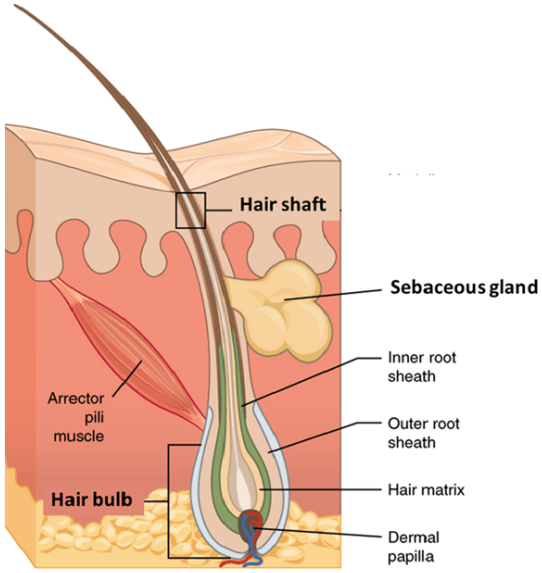


Figure 3.13.2: **Sebaceous Gland.** Schematic view of a hair follicle with sebaceous gland.

As mentioned earlier, **sebum** acts as a natural **lubricant** that helps moisturize the skin. It does this by slowing down the evaporation of water from the skin's surface. Sebum also plays a protective role by limiting the growth of certain bacteria. It contains antimicrobial compounds that help prevent bacteria from penetrating deeper layers of the skin. In addition, sebum helps **condition the hair**, keeping it from becoming too dry or brittle.

Sebaceous glands are involved in several common skin conditions. During puberty, hormonal changes trigger these glands to produce more sebum, which often leads to **oily skin**. If a sebaceous duct becomes clogged with sebum, it can form a **whitehead**. If that trapped material dries and oxidizes, it darkens into a **blackhead**. When a sebaceous gland becomes **infected**, it can lead to more serious forms of acne. (See the last page of the study guide for more details on acne.)

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3.14: No Extra Reading for Skin Discoloration

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3.15: No Extra Reading on the Arrector Pili Muscle

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3.16: Burns

A burn is a type of injury to flesh caused by heat, electricity, chemicals, light, radiation, or friction.

Master this section and you'll be able to

- List common causes of burn injuries.
- Classify burns according to their depth.
- Describe major complications that can result from severe burn wounds.
- Explain what an eschar is.
- Apply the Rule of Nines to estimate the percentage of total body surface area (TBSA) affected by a burn.

A **burn** is an injury to the skin caused by heat, electricity, chemicals, sun exposure, radiation, or friction. Most burns affect the outer layers of the skin — the **epidermis** and **dermis** — and result in the death of skin cells. This cell damage can cause a major loss of body fluids, leading to **dehydration**, **electrolyte imbalance**, and potentially **renal** (kidney) and **circulatory failure**, which can be life-threatening. To prevent these complications, burn patients are treated with **intravenous (IV) fluids** to restore hydration and **IV nutrients** to support tissue repair and protein replacement.

A serious additional risk is **infection** caused by impaired resistance from disruption of the skin's mechanical integrity by the burn and generalized immune suppression. This moist, protein-rich avascular environment encourages microbial growth. As a deep burn starts to heal, the skin barrier is replaced by **eschar** — dead, typically dry and black or brown tissue — that forms on the skin, often over a wound caused by burns. It may require removal to promote healing. Migration of immune cells is hampered by destruction of the vasculature (blood vessels), and there is a release of inflammatory intermediaries that impede the immune response. Eschar also restricts distribution of systemically administered antibiotics because of its avascularity.

As of 2023, the World Health Organization estimated that, globally, approximately 180,000 deaths occur every year from burn injuries (World Health Organization, 2023). The American Burn Association reported in their 2018 update that approximately 486,000 burn injuries occur every year in the United States (American Burn Association, 2018). Thermal injury is the main cause overall, accounting for 86% of burns, whereas electrical (4%) and chemical (3%) burns make up only a small portion of burn injuries.

Types of Burns

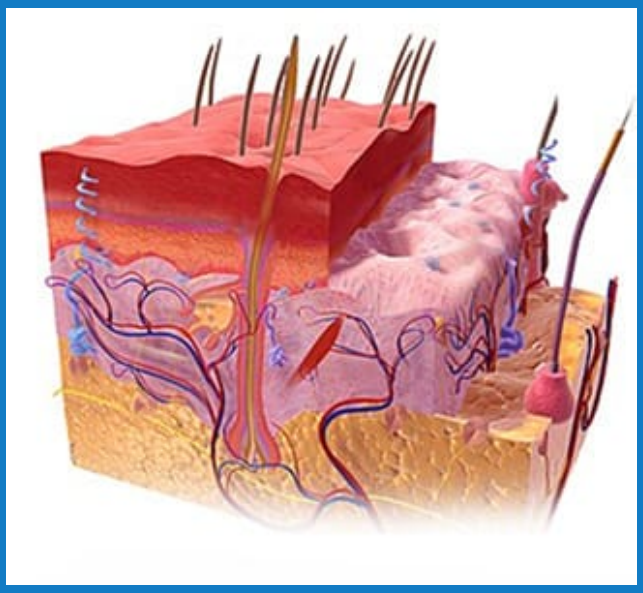
Burns are categorized in different ways:

- **By depth of injury**: Burns are described as **first-, second-, third-,** or **fourth-degree**, depending on how deep the tissue damage goes.
- Burns are also measured in terms of the **size of the total surface area affected.** This is referred to as the "**rule of nines**," which associates specific anatomical areas with a percentage that is a factor of nine.

Classification According to Depth of Injury

First degree burns are limited to the epidermis. Second degree burns extend into the superficial papillary dermis. Third degree burns extend through the entire dermis. Fourth degree burns involve all the skin layers as well as the underlying muscle and bone.







A first-degree burn is a superficial burn that affects only the epidermis. Although the skin may be painful and swollen, these burns typically heal on their own within a few days. Mild sunburn fits into the category of a first-degree burn.

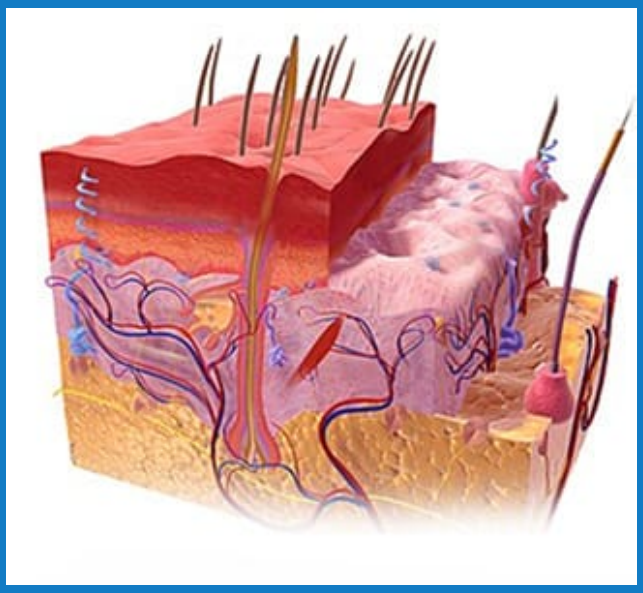


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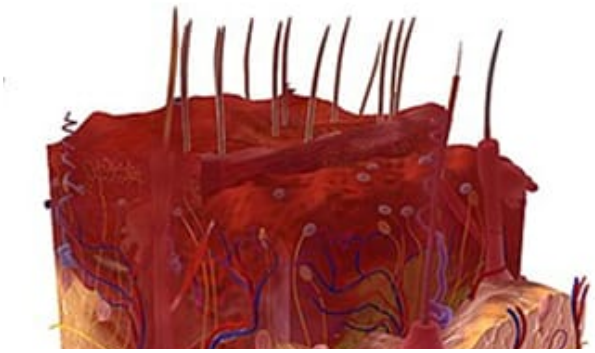




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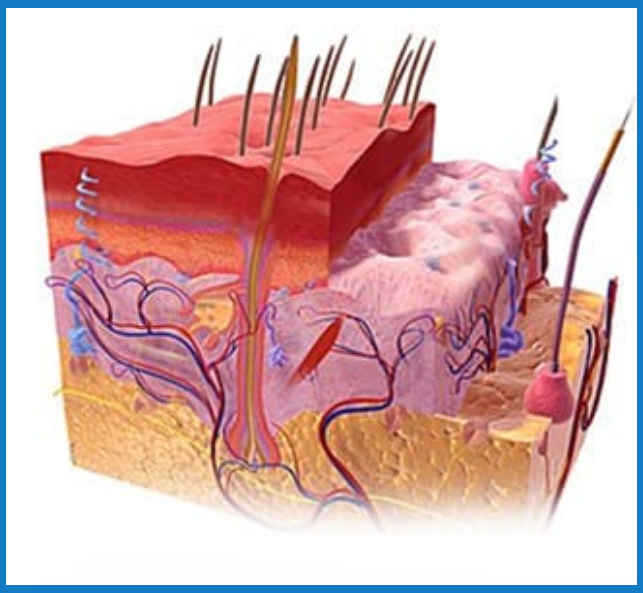


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A first-degree burn is a superficial burn that affects only the epidermis. Although the skin may be painful and swollen, these burns typically heal on their own within a few days. Mild sunburn fits into the category of a first-degree burn.



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A **third-degree burn** fully extends into the epidermis and dermis (= full-thickness burn), destroying the tissue and affecting the nerve endings and sensory function. The black, leathery, and dry areas — particularly around the ankle and lower calf — are characteristic of **eschar**, which is dead, necrotic tissue that forms after a deep burn. Eschar is typically avascular and must often be removed to allow proper healing.

Third-degree burns destroy blood vessels and nerve endings, so the wound may appear dry and insensate rather than wet or painful.

Classification According to the Rule of Nines

The **Rule of Nines** is a method used by medical professionals to quickly estimate the **total body surface area (TBSA)** affected by burns — particularly **second-degree (partial-thickness)** and **third-degree (full-thickness)** burns. This classification is crucial for guiding initial treatment decisions, such as determining the need for **fluid resuscitation** and whether **referral to a specialized burn center** is necessary.

The body is divided into regions that represent **9% or multiples of 9%** of the TBSA:

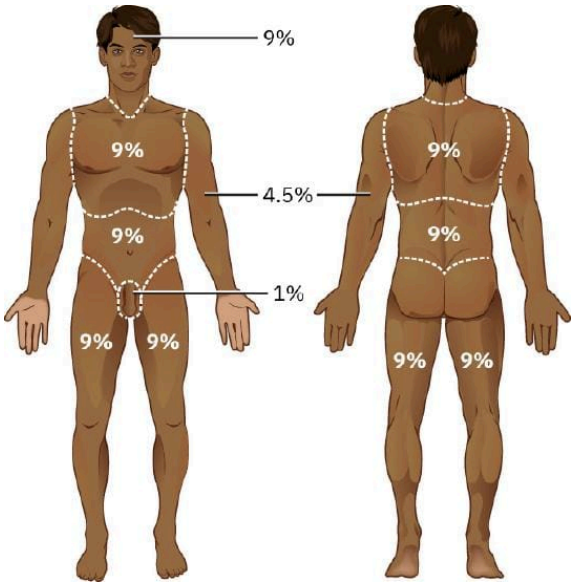


Figure 3.16.1: **Rule of Nines used to calculate the TBSA burned.** Anterior and posterior portions are separate, and the areas are summed to a total score. For example, if a person is burned on their anterior and posterior bilateral upper arms, the TBSA would total 18% (4.5% for left anterior arm + 4.5% for left posterior arm + 4.5% for right anterior arm + 4.5% for right posterior arm). (CC BY 4.0; Rice University & OpenStax)

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3.17: Skin Cancer

Skin cancer is the uncontrolled growth of abnormal skin cells, usually caused by damage from UV radiation.

Master this section and you'll be able to

- Describe what cancer is and how it differs from normal cell growth.
- Distinguish between benign and malignant tumors.
- Compare and contrast the three different types of skin cancer.
- Identify some common causes and risk factors associated with cancer.
- Describe the importance of early detection.

In the first part of this module, you learned what happens when abnormal cells grow and divide uncontrollably. You also discovered that, unlike benign tumors which stay in one place, malignant tumors can invade nearby tissues and spread throughout the body — a condition known as cancer.

Most cancers are identified by the organ or tissue in which they originate. One common form of cancer is skin cancer. The Skin Cancer Foundation reports that one in five Americans will experience some type of skin cancer in their lifetime. Non-melanoma skin cancer is the most common type of cancer in the U.S., but it is often left out of cancer rankings because it is usually easy to treat and rarely deadly.

The degradation of the ozone layer in the atmosphere and the resulting increase in exposure to UV radiation has contributed to its rise. Overexposure to UV radiation damages DNA and leads to mutations. These mutations can result in cell populations that do not die when they should, resulting in uncontrolled cell proliferation that leads to tumors. Although many tumors are benign (harmless), some produce cells that can mobilize and establish tumors in other organs of the body; this process is referred to as metastasis. Cancers are characterized by their ability to metastasize.

Although melanin offers some protection against DNA damage from the sun, often it is not enough. The fact that skin cancers can also occur on areas of the body that are normally not exposed to UV radiation suggests that there are additional factors that can lead to skin cancer.

Basal Cell Carcinoma

Basal cell carcinoma is a form of cancer that affects the mitotically active stem cells in the stratum basale of the epidermis. It is the most common of all cancers that occur in the United States and is frequently found on the head, neck, arms, and back, which are areas that are most susceptible to long-term sun exposure. Although UV rays are the main culprit, exposure to other agents, such as radiation and arsenic, can also lead to this type of cancer. Wounds on the skin due to open sores, tattoos, burns, etc. may be predisposing factors as well. Basal cell carcinomas start in the stratum basale and usually spread along this boundary. At some point, they begin to grow toward the surface and become an uneven patch, bump, growth, or scar on the skin surface. Like most cancers, basal cell carcinomas respond best to treatment when caught early. Treatment options include surgery, freezing (cryosurgery), and topical ointments.



Figure 3.17.1: **Basal Cell Carcinoma.** Basal cell carcinoma can take several different forms. It is marked with irregular, dark-red stripes that resemble tiny blood vessels. The surrounding skin is the same pink color as the carcinoma, but without the red striping or raised appearance. Similar to basal cell carcinoma, it is readily cured if caught early and treated. (credit: John Hendrix, MD)

Squamous Cell Carcinoma

Squamous cell carcinoma is a cancer that affects the keratinocytes of the stratum spinosum and presents as lesions commonly found on the scalp, ears, and hands (Figure 3.17.2). It is the second most common skin cancer. The American Cancer Society reports that two of 10 skin cancers are squamous cell carcinomas, and it is more aggressive than basal cell carcinoma. If not removed, these carcinomas can metastasize. Surgery and radiation are used to cure squamous cell carcinoma.



Figure 3.17.2: **Squamous Cell Carcinoma.** Squamous cell carcinoma presents here as a lesion on an individual's nose. (credit: the National Cancer Institute)

Melanoma

A melanoma is a cancer characterized by the uncontrolled growth of melanocytes, the pigment-producing cells in the epidermis. Typically, a melanoma develops from a mole. It is the most fatal of all skin cancers, as it is highly metastatic and can be difficult to detect before it has spread to other organs. Melanomas usually appear as asymmetrical brown and black patches with uneven borders and a raised surface. Treatment typically involves surgical excision and immunotherapy.



Figure 3.17.3: **Melanoma.** Melanomas typically present as large brown or black patches with uneven borders and a raised surface. (credit: the National Cancer Institute / Centers for Disease Control)

Doctors often give their patients the following **ABCDE mnemonic** to help with the diagnosis of early-stage melanoma. If you observe a mole on your body displaying these signs, consult a doctor.

- **A**symmetry — the two sides are not symmetrical
- **B**orders — the edges are irregular in shape
- **C**olor — the color is varied shades of brown or black
- **D**iameter — it is larger than 6 mm (0.24 in)
- **E**volving — its shape has changed

Some specialists cite the following additional signs for the most serious form, **nodular melanoma**:

- **E**levated — it is raised on the skin surface
- **F**irm — it feels hard to the touch
- **G**rowing — it is getting larger

Career Connection

Dermatologist

Have you ever had a rash that did not respond to over-the-counter creams, or a mole that you were concerned about? Dermatologists help patients with these types of problems and more, on a daily basis. Dermatologists are medical doctors who specialize in diagnosing and treating skin disorders. Like all medical doctors, dermatologists earn a medical degree and then complete several years of residency training. In addition, dermatologists may then participate in a dermatology

fellowship or complete additional, specialized training in a dermatology practice. If practicing in the United States, dermatologists must pass the United States Medical Licensing Exam (USMLE), become licensed in their state of practice, and be certified by the American Board of Dermatology.

Most dermatologists work in a medical office or private-practice setting. They diagnose skin conditions and rashes, prescribe oral and topical medications to treat skin conditions, and may perform simple procedures, such as mole or wart removal. In addition, they may refer patients to an oncologist if skin cancer that has metastasized is suspected. Recently, cosmetic procedures have also become a prominent part of dermatology. Botox injections, laser treatments, and collagen and dermal filler injections are popular among patients, hoping to reduce the appearance of skin aging.

Dermatology is a competitive specialty in medicine. Limited openings in dermatology residency programs mean that many medical students compete for a few select spots. Dermatology is an appealing specialty to many prospective doctors, because unlike emergency room physicians or surgeons, dermatologists generally do not have to work excessive hours or be “on-call” weekends and holidays. Moreover, the popularity of cosmetic dermatology has made it a growing field with many lucrative opportunities. It is not unusual for dermatology clinics to market themselves exclusively as cosmetic dermatology centers, and for dermatologists to specialize exclusively in these procedures.

Consider visiting a dermatologist to talk about why they entered the field and what the field of dermatology is like. Visit this site(opens in new window) for additional information.

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3.18: Acne

Acne, clinically known as acne vulgaris, is a common human skin disease affecting the skin of the face, upper parts of the chest, and back.

Master this section and you'll be able to

- Outline the role of the hair follicles and sebaceous glands in the development of acne.
- Explain the biological and hormonal factors that contribute to acne formation and inflammation.
- Identify a common treatment for acne.

Structure of a Hair Follicle

A hair follicle is a tiny, tube-like structure in your skin that surrounds the root of each hair and helps it grow. Hair follicles are located in both the epidermis and dermis layers of your skin. Together with the sebaceous gland and arrector pili muscle, they form what is called the **pilosebaceous unit** — a team that helps protect and maintain your skin and hair.

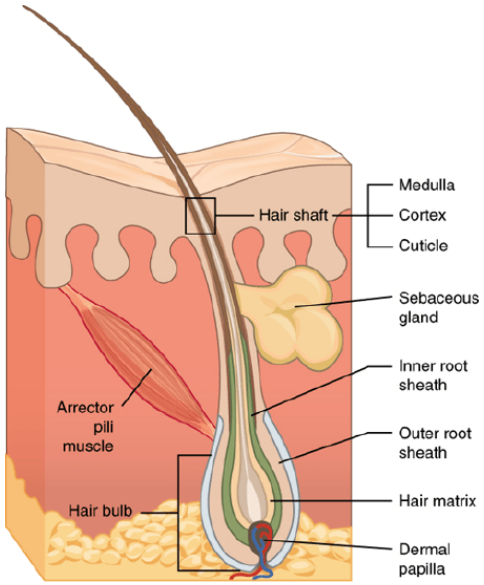


Figure 3.18.1: **Hair Follicle**. The sebaceous gland produces oily secretions that can block the follicle, resulting in a pimple.

What's the Deal with Acne?

Acne vulgaris — better known as just *acne* — is one of the most common (and most annoying) skin conditions out there. It usually pops up in areas loaded with sebaceous (oil) glands, like your **face**, **chest**, and **upper back**.

In fact, over **40 million people in the U.S.** are dealing with acne right now. It affects people of all racial and ethnic groups, and most often appears during the teen years, but it is not just a teenage problem — acne can show up in **infants** and linger into **adulthood**. For most people though, acne diminishes over time and tends to disappear — or at the very least decreases — by age 25.

Why Does Acne Happen?

Blame your hormones. During puberty and just before menstruation, **increased androgen hormone levels** trigger the enlargement of sebaceous glands and boost sebum production. Androgens are steroid hormones that stimulate or controls the development and maintenance of masculine characteristics in vertebrates.
The excess sebum, combined with a buildup of keratin, can clog hair follicles.

Enter ***Cutibacterium acnes*** — a gram-positive, anaerobic bacterium (formerly known as *Propionibacterium acnes*) that normally lives on our skin, especially in the oily environment of sebaceous glands. When pores get blocked, *C. acnes* gets a chance to overgrow and cause an infection. Although this bacterium is found on both acne-prone and clear skin, certain strains are more strongly linked to the development of acne.

The bacterial overgrowth prompts your immune system to respond. White blood cells swarm the area to combat the bacteria, leading to inflammation and the formation of those familiar acne lesions — pus-filled pimples known as "pustules." The pus itself is a mixture of sebum, keratin, and dead white blood cells.

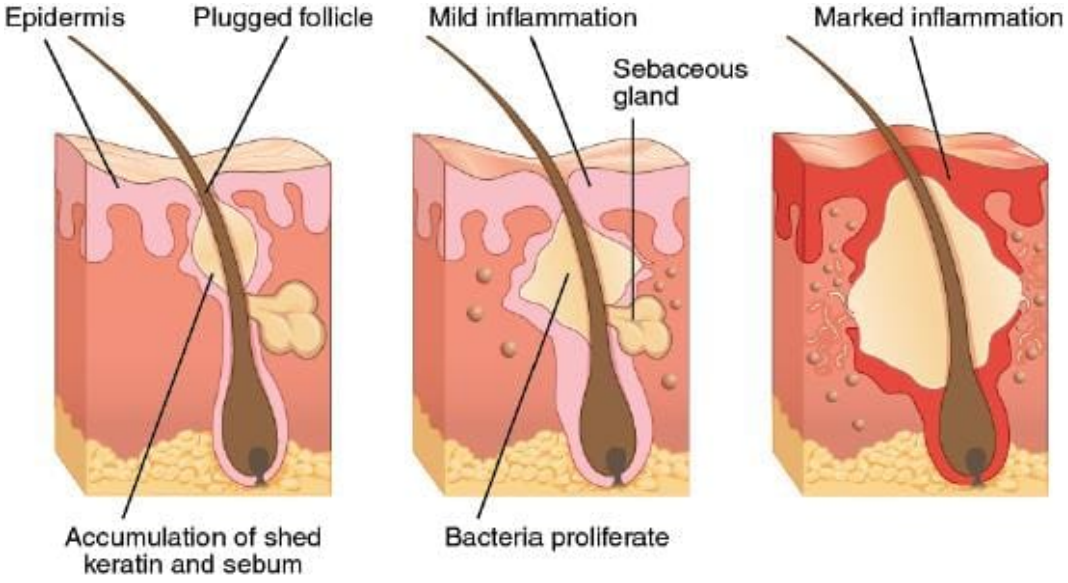


Figure 3.18.2: **Three Skin Cross-sections Showing Acne Stages.** Plugged up pore, backup of sebum, and inflammation leads to pus buildup.

What is the difference between a whitehead and a blackhead?

- If the clogged pore stays sealed under the skin, it forms a **whitehead** — a small, flesh-colored or white bump.
- If the plug is open to air, the sebum inside **oxidizes** and turns black, forming a **blackhead**. No, it is not dirt — it is chemistry!



Figure 3.18.3: **Acne**. Most common during adolescence. Visible here are whiteheads and blackheads.

Other Triggers

While puberty is the big one, acne can also flare up due to:

- **Hormonal changes** before menstruation
- **Stress**, which may increase hormone levels
- Certain **foods** and **medications**
- Using **heavy or greasy skincare and certain cosmetics products**

The Aftermath: Scars and Self-Esteem

Once the inflammation calms down, acne can leave behind **scars** — especially if you pick at it (tempting, but try to resist!).

But even more damaging than the skin effects can be the **emotional toll**. Acne often strikes during a time when people already feel insecure about their appearance. It can affect **self-esteem**, **social confidence**, and in severe cases, contribute to **anxiety** or **depression**.

The good news is that most people see acne improve by their mid-twenties. And thanks to science, there are **plenty of treatments** — from over-the-counter creams to prescription medications — that can help manage it. Understanding the biology behind acne is the first step toward **taking control** of it.

Treatments for Acne

Many different treatments exist for acne including benzoyl peroxide, antibiotics, retinoids, antiseborrheic medications, anti-androgen medications, hormonal treatments, salicylic acid, alpha hydroxy acid, azelaic acid, nicotinamide, and keratolytic soaps. They are believed to work in at least four different ways, including: normalizing shedding into the pore to prevent clogging, killing *Cutibacterium acnes*, anti-inflammatory effects, and hormonal manipulation. Laser treatment and dermabrasion can be used to reduce the appearance of scarring caused by acne.

One powerful prescription medication for severe acne that has not responded to other treatments is **Accutane** (brand name for **isotretinoin).** It is a derivative of vitamin A and works by:

- **Reducing the size and output of sebaceous glands**
- Slowing the rate of **skin cell turnover** to prevent clogged pores

- Reducing **inflammation** and the number of acne-causing bacteria

While very effective, isotretinoin can have **serious side effects**, including **birth defects**, so it requires close medical supervision and strict pregnancy prevention protocols.

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4: SKELETAL SYSTEM

4.1: Connective Tissues of the Skeletal System

4.2: Gross Anatomy of The Skeletal System

4.3: Long Bones — Anatomy, Blood Supply, and Innervation

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4.12: Diseases and Injuries of Joints

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4.1: Connective Tissues of the Skeletal System

Connective tissues of the skeletal system use specialized cells embedded in an extracellular matrix to provide support, movement, protection, and mineral storage through compact and spongy bone.

Master this section and you'll be able to

- Describe the three key components of connective tissue.
- Explain how the composition of bone's organic and inorganic matrix contributes to its strength and flexibility.
- Distinguish between compact bone and spongy bone in structure and function.
- Identify the parts of an osteon and explain the roles of osteoblasts, osteocytes, and osteoclasts.
- Describe how trabeculae in spongy bone support bone strength and provide space for red marrow and blood cell production.

Osseous Tissue, Cartilage, and Dense Connective Tissue

Do you remember from Module 3 that, unlike epithelial tissue, which is composed of cells closely packed with little or no extracellular space in between, **connective tissue cells are dispersed in an extracellular matrix?**

The matrix usually includes a large amount of extracellular material produced by the connective tissue cells that are embedded within it. The matrix plays a major role in the functioning of the specific connective tissue. The major component of the matrix is a **ground substance often crisscrossed by protein fibers.** This ground substance is usually a fluid or gel like, but it can also be mineralized and solid, as in bones. Connective tissues come in a vast variety of forms, yet they typically have in common three characteristic components:

1. **cells,**
2. **large amounts of amorphous ground substance, and**
3. **protein fibers.**

The amount and structure of each component correlates with the specific function of the tissue. In this module we will take a closer look at osseous tissue, cartilage, and dense connective tissue, all of them closely associated with the skeleton system as a whole.

Bone, or **osseous tissue**, is a hardened connective tissue that forms most of the adult skeleton, the support structure of the body. In the areas of the skeleton where bones move (for example joints), **cartilage**, a semi-rigid form of connective tissue, provides flexibility and smooth surfaces for movement.

The **skeletal system** is the body system composed of bones, cartilage, and ligaments. It performs the following critical functions for the human body:

- **supports the body,**
- **facilitates movement,**
- **protects internal organs,**
- **produces blood cells,**
- **stores and releases minerals and fat.**

Compact vs. Spongy: Osseous Tissue Types

Also known as bone tissue (or just simply bone), osseous tissue is the specialized connective tissue that forms the structural framework of bones in the skeletal system. It is the hardest connective tissue. Bone's rigid extracellular matrix is composed of about **one-third organic components —** mainly **collagen fibers** — and **two-thirds inorganic mineral salts** — primarily **hydroxyapatite**, a form of **calcium phosphate**. The organic matrix gives flexibility to bones, while the mineral content provides remarkable hardness and strength.

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

The differences between compact and spongy bone are best explored via their histology. Most bones contain compact *and* spongy osseous tissue, but their distribution and concentration vary based on the bone's overall function. Compact bone is dense so that it can withstand compressive forces, while spongy (cancellous) bone has open spaces and supports shifts in weight distribution.

Compact (Cortical) Bone

Compact bone is the **denser, stronger** of the two types of bone tissue. It can be found under the **periosteum (**thin, fibrous membrane that covers the outer surface of bones and contains blood vessels, nerves, and cells for bone growth and repair), and in the **diaphyses** (shafts) of long bones, where it provides support and protection.

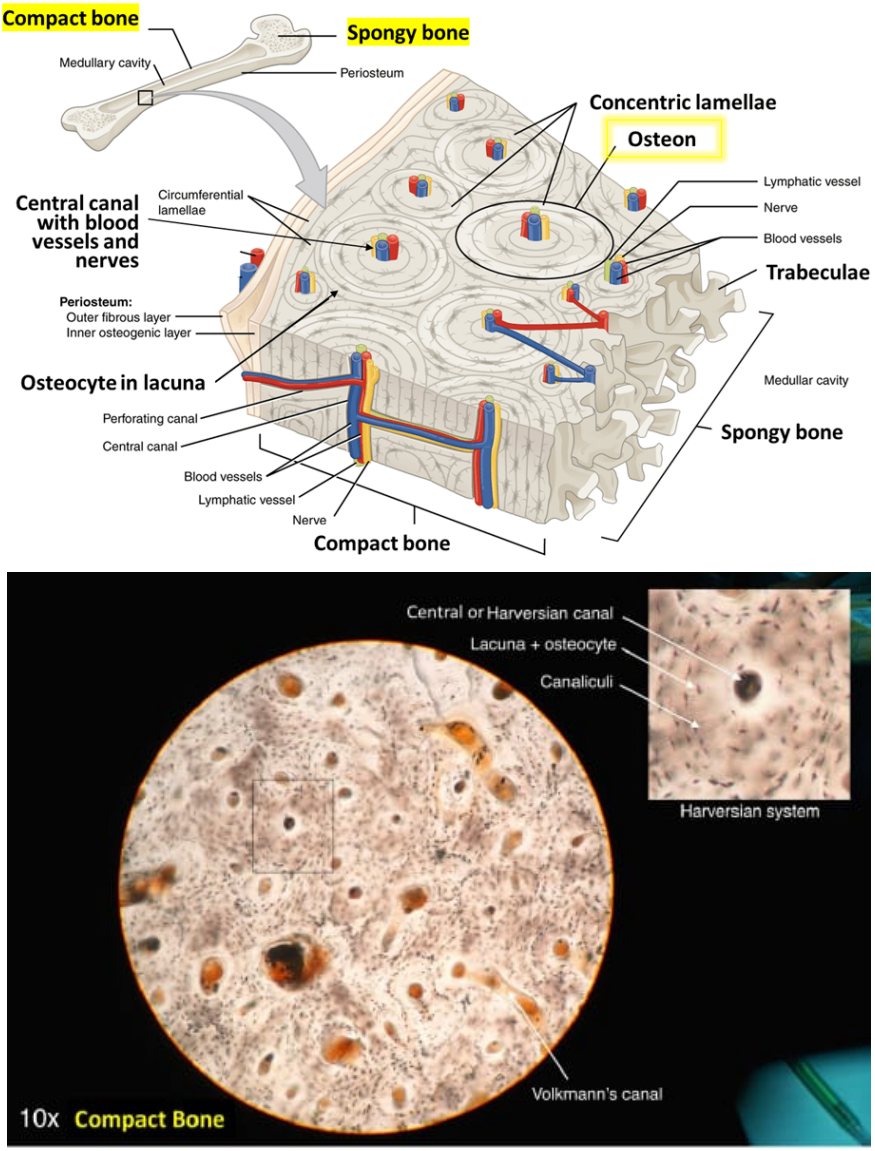


Figure 4.1.1: **Diagram of Compact and Spongy Bone.** In both images you can clearly see the highly organized concentric lamellae that make up the osteons in compact bone and central (or Haversian) canals with the blood vessels and nerves.

Osteon

The osteon, also called the **Haversian system**, is the basic structural unit of compact bone. It looks like a tiny cylinder made of concentric rings of calcified bone called **lamellae** (singular: lamella). These rings surround a **central (Haversian) canal** that contains nerves and blood vessels, which deliver nutrients to nearby bone cells and carry away their waste.

The Main Cells Involved in Forming and Maintaining Bone in an Osteon Are:

Osteoblasts:
These cells build new bone by secreting the bone matrix. Once they become trapped in this matrix, they turn into osteocytes.

Osteocytes:
These are mature bone cells that help maintain bone tissue. Osteocytes are arranged in concentric circles around a central canal, and each one is housed in a small space called a lacuna (plural: lacunae). The lacunae are found at the borders of adjacent lamellae (layers of bone tissue). Tiny channels called canaliculi connect neighboring lacunae and also extend toward the central canal. This network helps nutrients and waste products move between the osteocytes and the blood vessels in the central canal.

Osteoclasts:
These are large cells with more than one nucleus. Their job is to break down (resorb) bone tissue during bone remodeling.

Summary:
These three types of cells — osteoblasts, osteocytes, and osteoclasts — work together to build, maintain, and remodel the cylindrical structure of the osteon.

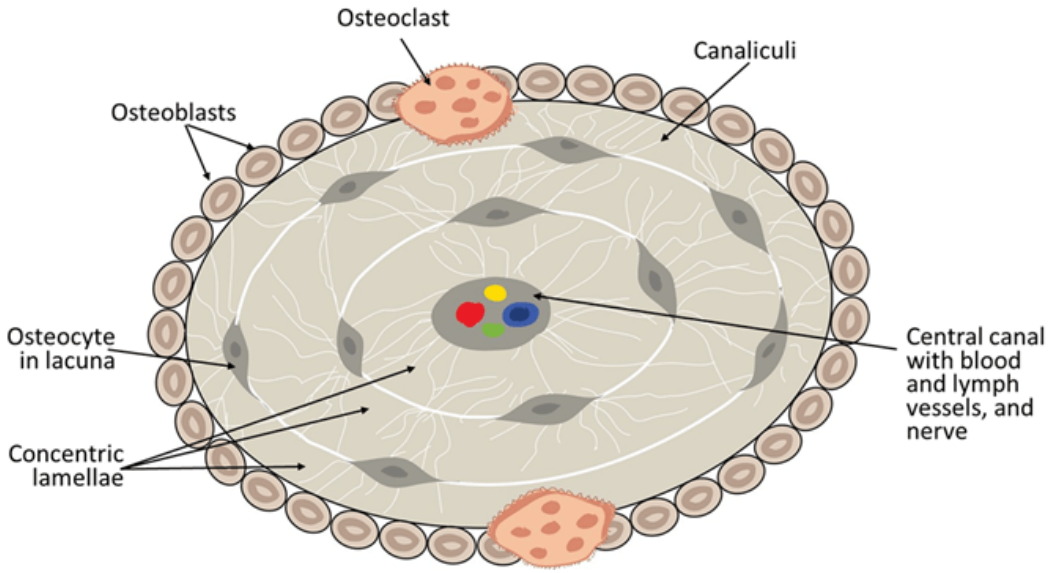


Figure 4.1.2: **Osteon.** The basic structural unit of compact bone - the osteon - consists of concentric rings of bone tissue (lamellae) arranged around a central canal that contains blood vessels and nerves.

Spongy (Cancellous) Bone

Spongy bone, also known as cancellous bone, looks like a sponge under the microscope. It contains empty spaces between **trabeculae** (or arches) of bone tissue. It is lighter than compact bone and found in the interior of some bones and at the end of long bones.

Like compact bone, spongy bone contains **osteocytes housed in lacunae**, but they are **not arranged in concentric circles.** Instead, the lacunae and osteocytes are found in a lattice-like network of matrix spikes called **trabeculae** (singular = trabecula). The trabeculae may appear to be a random network, but each trabecula forms along lines of stress to provide strength to the bone. The spaces of the trabeculated network provide balance to the dense and heavy compact bone by making bones

lighter so that muscles can move them more easily. In addition, the spaces in some spongy bones contain red marrow, protected by the trabeculae, where hematopoiesis occurs.

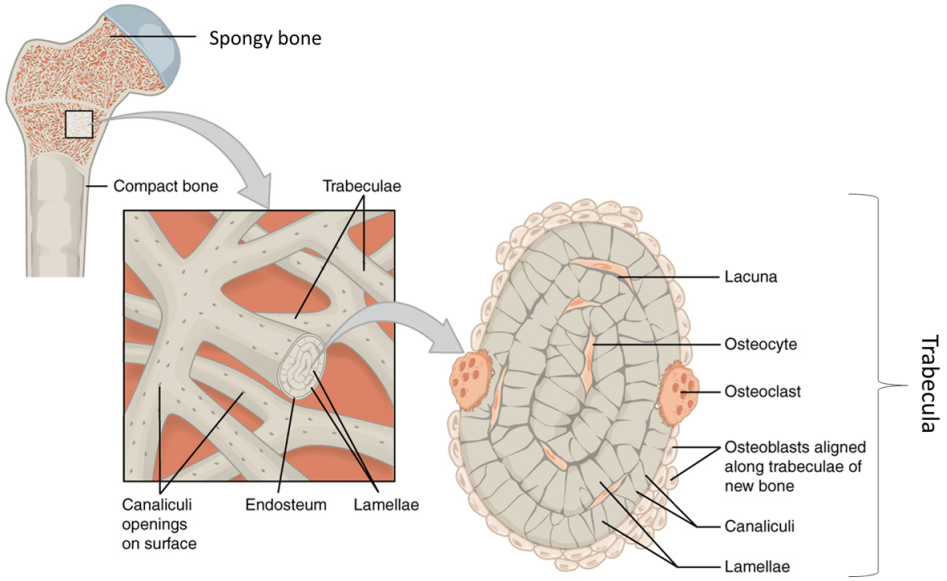


Figure 4.1.3: **Diagram of Spongy Bone.** Spongy bone is composed of trabeculae that contain the osteocytes. Red marrow fills the spaces between the trabeculae in some bones.

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4.2: Gross Anatomy of The Skeletal System

Bones form the body's rigid framework, providing support and protection while serving as the structural foundation for movement.

Master this section and you'll be able to

- Describe the functions of the skeletal system.
- Distinguish its two major subdivisions.
- Classify bones according to their shapes and give examples for each shape.

Bone Tissue Review

In the previous section you have already learned that bones support and protect the body and its organs. They also produce red and white blood cells, store minerals, and provide support for mobility in conjunction with muscles. Bone is made of bone tissue, a type of dense connective tissue. Bone (osseous) tissue is the structural and supportive connective tissue of the body that forms the rigid part of the bones that make up the skeleton. Overall, the bones of the body are an organ made up of bone tissue, bone marrow, blood vessels, epithelium, and nerves.

There are two types of bone tissue: **compact** and **spongy bone**. Compact bone forms the extremely hard exterior while spongy bone fills the interior. The tissues are biologically identical but differ in the arrangement of their microstructure.

The Skeleton: Your Body's Framework

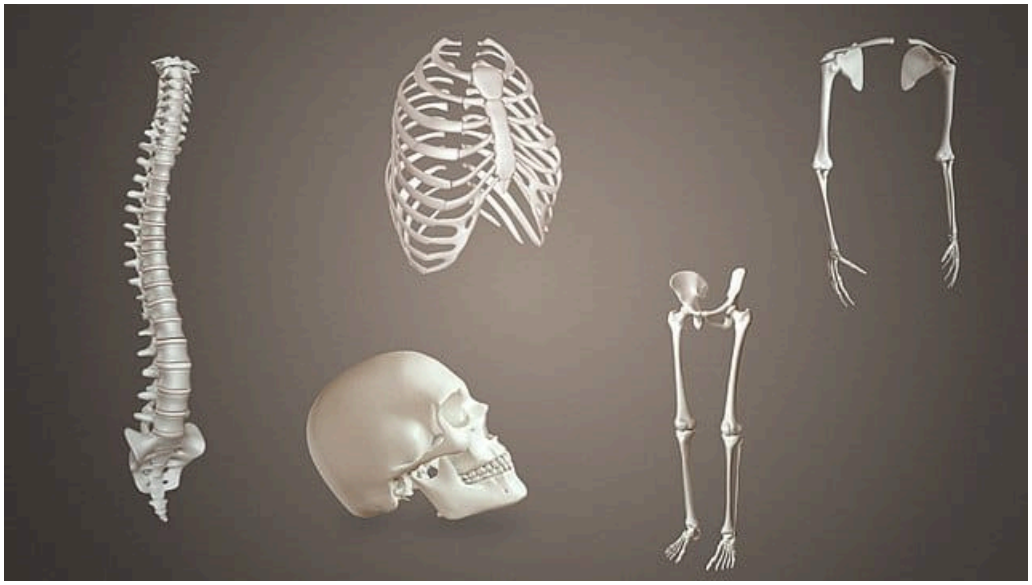


Figure 4.2.1: **Bones of the Human Skeleton.** (Image credit: "Bones of skeleton" by Scientific Animations(opens in new window) is licensed under CC BY-SA 4.0, via Wikimedia Commons)

Your skeletal system is like the **framework of a house** — it gives your body shape, support, and protection. This system is made up of **bones, cartilage, and ligaments.**, all working together to keep you upright and allow you to move. Quick review:

- **Bones** are the strong, rigid parts of the skeleton. They support your body weight, protect your organs, and — together with muscles — allow you to move.
- **Cartilage** is a firm but flexible tissue. It reinforces structures like your **rib cage, ear, trachea, and voice box (larynx)**. At joints, cartilage also **cushions bones** and sometimes even **connects them**.

- **Ligaments** are tough bands of connective tissue that **hold bones together at moveable joints** and prevent the joint from moving too far and causing injury.

Your muscles attach to bones, usually through **tendons**. When muscles contract, they **pull on bones like levers**, creating movement. Without your skeleton, you would not be able to **stand, walk, or even lift a fork to your mouth**!

Form Meets Function

Not all bones look alike, because **form follows function**! Therefore:

- **Weight-bearing bones**, like those in your **lower back and legs**, are **thick and strong** to support your body weight.
- **Bony bumps and ridges** (called landmarks) form where **powerful muscles attach**. Stronger muscles = larger bumps!

Your bones are not just hard and lifeless — they are actually very **dynamic organs** that respond to how you use your body:

- **Exercise** or gaining weight? Bones get **thicker and stronger**.
- **Lose muscle or spend weeks in bed?** Bones **thin and weaken**.
- Even your **diet** can change your bones. Eating only soft foods after losing teeth can make the **jawbone shrink** over time.

In other words, your skeleton is **alive and adaptable**. It quietly remodels itself to keep up with the demands you place on it — whether you are **training for a 10K, stuck in a cast, or floating in outer space**.

The Skeleton's Two Teams (Subdivisions): Axial and Appendicular

In adults, the skeleton consists of **206 bones**.

When you are young, you actually have more bones than an adult. This is because **some bones start out separate and later fuse together** as you grow, forming the adult skeleton.

Your skeleton has two main jobs:

1. **Support and stability:** It provides a strong internal framework that holds up your body against gravity.
2. **Movement:** It gives your muscles something to pull on, allowing your body to move in all sorts of ways.

The **lower part of your skeleton** — your pelvis and legs — is designed for **strength and stability**. This is what allows you to stand upright, walk, and run without losing your balance.

In contrast, the **upper part of your skeleton** — your arms, shoulders, and spine — is built for **flexibility and movement**. This gives you the ability to lift and carry things, twist your torso, and easily turn your head.

The Axial Skeleton

The **axial skeleton** forms the vertical, central axis of the body and includes all bones of the head, neck, chest, and back *(Figure 4.2.2)*. It serves to protect the brain, spinal cord, heart, and lungs. It also serves as the attachment site for muscles that move the head, neck, and back, and for muscles that act across the shoulder and hip joints to move their corresponding limbs.

The axial skeleton of the adult consists of 80 bones, including the **skull**, the **vertebral column**, and the **thoracic cage**. The skull has two main divisions, the cranial portion and the facial portion, and is formed by 22 bones. Also associated with the head are an additional seven bones, including the **hyoid bone** and the **ear ossicles** (three small bones found in each middle ear). The

vertebral column consists of 24 bones, each called a **vertebra**, plus the **sacrum** and **coccyx**. The thoracic cage includes the 12 pairs of **ribs**, and the **sternum**, the flattened bone of the anterior chest.

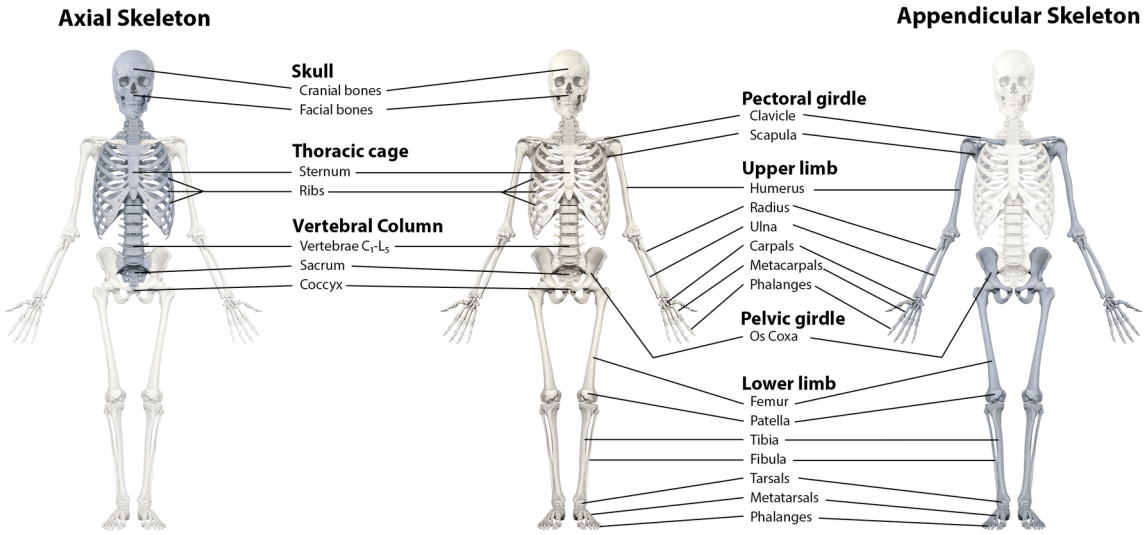


Figure 4.2.2: **Axial and Appendicular Skeleton.** The axial skeleton supports the head, neck, back, and chest and thus forms the vertical axis of the body. It consists of the skull, vertebral column (including the sacrum and coccyx), and the thoracic cage, formed by the ribs and sternum. The appendicular skeleton is made up of all bones of the upper and lower limbs.
(Image credit: "Axial and Appendicular Skeleton" by Jennifer Lange is licensed under CC BY-NC-SA 4.0(opens in new window), modification of images from Anatomy Standard(opens in new window) under CC BY-NC 4.0.(opens in new window))

The Appendicular Skeleton

The **appendicular skeleton** includes all bones of the upper and lower limbs, plus the bones that attach each limb to the axial skeleton. There are 126 bones in the appendicular skeleton of an adult. The bones that attach the upper limbs to the axial skeleton, include the **clavicle** and **scapula**, and are collectively known as the **pectoral (shoulder) girdle.** Bones of the upper limb include the **humerus, ulna, radius, carpals, metacarpals and phalanges.** The **pelvic girdle**, which attaches the lower limbs to the axial skeleton, is made up of the **hip bones (coxae; singular coxa).** Bones of the lower limb include the **femur, patella, tibia, fibula, tarsals, metatarsals, and phalanges.** The bones of the appendicular skeleton serve as attachment sites for muscles that move the appendages. The bones of the lower limb are structured to bear the weight of the body as well.

Bone Types

The 206 bones that make up the adult skeleton are **divided into five categories based on their shapes** (Figure 4.2.3). Their shapes and their functions are related such that each categorical shape of bone has a distinct function.

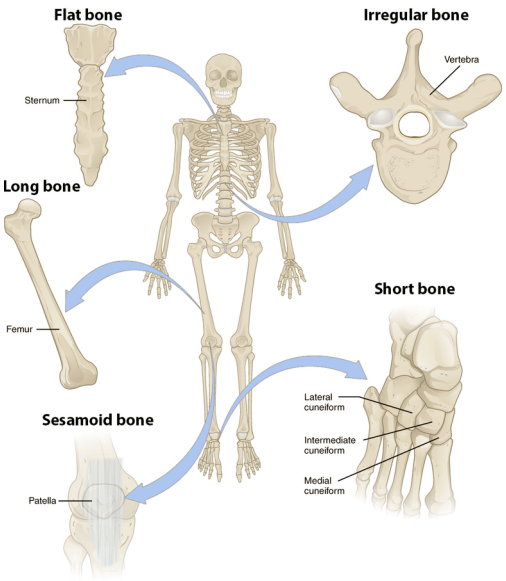


Figure 4.2.3: **Classifications of Bones by Shape.** The five classifications of bones based on their shape.
(Image credit: "Bone Classifications" by Jennifer Lange is licensed under CC BY-NC-SA 4.0(opens in new window) , modification of original by OpenStax (opens in new window) .)

Long Bones

A **long bone** is one that is cylindrical in shape, being longer than it is wide. Keep in mind, however, that the term describes the shape of a bone, not its size. Long bones are found in the arms (humerus, ulna, radius) and legs (femur, tibia, fibula), as well as in the hands (metacarpals, phalanges) and feet (metatarsals, phalanges). Long bones function as levers; they move when muscles contract.

Short Bones

A **short bone** is one that is cube-like in shape, being approximately equal in length, width, and thickness. Short bones provide support and stability with limited motion. The only short bones in the human skeleton are in the **carpals** of the wrists and the **tarsals** of the ankles. They consist of a thin layer of compact bone with spongy interiorly.

Flat Bones

The term **flat bone** is somewhat of a misnomer because, although a flat bone is typically thin, it is also often curved. Flat bones are composed of two thin layers of compact bone that surround a layer of spongy bone. The broad surfaces of flat bones help with protection and serve muscular attachment.

In an adult, most **red blood cells** are formed in the marrow in flat bones.Examples include the **cranial (skull) bones**, the **scapulae** (shoulder blades), the **sternum** (breastbone), and the **ribs**. Flat bones serve as points of attachment for muscles and often protect internal organs.

Irregular Bones

An **irregular bone** is one that does not have any easily characterized shape and therefore does not fit any other classification. These bones tend to have more complex shapes, like the **vertebrae** that support the spinal cord and protect it from compressive forces. **Many facial bones, particularly the ones containing sinuses,** are classified as irregular bones. While most irregular

bones function to protect internal organs, because each is irregular in its own way, there is no one general function that fits this class of bones.

Sesamoid Bones

Sesamoid bones are named because many of them are **small and shaped somewhat like a sesame seed.** The term comes from the Greek word for "sesame seed". These bones are typically **small, round or oval**, and are embedded within **tendons,** the sheaths of tissue that connect bones to muscles. The sesamoid bones protect tendons by helping them overcome compressive forces. Sesamoid bones **vary in number and placement from person to person** but are typically found in tendons associated with the feet, hands, and knees.

The **patellae** (kneecaps) — singular = **patella —** are the only sesamoid bones found in every person. They are much larger than a sesame seed.

The table below summarizes the different types of bones along with their key features, functions, and examples.

Bone Classifications

Bone classification	Features	Function(s)	Examples
Long	Cylinder-like shape, longer than it is wide	Leverage	Femur, tibia, fibula, metatarsals, humerus, ulna, radius, metacarpals, phalanges
Short	Cube-like shape, approximately equal in length, width, and thickness	Provide stability, support, while allowing for some motion	Carpals, tarsals
Flat	Thin and curved	Points of attachment for muscles; protectors of internal organs	Sternum, ribs, scapulae, cranial bones
Irregular	Complex shape	Protect internal organs	Vertebrae, facial bones
Sesamoid	Small and round; embedded in tendons	Protect tendons from compressive forces	Patellae

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4.3: Long Bones — Anatomy, Blood Supply, and Innervation

Long bones are elongated, living organs that support movement and contain specialized regions for strength, growth, blood cell production, and repair.

Master this section and you'll be able to

- Identify and describe the key structural regions of a long bone.
- Explain how blood vessels and nerves enter and travel through a long bone to support bone health and repair.
- Relate the structure of long bones to their primary functions in support, movement, and blood cell production.

Anatomy of Long Bones

Long bones are key players in your skeleton. They have a distinctive elongated shape and contain several important parts, including the diaphysis (shaft), the epiphyses (ends), and the medullary cavity inside. These bones are not just static supports, they grow during childhood, remodel as you use them, and even repair themselves after injury.

The long bones in the body are as follows:

- *Legs:* The **femur**, **tibia**, and **fibula**.
- *Arms:* The **humerus**, **radius**, and **ulna**.
- The **clavicles** or collar bones.
- **Metacarpals** (hand bones: the long bones in your palm), **metatarsals** (foot bones: the long bones in your arch), **phalanges** .

The outer surface of every bone is covered by a connective tissue layer called the **periosteum**. This tough, fibrous layer is rich in blood vessels and nerves. It plays a vital role in nourishing the bone, supporting its growth, repair, and maintenance, and providing attachment points for tendons and ligaments. The only areas without periosteum are where the bone is capped by **articular (hyaline) cartilage** at joints.

A long bone has *two main regions* with different structures and functions:

- **Diaphysis (shaft)** – This is the **long, central part of the bone**. Its thick **compact bone** provides strength and supports movement like a lever. Inside is the **medullary cavity**, which in adults mostly contains **yellow bone marrow**, a storage site for fat.

- **Epiphyses (ends)** – These are the **rounded ends of a long bone**. They are made mostly of **spongy bone** surrounded by a thin shell of **compact bone**. The spaces within the spongy bone often contain **red bone marrow**, which produces blood cells. The epiphyses form **joints with neighboring bones** and are capped with **hyaline cartilage**, which reduces friction and cushions the joint against impact.

  The **epiphyseal plate**, or **growth plate**, is a layer of cartilage near the ends of the long bones where new bone is made during **childhood and adolescence**. This plate allows the bone to grow in length and is **only present in young, growing bones**. Once growth is complete, the cartilage of the epiphyseal plate is replaced by bone, leaving the **epiphyseal line**, which marks where the growth plate used to be.

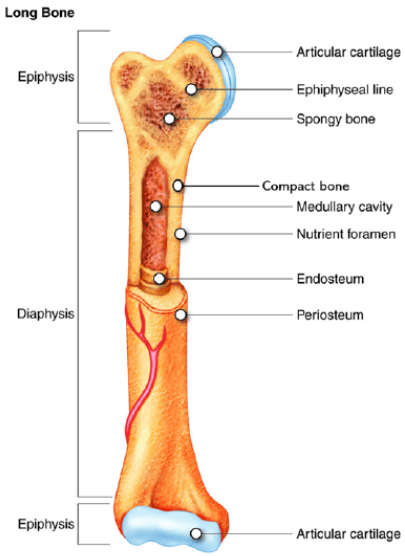


Figure 4.3.1: **Long Bone.** A long bone is longer than it is wide. Growth occurs by a lengthening of the diaphysis. located in the center of the long bone.

Blood and Nerve Supplies of Long Bones

Blood Vessels in Long Bones

- **Periosteal arteries** nourish the outer surface of the bone (except at the joint surfaces).
- **Perforating canals** are channels that carry **blood vessels and nerves** from the **periosteum** into the bone and connect to the **central canals** of osteons.
- **Nutrient arteries** are the main blood vessels for the shaft (diaphysis). They enter the bone through small openings called **nutrient foramina** (plural for **foramen**), usually found in the **middle third of the shaft.** Except for a few with double or no foramina, 90% of long bones have a single nutrient foramen.
- Inside the **medullary cavity**, the nutrient artery **divides into upward and downward branches**, which send smaller vessels toward the ends of the bone.
  Within the marrow and spongy bone, blood flows through **sinusoidal networks** — special, wide capillaries that slow blood flow and therefore allow more time for nutrients and oxygen to reach the bone cells.
- Near the epiphyses, nutrient artery branches **join (anastomose)** with the **epiphyseal arteries**, forming a network that ensures the whole bone gets blood.

This arrangement makes sure the **entire bone**, from the shaft to the ends, receives a reliable blood supply for **growth, repair, and maintenance**.

Blood then exits through **venous channels** located on all surfaces, **except again, where articular cartilage covers the bone**. Articular cartilage has **no direct blood supply** and receives nutrients by **diffusion** instead. That is why cartilage heals so poorly and so slowly!

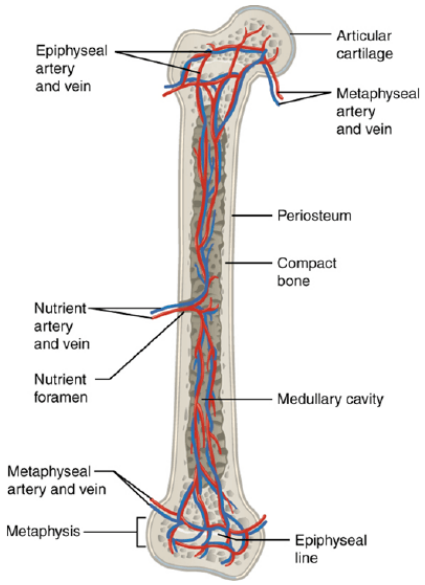


Figure 4.3.2: **Blood Supply to Long Bone** — A long bone is supplied by the **nutrient artery** to the medullary cavity and inner compact bone, **periosteal arteries** to the outer cortex, and **metaphyseal and epiphyseal arteries** to the bone ends and spongy bone. Together, these vessels support bone growth, maintenance, and repair.

Use the figure below to review the **osteon** and see how it receives its **blood supply**. In mature compact bone, **blood flows through tiny central canals** inside each osteon. These canals run **lengthwise along the bone, parallel to its surface**, carrying blood vessels that nourish the bone cells, and nerves that pick up sensory information and signal it to the brain.

Around each central canal are **concentric rings of bone tissue** called **lamellae**, and together the central canal plus its rings form an **osteon**, the basic structural unit of compact bone.

The **osteocytes** live in small spaces called **lacunae**, and they connect to each other and to the central canal through **canaliculi**, which are like tiny passageways. This arrangement allows the osteocytes to get nutrients, remove waste, and store the **mineral salts** that make bone strong.

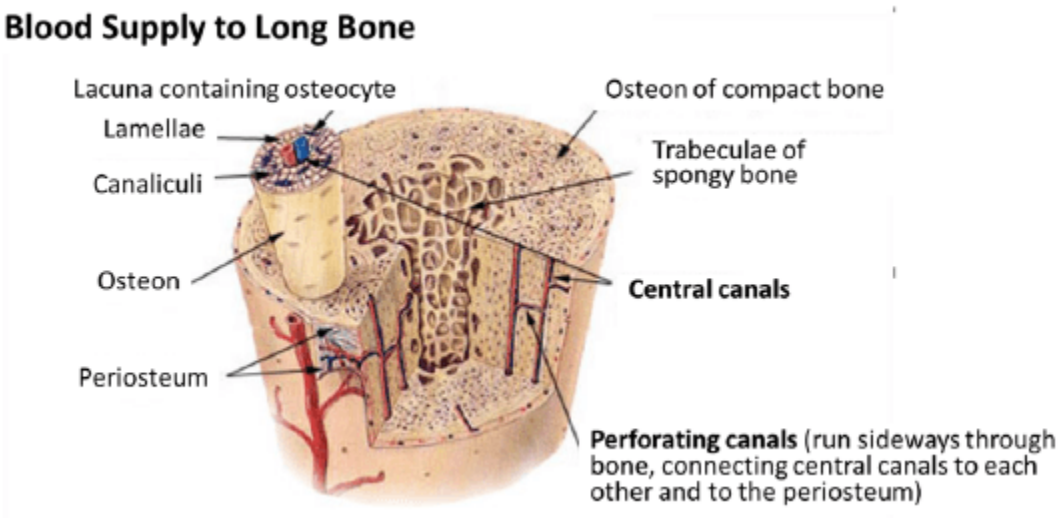


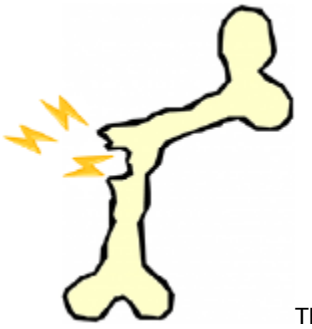
Figure 4.3.3: **Central canal**: The central canals surround blood vessels and nerve cells throughout the bone.

Nerve Supply in Long Bones

The nerve supply is mainly **sensory** and **autonomic**, supporting **pain sensation**, but also blood flow regulation, and bone growth.

The nerve supply to a long bone primarily enters **through the nutrient foramen alongside the blood vessels** and extending

into the bone via perforating and central canals. The nerves innervate the periosteum, endosteum, bone marrow, and spongy bone.



The periosteum is especially rich in nerve endings, which is why breaking a bone is extremely painful. When a bone fractures, these nerves are **damaged or irritated**, sending strong pain signals to the brain.

Bone injury also causes swelling, bleeding, and inflammation, all of which increase pressure on nearby nerves. Chemicals released during inflammation, like prostaglandins, make the nerves even more sensitive.

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4.4: Bone Formation and Remodeling

Bone forms during development by replacing fibrous tissue or cartilage through two pathways, intramembranous and endochondral ossification, allowing bones to grow, reshape, and renew throughout life.

Master this section and you'll be able to

- Explain the function of cartilage for bone development.
- Outline the two main processes of bone formation.
- Explain how bones grow in length and diameter.
- Identify the roles of key bone cells (osteoblasts, osteoclasts, and chondrocytes) in bone development and growth.

In the early stages of embryonic development, the embryo's skeleton consists of **fibrous membranes and hyaline cartilage**. By the **sixth or seventh week of embryonic life**, the actual process of bone development, **ossification (osteogenesis), begins**.

There are two osteogenic pathways — **intramembranous ossification** and **endochondral ossification** — but bone is the same regardless of the pathway that produces it.

Brief overview of the two main bone formation processes:

- **Intramembranous Ossification** (sometimes referred to as "intradermal/dermal ossification"): This is the process in which bone develops directly from sheets of mesenchymal (undifferentiated) connective tissue without a cartilage stage. Mesenchymal cells differentiate into osteoblasts, which form bone tissue. This process is responsible for creating most flat bones, such as those in the skull and the clavicle.

- **Endochondral Ossification**: In this process, bone develops by first forming a **cartilage model**. Mesenchymal cells transform into chondrocytes to make a cartilage template, which is then gradually replaced by bone as osteoblasts invade and lay down mineralized bone matrix. Endochondral ossification forms most of the bones of the body, especially long bones like the femur and humerus.

Cartilage Templates

Bone develops as a **replacement tissue**, meaning it first forms on a softer **template** before it hardens. In most cases, this template is **cartilage**. During fetal development, a flexible framework of cartilage shows where future bones will grow. This framework is made by **chondroblasts**, cells that produce a semi-solid matrix containing **hyaluronic acid, chondroitin sulfate, collagen fibers, and water**. Once these cells are trapped in the matrix, they are called **chondrocytes**.

Unlike most connective tissues, **cartilage** is **avascular,** meaning it has no blood vessels. Nutrients and waste must move through the matrix by **diffusion**, which is slow. This is why **cartilage heals poorly** after injury.

As the fetus develops and continues to grow into childhood, bone tissue gradually replaces the cartilage. At birth, most of the skeleton is already bone, with some cartilage remaining to allow for further growth. In adults, small areas of cartilage persist, especially where bones need flexibility or cushioning.

Endochondral Ossification

In this course, we will focus on **endochondral ossification**, the process where **bone develops by replacing hyaline cartilage**. It is important to note that **cartilage does not turn into bone**. Instead, the cartilage acts as a **template** that is gradually **broken down and replaced by new bone tissue**.

Endochondral ossification is a **slower process** than intramembranous ossification. It forms the **long bones** of the arms and legs,

the **short bones** of the wrist, as well as many **irregular bones** such as the ribs and vertebrae and others.

In a long bone, for example, at about 6 to 8 weeks after conception, some of the **mesenchymal cells** (multipotent stem cells originating from the mesoderm layer during embryonic development) **differentiate into** chondrocytes (cartilage cells) and **various other connective tissue cell types.** They also produce the extracellular matrix that forms the foundation of connective tissue.

As the cartilage model of a future bone grows, the **chondrocytes** (cartilage cells) in the center **enlarge**. Eventually, the surrounding **matrix calcifies**, blocking nutrients from reaching these cells. The chondrocytes **die**, and the surrounding cartilage **breaks down**, leaving spaces behind. **Blood vessels** then grow into these spaces, carrying **osteogenic cells**, many of which become **osteoblasts**. As these spaces enlarge and merge, they form the **medullary cavity** in the diaphysis.

At the same time, **capillaries penetrate the outer cartilage**, triggering the **perichondrium** to transform into the **periosteum**, the bone-producing layer. **Osteoblasts** here build a periosteal collar of compact bone around the diaphysis. By the **second or third month of fetal life**, these processes accelerate and create the **primary ossification center** deep in the diaphysis.

Meanwhile, the **ends of the bone (future epiphyses)** continue to grow in cartilage. This allows the bone to **lengthen** even as cartilage is replaced by bone in the diaphysis. By the time the fetal skeleton is fully formed, cartilage remains only in two places:

- **Articular cartilage** at the joint surfaces
- **Epiphyseal plates** between the diaphysis and epiphyses, which allow bones to keep lengthening after birth

After birth, the **same sequence** — matrix calcification, chondrocyte death, blood vessel invasion, and osteoblast formation — occurs in the epiphyses, forming **secondary ossification centers**.

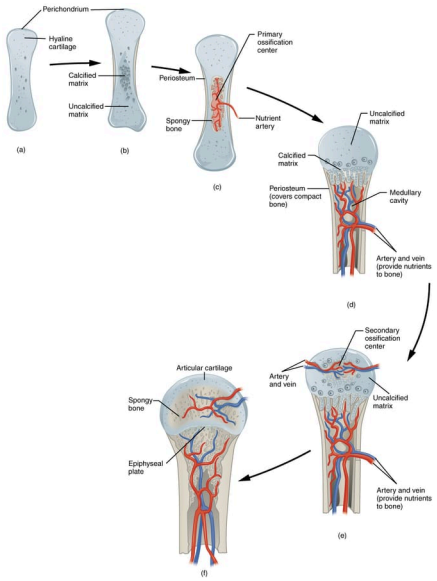


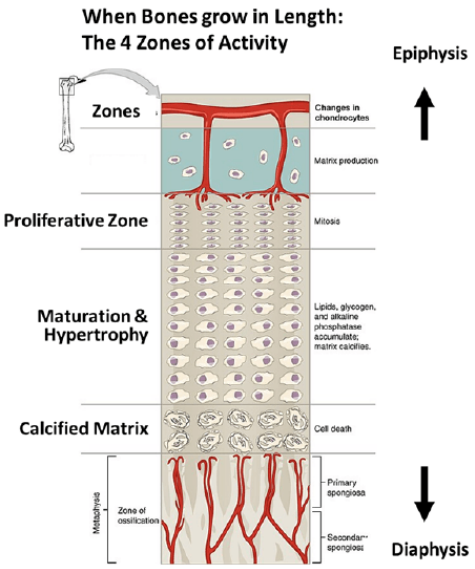
Figure 4.4.1: **Endochondral Ossification.** Endochondral ossification follows five steps. (a) Mesenchymal cells differentiate into chondrocytes. (b) The cartilage model of the future bony skeleton and the perichondrium form. (c) Capillaries penetrate cartilage. Perichondrium transforms into periosteum. Periosteal collar develops. Primary ossification center develops. (d) Cartilage and chondrocytes continue to grow at ends of the bone. (e) Secondary ossification centers develop. (f) Cartilage remains at epiphyseal (growth) plate and at joint surface as articular cartilage.

How Bones Grow in Length

The **epiphyseal plate**, or growth plate, is the region where **long bones grow in length**. It is made of **hyaline cartilage** in immature bones, and **ossification** occurs here as the bone elongates.

- On the **epiphyseal side:** new cartilage is produced.

- On the **diaphyseal side**, the cartilage is gradually replaced by bone, lengthening the diaphysis.



The epiphyseal plate has **four zones of activity** *(See image on the right)*

1. **Reserve Zone**
   - Closest to the epiphysis.
   - Contains **small, inactive chondrocytes** embedded in matrix.
   - **Anchors** the epiphyseal plate to the bone of the epiphysis.

2. **Proliferative Zone**
   - Next layer toward the diaphysis.
   - Slightly larger **chondrocytes divide (mitosis)** producing new chondrocytes and creating **stacks of cells.**
   - Produces new chondrocytes to **replace those dying at the diaphyseal side.**

3. **Zone of Maturation and Hypertrophy**
   - **Older, larger chondrocytes** closer to the diaphysis.
   - **Cells grow in size (hypertrophy).**
   - **Bone lengthens** due to both cell division in the proliferative zone and cell growth here.

4. **Zone of Calcified Matrix**
   - **Closest to the diaphysis**
   - **Chondrocytes die** as the surrounding matrix **calcifies**
   - **Capillaries and osteoblasts invade**
   - **Osteoblasts deposit bone tissue** on the calcified cartilage, connecting the plate to the diaphysis

The longitudinal growth of bone is a result of cellular division in the proliferative zone and the maturation of cells in the zone of maturation and hypertrophy.

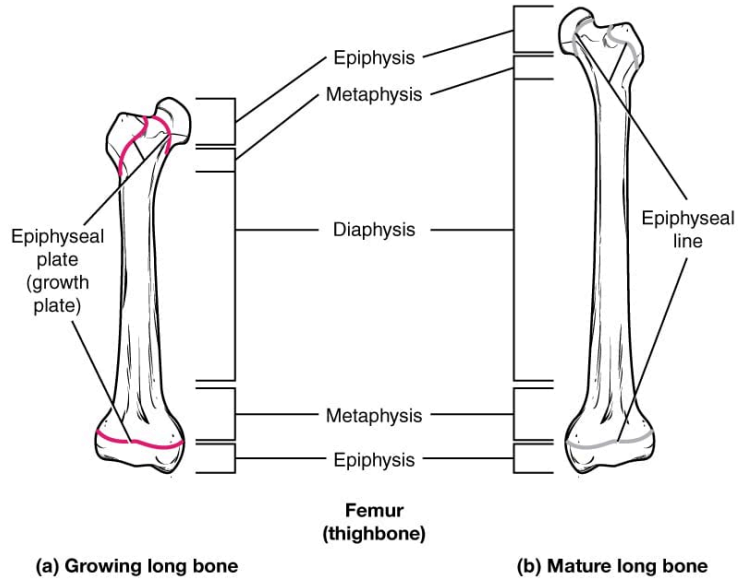


Figure 4.4.2: **Progression from Epiphyseal Plate to Epiphyseal Line.** As a bone matures, the epiphyseal plate progresses to an epiphyseal line. (a) Epiphyseal plates are visible in a growing bone. (b) Epiphyseal lines are the remnants of epiphyseal plates in a mature bone.

How Bones Grow in Diameter

As bones grow in **length**, they also **increase in diameter**. This **appositional growth** can continue **even after a bone stops lengthening**.

- **Osteoclasts** break down (resorb) old bone along the **medullary cavity**.
- **Osteoblasts** add **new bone beneath the periosteum** through **intramembranous ossification**.

This combination of **bone removal on the inside** and **bone deposition on the outside**:

- **Widens the diaphysis**
- **Enlarges the medullary cavity**

This overall reshaping of the bone is called **modeling**.

Bone Remodeling

Bone remodeling occurs when bone matrix is **removed from one surface** and **deposited on another**. This process is most active **during bone growth**, helping to shape and enlarge bones.

In **adults**, bones mainly undergo **remodeling** instead. During remodeling, **old or damaged bone is resorbed and new bone is deposited on the same surface**. This process:

- Repairs **injuries**
- Responds to **stress and exercise**
- Continuously **refreshes bone tissue**

Even without injury or heavy activity, about **5–10% of the skeleton is naturally renewed each year** as old bone is replaced with new bone.

Diseases of the...

Skeletal System

Osteogenesis imperfecta (OI) is a genetic disease in which bones do not form properly and therefore are fragile and break easily. It is also called brittle bone disease. The disease is present from birth and affects a person throughout life.

The genetic mutation that causes OI affects the body's production of collagen, one of the critical components of bone matrix. The severity of the disease can range from mild to severe. Those with the most severe forms of the disease sustain many more fractures than those with a mild form. Frequent and multiple fractures typically lead to bone deformities and short stature. Bowing of the long bones and curvature of the spine are also common in people afflicted with OI. Curvature of the spine makes breathing difficult because the lungs are compressed.

Because collagen is such an important structural protein in many parts of the body, people with OI may also experience fragile skin, weak muscles, loose joints, easy bruising, frequent nosebleeds, brittle teeth, blue sclera, and hearing loss. There is no known cure for OI. Treatment focuses on helping the person retain as much independence as possible while minimizing fractures and maximizing mobility. Toward that end, safe exercises, like swimming, in which the body is less likely to experience collisions or compressive forces, are recommended. Braces to support legs, ankles, knees, and wrists are used as needed. Canes, walkers, or wheelchairs can also help compensate for weaknesses.

When bones do break, casts, splints, or wraps are used. In some cases, metal rods may be surgically implanted into the long bones of the arms and legs. Research is currently being conducted on using bisphosphonates to treat OI. Smoking and being overweight are especially risky in people with OI, since smoking is known to weaken bones, and extra body weight puts additional stress on the bones.

Interactive Link

Watch this video (opens in new window) to see how a bone grows.

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4.5: Fractures and Bone Repair

A fracture is a break in a living bone that must be properly aligned to heal correctly and restore normal function.

Master this section and you'll be able to

- Differentiate among the different types of fractures
- Describe the steps involved in bone repair

A **fracture** is simply a broken bone, but not all fractures are the same. Bones are living tissues, and they will try to heal themselves whether or not a doctor helps. The problem is that if the pieces of bone are not lined up properly, the bone will happily heal in a **crooked or deformed position**.

To prevent this, doctors use two main approaches:

- **Closed reduction**: The bone is gently manipulated back into place **without surgery**.
- **Open reduction**: **Surgery** is needed to expose the fracture and realign the bone.

While some fractures are mostly painful and inconvenient, others can be **life-threatening**. For example, breaking the **shaft (diaphysis) of the femur** can allow **fat droplets from the bone marrow** to enter the bloodstream. These **fat emboli** can travel to the tiny blood vessels (capillaries) of the lungs, causing **severe breathing problems** — a condition called **fat embolism syndrome** — similar to pulmonary embolism which is caused by blood clots. Without quick treatment, this complication can become fatal.

Types of Fractures

Fractures are classified by their complexity, location, and other features (see figure and table below). Some fractures may be described using more than one term because it may have the features of more than one type (e.g., an open transverse fracture).

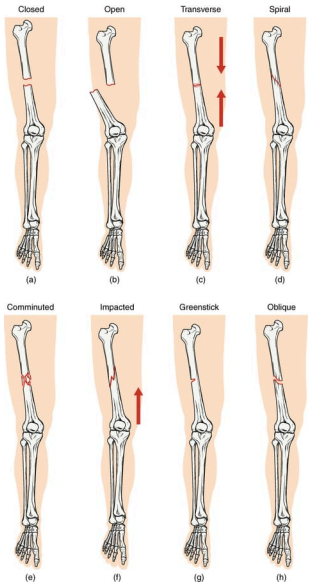


Figure 4.5.1: **Types of Fractures** — Compare healthy bone with different types of fractures: (a) closed fracture, (b) open fracture, (c) transverse fracture, (d) spiral fracture, (e) comminuted fracture, (f) impacted fracture, (g) greenstick fracture, and (h) oblique fracture.

The Various Types of Bone Fractures

Type of fracture	Description
Transverse	Occurs straight across the long axis of the bone
Oblique	Occurs at an angle that is not 90 degrees
Spiral	Bone segments are pulled apart as a result of a twisting motion
Comminuted	Several breaks result in many small pieces between two large segments
Impacted	One fragment is driven into the other, usually as a result of compression
Greenstick	A partial fracture in which only one side of the bone is broken
Open (or compound)	A fracture in which at least one end of the broken bone tears through the skin; carries a high risk of infection
Closed (or simple)	A fracture in which the skin remains intact

Bone Repair

When a bone breaks, blood flows from any vessel torn by the fracture. These vessels could be in the periosteum, osteons, and/or medullary cavity. The blood begins to clot, and about six to eight hours after the fracture, the clotting blood has formed a **fracture hematoma.** The disruption of blood flow to the bone results in the death of bone cells around the fracture.

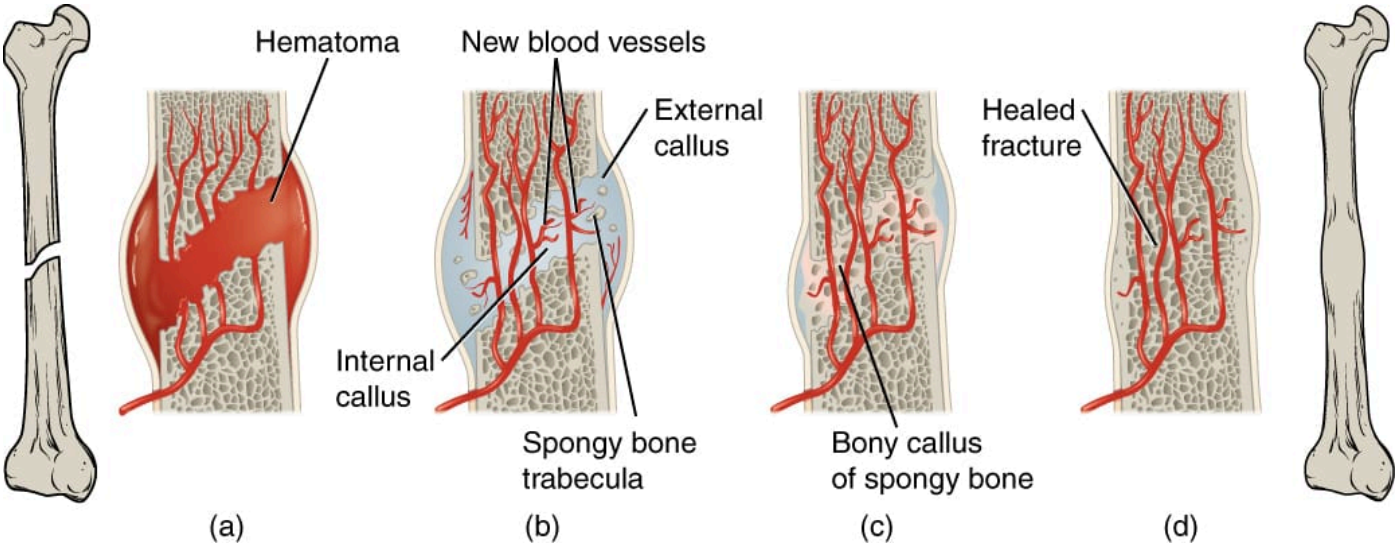


Figure 4.5.2: **Stages in Fracture Repair** — The healing of a bone fracture follows a series of progressive steps: (a) A fracture hematoma forms. (b) Internal and external calli form. (c) Cartilage of the calli is replaced by trabecular bone. (d) Remodeling occurs.

Within about 48 hours after the fracture, chondrocytes from the endosteum have created an **internal callus (plural = calli) by secreting a fibrocartilaginous matrix** between the two ends of the broken bone, while the periosteal chondrocytes and osteoblasts create an **external callus of hyaline cartilage and bone,** respectively, around the outside of the break. This stabilizes the fracture. (Figure 4.5.2 **b**).

Over the next several weeks, osteoclasts resorb the dead bone; osteogenic cells become active, divide, and differentiate into osteoblasts. The cartilage in the calli is replaced by trabecular bone via endochondral ossification (Figure 4.5.2 **c**).

Eventually, the internal and external calli unite, compact bone replaces spongy bone at the outer margins of the fracture, and healing is complete. A slight swelling may remain on the outer surface of the bone, but quite often, that region undergoes remodeling (Figure 4.5.2 **d**), and no external evidence of the fracture remains.

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4.6: The Functions of the Skeletal System

The skeletal system supports and protects the body, enables movement through muscle attachment and leverage, produces blood cells, and stores essential minerals and energy.

Master this section and you'll be able to

- List and describe the functions of the skeletal system

The skeletal system is like the framework of a house for your body — it gives you structure, support, and protection while allowing for movement. You learned that bone, or **osseous tissue**, is a hard and dense type of connective tissue that makes up most of the adult skeleton. This rigid material provides the strong scaffolding that supports your weight and anchors your muscles. In areas where flexibility and smooth motion are needed, such as at joints or in the ribcage, the skeleton incorporates **cartilage**, a semi-rigid connective tissue that cushions movement and prevents bone-on-bone friction.

Beyond simply “holding you up,” the skeletal system performs a remarkable list of jobs that keep you alive and healthy. It:

- **Protects internal organs**, like the skull guarding your brain or the ribcage shielding your heart and lungs.
- **Supports the body** so you do not crumple into a pile of soft tissue.
- **Facilitates movement** by serving as a system of levers for your muscles.
- **Stores and releases minerals and fat**, acting as a warehouse for calcium, phosphorus, and energy-rich lipids.
- **Produces blood cells** in the red bone marrow, a process called hematopoiesis.

In short, your skeletal system is not just a passive framework; it is a dynamic, living system that grows, repairs, and responds to the demands you place on your body every day.

Protection, Support, and Movement

The most obvious roles of the skeletal system are its **gross functions** — the ones you can easily observe just by looking at the human body. Your bones clearly **support your frame**, **facilitate movement**, and **protect your organs**.

Think of bones like the steel beams in a building. Without this internal framework, your body would collapse into a squishy heap of organs, muscles, and skin. Bones and cartilage form the **scaffold** that holds you upright and gives your body its recognizable shape.

Movement is made possible because bones serve as **attachment points for muscles**. When a muscle contracts, it pulls on the bone to which it is attached. In this way, bones act as **levers**, and the **joints** where they meet serve as **fulcrums**. From a mechanical standpoint, no muscle means no movement — bones cannot move themselves! This teamwork between bones and muscles is why we often talk about the **musculoskeletal system**, which combines the strength of the skeleton with the power of muscles to produce motion.

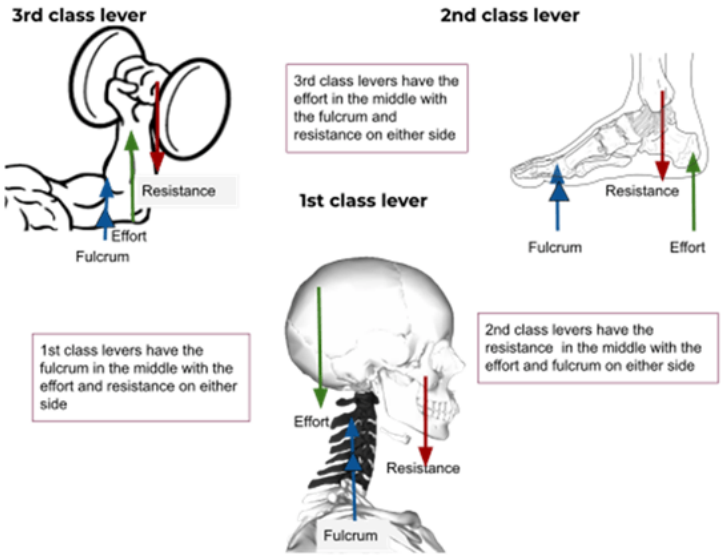


Figure 4.6.1: **Bones Support Movement.** Bones act as levers when muscles span a joint and contract.

Bones also act as **bodyguards for your vital organs**, shielding them from injury. Your **ribs** form a protective cage around your heart and lungs, your **vertebral column (spine)** surrounds and safeguards the delicate spinal cord, and your **cranium (skull)** forms a sturdy helmet for your brain (Figure \PageIndex2{4{.}6{.}\eatSpaces{2} \endSpaces}\PageIndex2). Without this bony armor, even minor bumps could cause serious damage.

Bones also protect internal organs from injury by covering or surrounding them. For example, your **ribs protect your lungs and heart**, the bones of your vertebral column (spine) protect your spinal cord, and the bones of your cranium (skull) protect your brain.

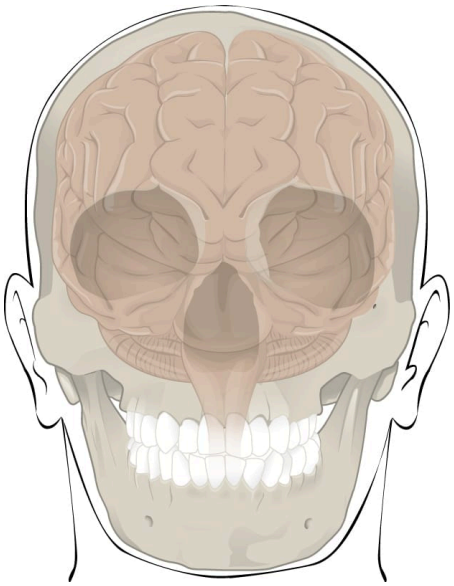


Figure 4.6.2: **Bones Protect Brain.** The cranium completely surrounds and protects the brain from non-traumatic injury.

Career Connection



Orthopedist

Figure 4.6.3: **Complex Brace.** An orthopedist will sometimes prescribe the use of a brace that reinforces the underlying bone structure it is being used to support. (credit: Becky Stern/Flickr)

An **orthopedist** is a physician who specializes in diagnosing and treating injuries and disorders of the **musculoskeletal system** — your bones, joints, muscles, ligaments, and tendons. Many orthopedic problems can be managed with medications, physical therapy, braces, or other supportive devices, but some cases require surgical treatment.

The word **"orthopedics"** comes from the Greek roots *ortho-* ("straight") and *paed-* ("child"), originally referring to "straightening the child." Today, orthopedists treat patients of all ages, from infants to older adults. In fact, modern orthopedists can even perform **prenatal surgery** to correct conditions like **spina bifida**, a birth defect where the fetal spinal canal does not fully close during development.

Orthopedists often treat **bone and joint injuries**, but they also manage conditions like **abnormal spinal curvatures**:

- **Scoliosis** – A sideways (lateral) curve of the spine that can cause a shoulder blade to protrude as a hump.
- **Kyphosis** – An exaggerated forward (dorsoventral) curve in the thoracic region, sometimes called a "hunchback."

These curvatures often develop in **preteens** due to poor posture, uneven growth, or unknown causes and are usually treatable. In older adults, **osteoporosis** and accumulated spinal injuries can also produce a stooped posture.

Some orthopedists specialize in **sports medicine**, treating everything from **minor injuries** (like sprained ankles) to **complex joint injuries** (like torn rotator cuffs). Treatment plans can range from simple exercises and therapy to full surgical repair.

Storage and Hematopoiesis

On a **metabolic level**, your bones are far from passive — they are busy performing critical tasks that keep you alive and well.

First, the **bone matrix** acts like a **mineral bank** for your body. It stores important minerals, especially **calcium** and **phosphorus**, which are essential for everyday life. When your body needs them, bones can "withdraw" these minerals and release them into the bloodstream. This is vital because **calcium ions** play key roles in **muscle contraction** and in **nerve signaling**, allowing your brain and body to communicate. Without a steady supply, even simple movements and reflexes would not work properly.

Bones also have some surprising **bonus functions**:

- **Fat storage:** The soft tissue inside bones, called **bone marrow** comes in two forms. **Yellow bone marrow** is rich in fat-storing cells (**adipocytes**), providing an energy reserve your body can tap into during lean times.
- **Blood cell production: Red bone marrow** is a biological factory where **hematopoiesis** — the production of blood cells — takes place. It generates your **red blood cells** (oxygen carriers), **white blood cells** (infection fighters), and **platelets** (clot makers).

So, next time you think about your skeleton, remember: it is not just holding you up!

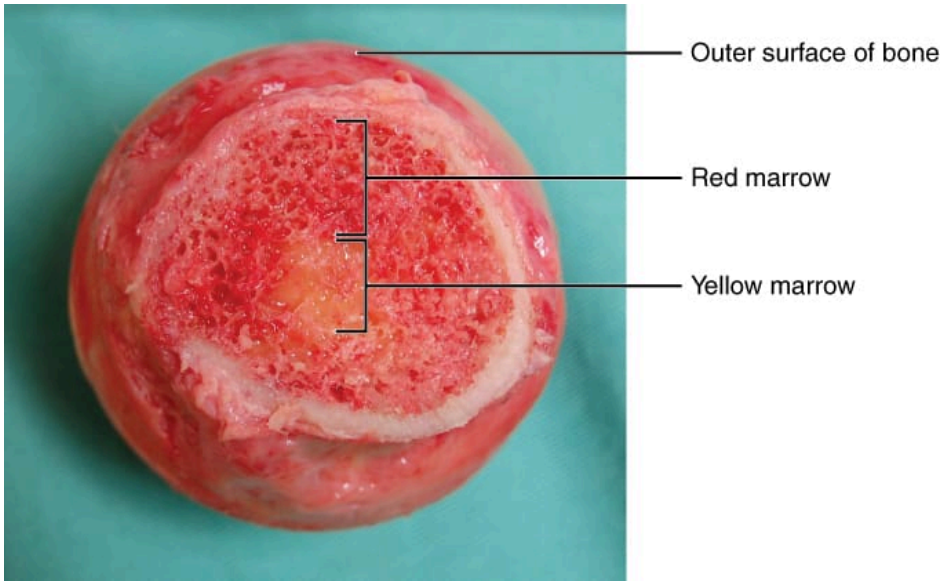


Figure 4.6.3: **Head of Femur Showing Red and Yellow Marrow.** The head of the femur contains both yellow and red marrow. Yellow marrow stores fat. Red marrow is responsible for hematopoiesis. (credit: modification of work by "stevenfruitsmaak"/Wikimedia Commons)

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4.7: The Vertebral Column

The vertebral column is a flexible yet sturdy column of vertebrae and intervertebral discs that protects the spinal cord, supports the body's weight, and allows controlled movement of the head, neck, and trunk.

Master this section and you'll be able to:

- Describe each region of the vertebral column and the number of bones in each region.
- Discuss the curves of the vertebral column and how these change after birth.
- Describe the basic structure of a typical vertebra and its key parts.
- Recognize the unique features of the atlas, axis, sacrum, and coccyx.

Vertebral Column: Your Body's Flexible Backbone

Your vertebral column — also called your backbone, spinal column, or just "spine" — is an incredible structure made up of **33 individual bones called vertebrae** (singular = **vertebra**). Between each two vertebrae sits an **intervertebral disc**, a little cushion of fibrocartilage that keeps the bones from grinding together and allows for movement and flexibility.

Naming Vertebrae: Each vertebra is given an **alphanumeric code**: the **letter** shows the region (C, T, L, S, or Co), and the **number** increases as you move downward. **Example:** The topmost vertebra is **C1 (atlas)**, followed by **C2 (axis)**, then C3...C7, and next comes **T1** of the thoracic spine.

Together, the vertebrae and discs form a **flexible yet protective column** that:

- **Shields your spinal cord**, which acts like a **superhighway for information**, carrying nerve signals between your brain and the rest of your body. Thanks to this nerve highway, you can **move, feel, and respond** to the world around you.
- **Supports your head, neck, and torso** so you do not collapse into a floppy heap.
- **Provides attachment points for muscles**, helping you bend, twist, lift, and move.

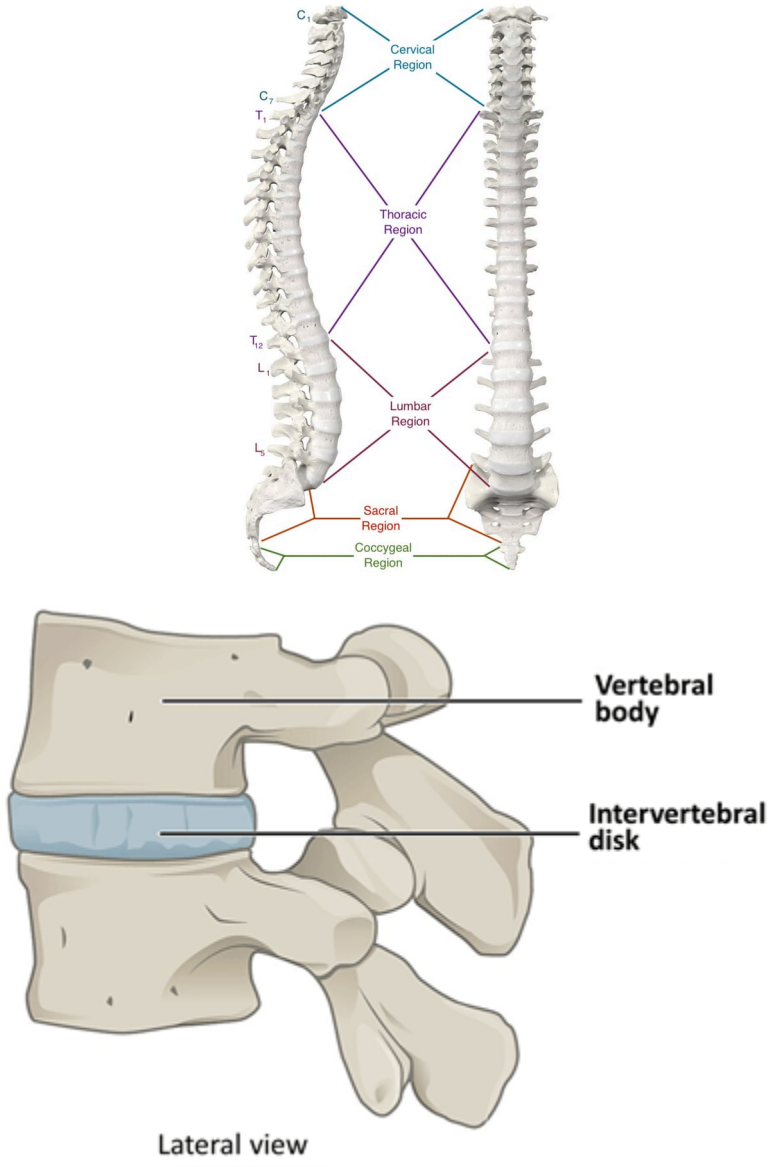
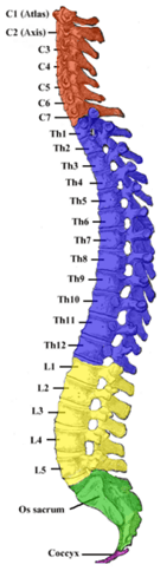


Figure 4.7.1: **Vertebral Column.** The image on the left shows the vertebral column consisting of 33 vertebrae divided into 5 regions. cervical C1–C7, thoracic T1–T12, lumbar L1–L5, sacral vertebrae. *(Image credit: "Vertebral Column Regions" by Jennifer Lange is licensed under CC BY-NC-SA 4.0>, modification of image from Anatomy Standard under CC BY-NC 4.0.* The image on the right shows two vertebrae separated by an intervertebral disk.

Regions and Curves of the Vertebral Column



Five Regions

1. **Cervical Region (Neck)** – 7 vertebrae (C1–C7). The first two vertebrae have special names:
    - **C1: Atlas** – Supports the skull, like the mythological Atlas holding the world
    - **C2: Axis** – Acts as a pivot for head rotation (side-to-side motion)
2. **Thoracic Region (Upper/Mid-Back)** – 12 vertebrae (T1–T12)
    - Attach to the ribs, providing protection for the heart and lungs
3. **Lumbar Region (Lower Back)** – 5 vertebrae (L1–L5)
    - Large and strong, built for weight-bearing and stability
4. **Sacral Region (Pelvic Area)** – (S1–S5) fused vertebrae forming the **sacrum**
    - Connects the spine to the pelvic bones
5. **Coccygeal Region (Tailbone)** – Co1–Co4) fused vertebrae forming the **coccyx**
    - Vestigial structure; provides attachment for ligaments and small muscles

Four Spinal Curves

1. **Cervical curve:** C1 to T2; the least pronounced curve.
2. **Thoracic curve:** T2 to T12.
3. **Lumbar curve:** T12 to L5; more pronounced in females due to pelvic anatomy.
4. **Sacrococcygeal curve:** From the top of the sacrum to the tip of the coccyx.

The **thoracic and sacral curves** are **primary curves** which are present at birth, the **cervical and lumbar curves** are **secondary curves**, developing after birth:

- The **cervical curve** forms when a baby can lift its head.
- The **lumbar curve** forms when the child begins to walk.

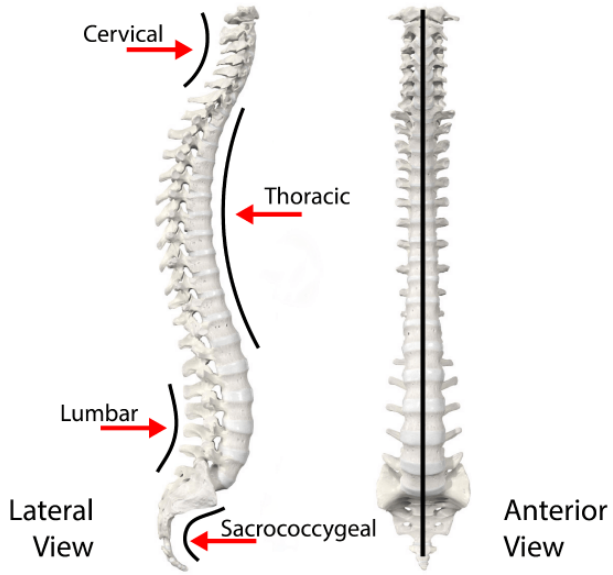


Figure 4.7.2: **The Four Curves of the Vertebral Column.** When viewed laterally, the vertebral column has four curves: the thoracic and sacrococcygeal regions are concave on the anterior side while the cervical and lumbar regions are concave on the posterior side. When viewed anteriorly (or posteriorly) the vertebral column is straight. *(Image credit: "Vertebral Column Curvatures" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

General Structure of a Vertebra

The **vertebrae** (plural of vertebra) are the small bones that form your spinal column, or backbone. While vertebrae look slightly different depending on which region of the spine they are in, they all share the same basic parts:

- **Body:** The large, front portion that supports most of your body weight. The bodies get bigger and thicker as you go down the spine because they carry more weight.
- **Vertebral arch:** The curved back portion that helps form the opening for the spinal cord.
- **Processes:** Small bony projections. The only ones you need to remember are the **two transverse processes** (sticking out to the sides) and the **spinous process** (the bony “spike” you can feel down the middle of your back).

Between the bodies of neighboring vertebrae is an **intervertebral disc**, which separates and cushions the bones while also holding them firmly together. These discs, along with the increasing size of the lower vertebrae, allow the spine to safely bear more and more weight as it descends toward the lower back.

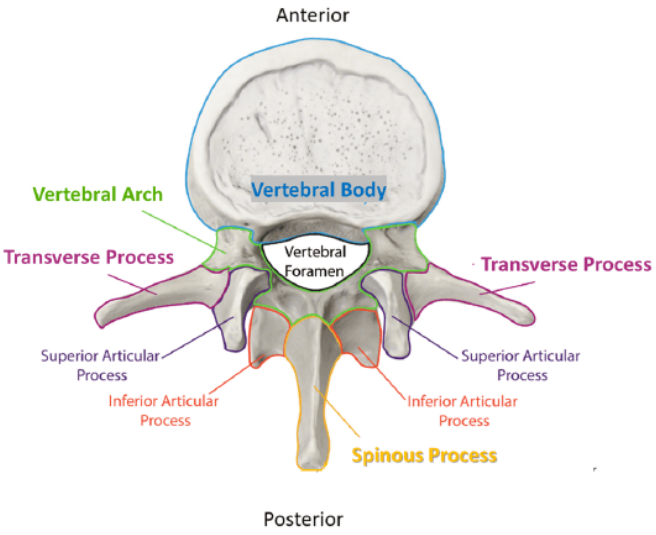


Figure 4.7.3: **Parts of a Typical Vertebra.** A typical vertebra consists of a body and a vertebral arch. Arising from the vertebral arch are the transverse, spinous, superior articular, and inferior articular processes. *(Image credit: "Typical Vertebral Structure" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

- Here is a list of the key parts of a vertebra that you need to know:
- **Vertebral Body**: This is the large, round part at the front of the vertebra. It supports most of your body's weight and is where your vertebrae are separated by cushioning intervertebral discs.
- **Vertebral Arch**: Located behind the vertebral body, this arch surrounds and protects the spinal cord. The arch forms a hole called the **vertebral foramen**. When all the vertebrae are stacked, these holes line up to **create the spinal canal for the spinal cord**.
- **Processes**: Sticking out from the arch are several bony projections:
  - **Spinous process:** The "spine" you can feel if you run your hand down your back.
  - **Transverse processes:** Extend to each side for muscle and ligament attachment.
  - Articular processes: (superior and inferior) Connect one vertebra to another, allowing movement but keeping the spine aligned.

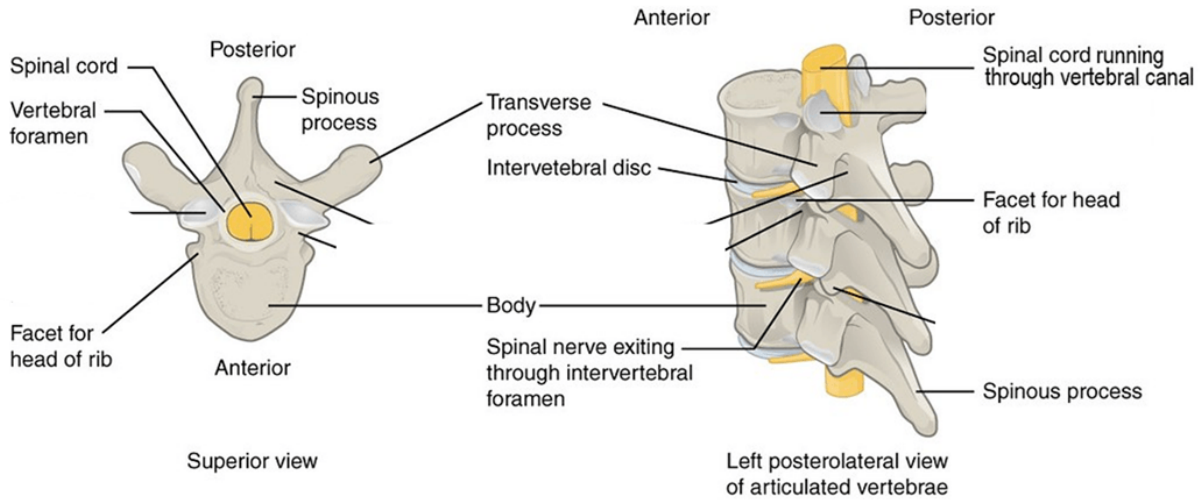


Figure 4.7.4: **Intervertebral Features and Nervous System.** Diagram of thoracic vertebrae showing spinal cord, vertebral foramen, discs, and rib facets. The intervertebral foramen is the space through which spinal nerves pass that is located between the adjacent vertebrae. *(Image credit: "Intervertebral Foramen" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

Regional Modifications of Vertebrae

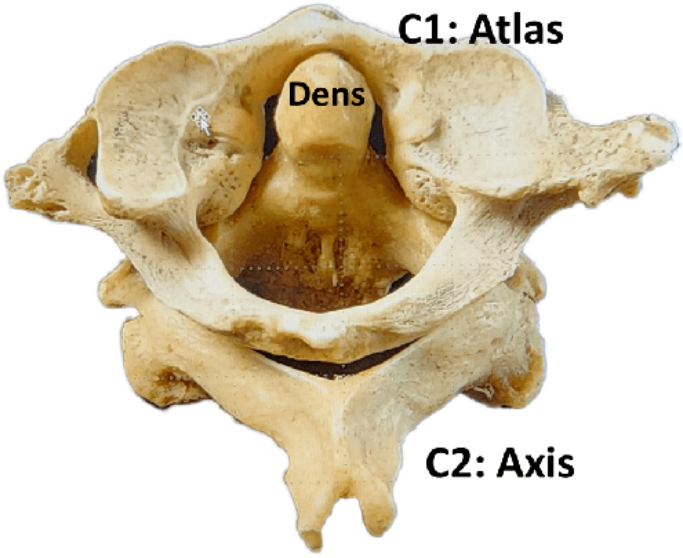
In addition to the general features that all vertebrae share, each region of the vertebral column has its own unique characteristics:

- **Size differences:** Cervical vertebrae are the smallest because they only support the weight of the head. Lumbar vertebrae are the largest since they carry much more of the body's weight.
- **Specialized functions:** Only thoracic vertebrae have facets for rib attachment, making them key players in forming the rib cage.
- **Fused vertebrae:** In adulthood, the vertebrae of the sacrum and coccyx fuse into single bones, providing a solid foundation for the spine.

These differences reflect how each region of the spine is built for a slightly different job—supporting weight, allowing movement, or forming protective structures.

Cervical Vertebrae

The first two cervical vertebrae (C1 and C2) are **special** because they look and work differently from the rest of the spine:



C1 – The Atlas

The **first cervical vertebra (C1)** is called the **atlas** because, like the Titan Atlas from Greek mythology who held up the sky, this vertebra **holds up your skull**.

- It does **not** have a body or a spinous process, instead, it is shaped like a **ring.**
- Its **transverse processes** are longer than those of any other cervical vertebra and stick out more to the sides.
- The **superior articular processes** (upper joints) are **deeply curved** so they can cradle the **occipital condyles** at the base of your skull.
- The **inferior articular processes** (lower joints) are **flat** and face downward to connect with the **C2 vertebra** below.

C2 – The Axis

The **second cervical vertebra (C2)** is called the **axis** because it acts as the pivot point that allows your head to rotate side to side, like shaking your head "no." Key features include:

- **General shape:** Most of the axis looks like a typical cervical vertebra.
- **Dens (odontoid process):** unique, tooth-like bony projection that sticks up from the body of C2. The dens fits against the **anterior arch of the atlas (C1)** and serves as the pivot for head rotation.
- **Transverse ligament:** Holds the dens securely in place, allowing safe rotation without the dens slipping out of position.

Watch the animation below to see how the atlas and axis work together to turn your head:

Interactive Content

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this Interactive Content online

The Sacrum and Coccyx: The Spine's Foundation

The **sacrum** is the **large, triangular bone at the base of your spine**. It is formed by the **fusion of five sacral vertebrae** into

one strong structure.

- **Top (superior aspect):** The sacrum **articulates with the lowest lumbar vertebra (L5)**, forming the **lumbosacral joint**, which allows the spine and pelvis to move together.
- **Back (posterior view):** The fused “spines” of the vertebrae form a **bumpy ridge called the median sacral crest**.
- **Sides:** Each side has a **smooth, ear-shaped (auricular) surface**, which connects the sacrum to the **iliac bones of the pelvis** to form the **sacroiliac joints** — key to weight transfer from the spine to the legs.

Beneath the sacrum is the **coccyx** (in red in the animation below), or **tailbone**, which is **much smaller** and formed by **four tiny fused vertebrae**.

Together, the **sacrum and coccyx** form the **foundation of the spine**, securely linking it to the pelvis.

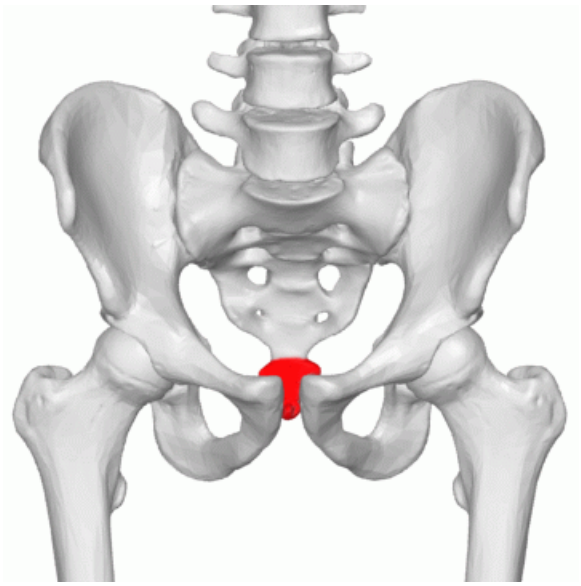


Figure 4.7.5: **Sacrum and Coccyx.** This animation demonstrates how the superior aspect of the sacrum provides the articular surfaces for the lumbosacral joint, laterally visible is the connection to the ileum (sacroiliac joint). In the posterior view, the fused spinous processes forming the median sacral crest are visible. The coccyx (in red) is formed by the fusion of four small coccygeal vertebrae.

There are many more specific regional modifications of the vertebrae, but we will not cover them in this course.

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4.8: Disorders of the Vertebral Column

The spine's natural curves provide strength, balance, and shock absorption, and when these curves become exaggerated or misaligned, they result in abnormal curvatures such as kyphosis, lordosis, and scoliosis.

Master this section and you'll be able to

- Outline the spine's four natural curves and explain why they are important.
- Recognize and differentiate the three main abnormal spinal curvatures based on their appearance, causes, and effects on posture.
- Demonstrate the proper method for visually assessing the spine to identify normal and abnormal curvatures.

The Spine's Natural Curves: Built for Strength, Balance, Flexibility, and Shock Absorption

In the previous section, you learned that the **vertebral column**, or spine, forms the central axis of the human skeleton. This flexible column of interconnected vertebrae stretches from the base of the skull to the pelvis, protecting the spinal cord, supporting the head and trunk, and serving as an anchor for the muscles and ligaments that move the body.

You also explored the **spine's natural curves** — gentle bends in the cervical, thoracic, lumbar, and sacral regions. These curves help maintain balance, absorb shock, and allow the spine to function like a spring rather than a rigid rod.

In this section, we will **review these normal curves briefly** (see image below) and then focus on **what happens when they become exaggerated or misaligned**, leading to **abnormal spinal curvatures**.

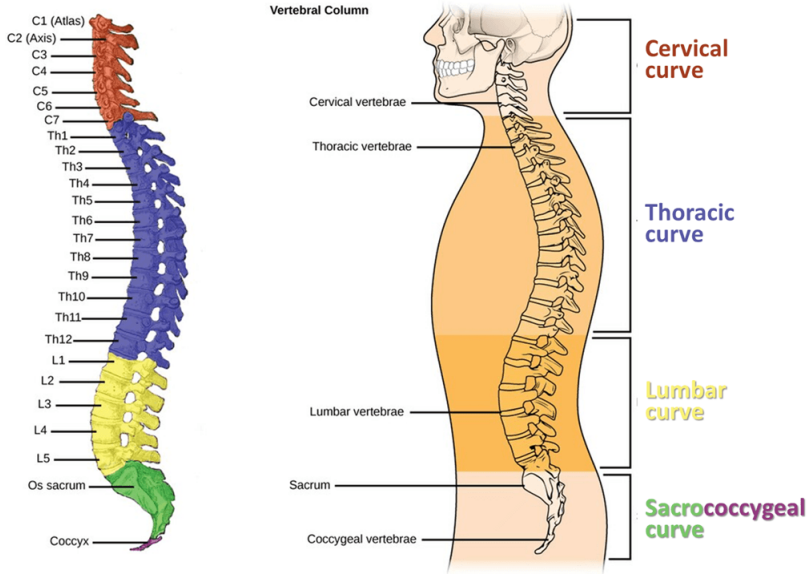
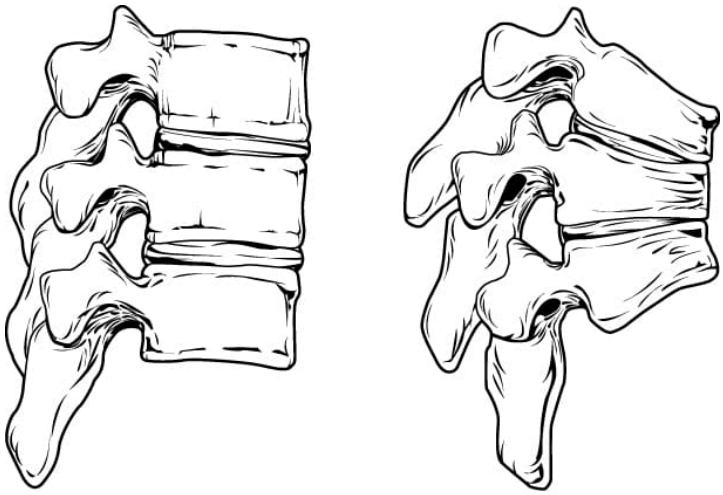


Figure 4.8.1: **Human Vertebral Column.** Normal cervical, thoracic, lumbar, and sacrococcygeal curves.

When Spinal Curves Go Wrong: Abnormal Curvatures

Abnormal curvatures happen when the natural curves become exaggerated or move out of their typical alignment due to development, disease, or changes in body weight. The main types are:



Normal vertebrae

Bone loss amplifies curvature

1. Kyphosis (“Hunchback”)

- **What it is:** An excessive **posterior curve** in the **thoracic region**.
- **Causes:** Often due to **osteoporosis**, which weakens the front part of the vertebrae and causes them to **collapse** over time. (See image on the right).
- **Appearance:** The upper back rounds forward, creating a “hunchback” look.

2. Lordosis (“Swayback”)

- **What it is:** An excessive **anterior curve** in the **lumbar region**.
- **Causes:** Most common with **obesity** or **late pregnancy**, where extra weight in the abdomen pulls the pelvis forward.
- **Appearance:** The lower back arches inward more than usual.

3. Scoliosis

- **What it is:** An **abnormal sideways (lateral) curve** of the spineUsually with a **twist** in the vertebrae.
- **Causes:** Often **unknown**, (idiopathic), but it is believed to involve a combination of genetic and environmental factors. Scoliosis **most commonly occurs during growth spurts** between the ages of ten and twenty, often right before puberty. It occurs in about 3% of people, and typically **females are more severely affected than males** with a ratio of 4:1. Predisposing factors can be:
    - Weak back muscles.
    - Unequal growth on the right and left sides of the vertebral column.
    - Uneven leg lengths.
- **Appearance:** instead of presenting as a straight line, the spine takes on an "S" or "C" shape when viewed from behind, due to a characteristic sideways curvature of the spine. This condition frequently causes visible signs such as uneven shoulders or hips, one shoulder blade or rib sticking out more than the other, and a body that may lean to one side.

Identifying Abnormal Spinal Curves

You can often **spot kyphosis and lordosis** by simple observation with the person standing in **anatomical position** (upright, feet together, arms at the sides). Since the side view highlights the **front-to-back curves** that are involved with kyphosis and lordosis,

you want to stand at the person's side to view the spine in profile when evaluating kyphosis and lordosis. In case of a curvature anomaly, you will observe the following:

- **Kyphosis** you will notice an exaggerated **rounding of the upper back** (“hunchback”).
- **Lordosis** you will notice an exaggerated **inward/forward (sway) of the lower back** (“swayback”).

In order to evaluate for **scoliosis (lateral curvature of the spine),** ask the person to **bend forward at the waist** with arms hanging loosely toward the floor.

- In a healthy spine, **both sides of the back appear level and symmetrical** in this position.
- In scoliosis, one side of the rib cage or lower back will appear **higher than the other**, creating a noticeable **asymmetry or “rib hump.”**
- The person may also **struggle to bend straight forward**, as the spine curves and rotates out of alignment.

Treatments

Treatments for all three spinal deformities typically begin with **conservative approaches,** including physical therapy to **strengthen and stretch back muscles**, postural training, and **pain management** such as medication or heat therapy. **Bracing** may be used, especially for children and adolescents whose bones are still growing, to prevent progression of the abnormal spinal curvature.

In more **severe cases,** when these measures are not effective or if the spinal curve is rapidly progressing, **surgical intervention** — most commonly spinal fusion — may be recommended to correct and stabilize the spine. The specific treatment approach depends on the severity, symptoms, and underlying cause of the curvature.

Identifying Abnormal Curves

- **Kyphosis and Lordosis:** View the person’s spine from the **side** while they stand in the **anatomical position**.
- **Scoliosis:** View the person’s spine from behind to check if it is straight or not. You can also have the person **bend forward**. If scoliosis is present, the right and left sides of the back will not be level with each other in the bent position. An individual might also have difficulty in bending directly forward.

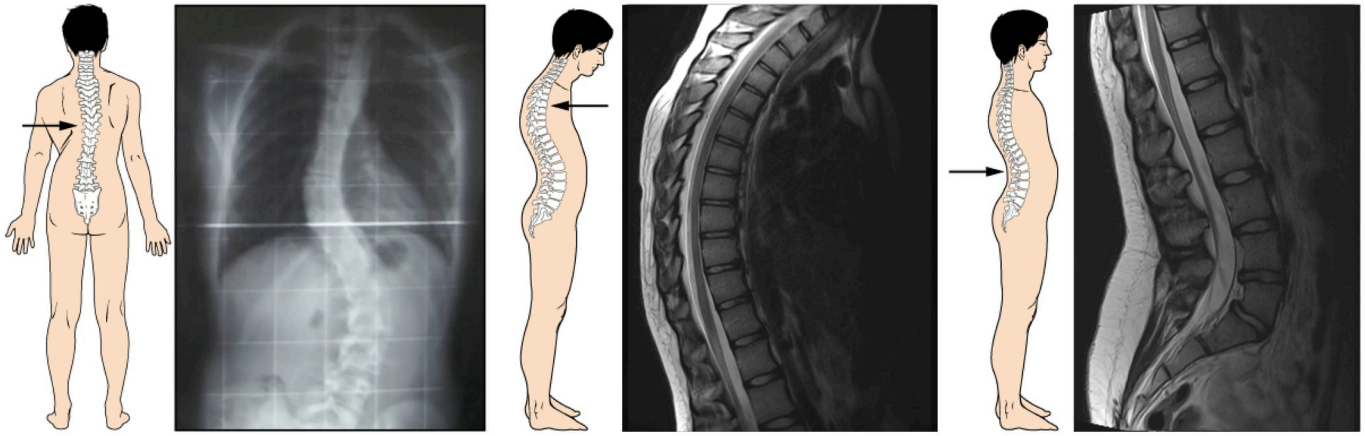


Figure 4.8.2: **Abnormal Curvatures of the Vertebral Column.** (a) Scoliosis is an abnormal lateral bending of the vertebral column. (b) An excessive curvature of the upper thoracic vertebral column is called kyphosis. (c) Lordosis is an excessive curvature in the lumbar region of the vertebral column. (*Image credit: "Abnormal Curves of Vertebral Column" by Jennifer Lange is licensed under CC BY-NC-SA 4.0(opens in new window). Modification of original by OpenStax(opens in new window). "Kyphosis" and "Lordosis" MRI images from Radiopedia(opens in new window). Case courtesy of Mostafa El-Feky.)*

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4.9: Structural and Functional Classification of Joints

There are three structural three functional classifications of joints.

Master this section and you'll be able to

- Describe the three structural classification of joints, including their defining features.
- Explain the functional classification of joints based on the degree of movement permitted.
- Compare and relate structural and functional classifications to explain how joint structure determines its range of motion.

A **joint**, also called an **articulation**, is where two bones meet in the skeletal system. Joints provide the means for movement. The type and characteristics of a given joint determines its degree and type of movement. Joints are classified in two main ways: by their **structure**, which describes what specifically holds the bones together, and by their **function**, which describes how much movement the joint allows.

Learning both systems gives a complete picture of joint anatomy and physiology.

Structural Classification of Joints

Structural classification categorizes the joints based on the **type of tissue involved in formation**. There are **three structural classifications** of joints: fibrous, cartilaginous, and synovial.

1) Fibrous Joints: Built for Strength, Not Movement

Fibrous joints are places where bones are held together by **dense connective tissue** rich in collagen fibers (remember the tissue name is dense fibrous connective tissue). These joints are usually **fixed or allow very little movement** because the bones are tightly bound together. Their edges are often **irregular and interlock** like puzzle pieces. Two examples of fibrous joints are:

1. **Sutures:** found in the **skull (cranium)**. In infants, sutures allow slight movement to help during birth and early brain growth. In adults, they become **mostly immovable** but retain tiny flexibility for shock absorption.

2. **Syndesmoses:** two bones are held together by **dense fibrous connective tissue** (usually a ligament or interosseous membrane) that allows **slight movement**. This type of joint is found between **long bones**, such as the **radius and ulna** (**radioulnar interosseous membrane**) or the interosseous membrane between the **tibia and fibula.**

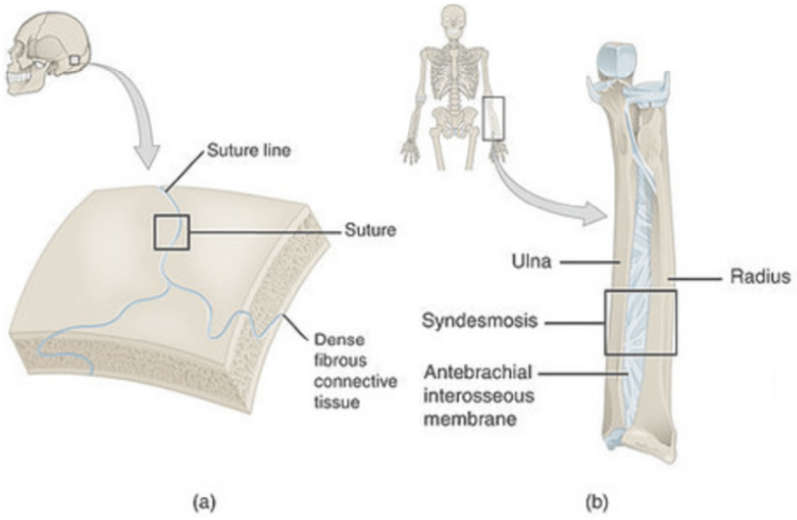


Figure 4.9.1: **Fibrous joints.** Image demonstrating the three types of fibrous joints. (a) Sutures (b) Syndesmosis.

2) Cartilaginous Joints: Built with Cartilage, Made to Bend

Cartilaginous joints are joints where the bones are connected by cartilage — either **hyaline cartilage** or **fibrocartilage**. These joints allow **a little movement**, more than fibrous joints but less than freely movable synovial joints.

Cartilaginous joints come in **two types**:

Primary Cartilaginous Joints (Synchondroses)

Primary cartilaginous joints are connected by **hyaline cartilage.** They are called primary because they appear first during development and are usually **temporary**, associated with early bone growth where cartilage is later replaced by bone.

Example: The **epiphyseal (growth) plates** in long bones.

Secondary Cartilaginous Joints (Symphyses).

Secondary cartilaginous joints are connected by **fibrocartilage**, often with some hyaline cartilage at the edges. They are called secondary because they develop after the primary joints and are formed of fibrocartilage — which appears later in development and remains throughout life.they are **permanent** joints, providing **strength and flexibility** where a **combination of stability and a small degree of movement** is required (e.g.: spine, pelvis)

Examples:

- **Intervertebral discs** between vertebrae
- **Pubic symphysis** between the two hip bones

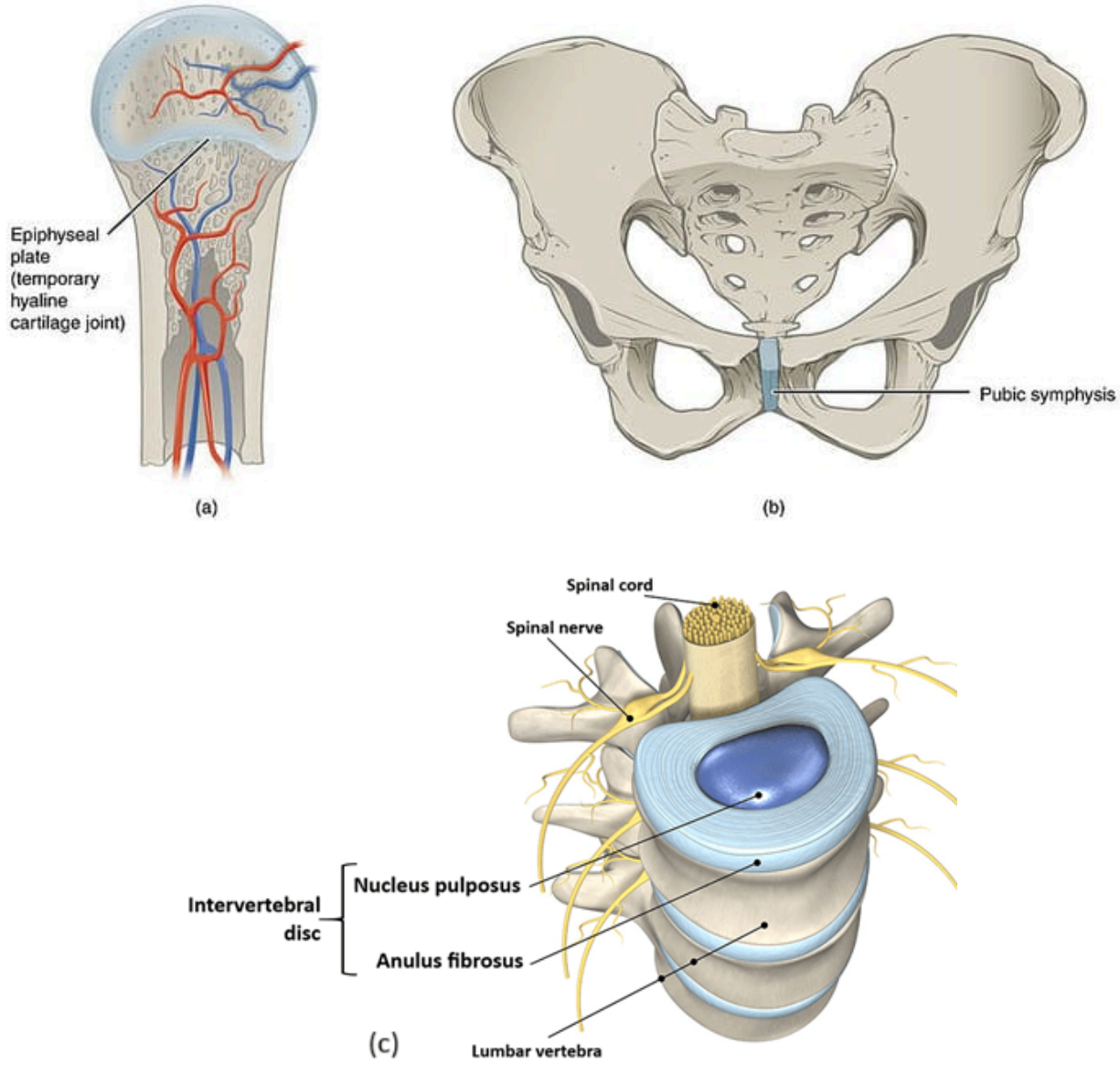
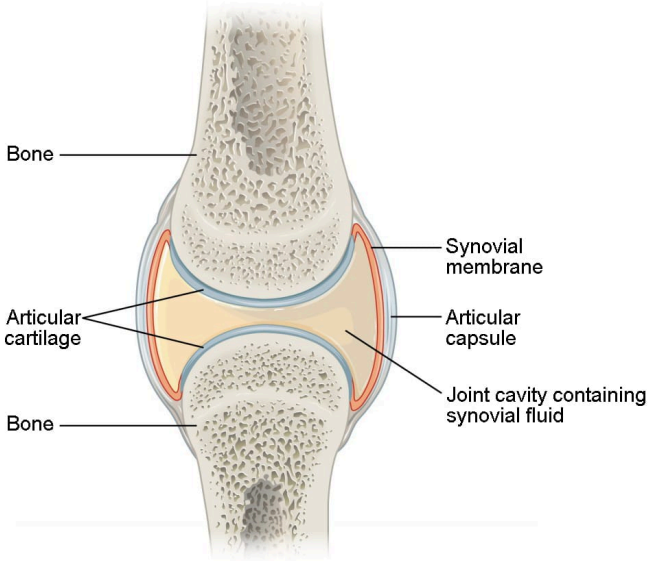


Figure 4.9.2: **Cartilaginous Joints.** Images from left to right show: (a) A **synchondrosis**, specifically an **epiphyseal plate** (a temporary hyaline cartilage joint); (b, c) two examples of **secondary cartilaginous joints (symphyses)**: the **pubic symphysis** on the left and an **intervertebral disc** on the right.

3) Synovial Joints: Encased in Fluid, Movement Made Easy

Synovial joints are the **most common and most freely movable** type of joint in the body. Examples include the **shoulders, elbows, knees, hips, and fingers**.

The Key features of a generic synovial joint are listed below. Please compare to the image on the right:



- **S ynovial Cavity**
  - A small **fluid-filled space** between the bones
  - Allows the bones to **move smoothly without rubbing directly against each other**
- **Articular Capsule**
  - **Outer layer:** Dense irregular connective tissue, continuous with the **periosteum** of the bones
  - **Function:** Forms a **protective sleeve** around the joint and helps **hold the bones together**
- **Articular Cartilage**
  - Layer of **smooth hyaline cartilage** covering bone surfaces inside the joint
  - Prevents bones from **grinding** against each other
- **Synovial Fluid**
  - **Thick, slippery fluid** inside cavity
  - **Functions:** Synovial fluid lubricates the joint to reduce friction, nourishes the cartilage, and helps with shock absorption during movement

---

Functional Classification of Joints

Above, you explored the structural classification of joints, which explains how a joint is physically built. Now it is time to shift gears and look at how joints move. Again, there are **three functional classifications** based on how much (or how little) motion a joint allows. In other words, while structural classification tells you *what* the joint is made of, functional classification focuses on *how* it moves.

1) Synarthrosis – No Movement

Most (but not all!) fibrous joints are synarthroses, meaning they allow little to no movement. These joints provide stability and protection. A good example: the **sutures of the skull.**

Exception: The epiphyseal plate, although NOT a fibrous joint (it is made of hyaline cartilage), is functionally classified as a synarthrosis, because it is immobile. Eventually, it ossifies and becomes solid bone.

2) Amphiarthrosis – Slightly Moveable

Most (but again, not all) cartilaginous joints fall into this category. Amphiarthroses allow limited movement, helping with flexibility and shock absorption. Examples include the pubic symphysis and the intervertebral discs.

Exceptions: The radioulnar and tibiofibular interosseous membranes are both amphiarthroses because, even though they are structurally fibrous joints, they allow a small degree of movement.

3) Diarthrosis – Freely Movable

All synovial joints are diarthroses. These joints allow a wide range of movement and include the knee, hip, shoulder, and essentially any joint joint in your body that you can move freely. Synovial joints are subdivided based on the shapes of the articulating surfaces of the bones that form each joint. The six types of synovial joints are pivot, hinge, condyloid, saddle, plane, and ball-and socket-joints. *(See figure below).* For more detail, see the next sections (4.10)

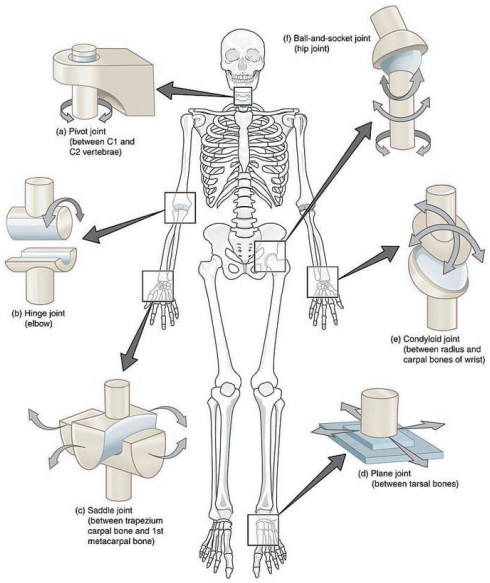


Figure 4.9.3: **Types of Synovial Joints —** Image of a skeleton showing the different classes of synovial joints.

💡*Note:* "-is" vs. "-es" Endings in Joint Anatomy and General Medical Language

In anatomy, you will often see joint names that end in **-is** or **-es**.
This is not a spelling mistake — it is just grammar! Why is that so? In **Greek**, words ending in **-sis** change to **-seis** in the plural. When adapted into **Latin-based anatomy terms** and then into **English**, this became **-ses**.

- **-is** = singular (one joint)
- **-es** = plural (two or more joints)

Examples

Singular (-is)	Plural (-es)	Meaning
Synarthrosis	**Synarthroses**	Immovable joint(s)
Amphiarthrosis	**Amphiarthroses**	Slightly movable joint(s)
Diarthrosis	**Diarthroses**	Freely movable joint(s)

Other common examples you are probably familiar with:

Diagnosis → Diagnoses

Oasis → Oases

Analysis → Analyses

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4.10: Synovial Joints

Synovial joints are freely movable joints defined by a fluid-filled joint cavity, articular cartilage, and supportive capsules, ligaments, and muscles that together allow smooth, stable, and highly flexible movement between bones.

Master this section and you'll be able to

- Describe all the the structural components of a synovial joint.
- Classify and compare the six types of synovial joints (ball-and-socket, plane, pivot, hinge, saddle, and condyloid) based on their anatomical structure, axes of movement, and range of motion.
- Explain bursitis, a common disorder of synovial joints (include causes, symptoms, and treatment options).

Synovial joints are the most common type of joint in the body. A key structural characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a **joint cavity**. This **fluid-filled** space is the site at which the articulating surfaces of the bones contact each other. Also unlike fibrous or cartilaginous joints, the articulating bone surfaces at a synovial joint are not directly connected to each other with fibrous connective tissue or cartilage. This gives the bones of a synovial joint the ability to move smoothly against each other, allowing for increased joint mobility.

Structural Features of Synovial Joints

You have learned that synovial joints are special because they have a **joint cavity** — a space between the bones that allows for free movement. This cavity is enclosed by the **articular capsule**, a tough sleeve of fibrous connective tissue that attaches to each bone just outside the joint surface.

Inside the cavity, the bones do not rub directly against each other. Instead, each articulating surface is covered with a smooth layer of **articular cartilage** (made of hyaline cartilage). Think of this cartilage like a **Teflon® coating** — it reduces friction and protects the bone beneath it. Unlike cartilaginous joints, the cartilage on each bone stays separate; the gap is filled with **synovial fluid**.

The **synovial membrane**, which lines the inside of the capsule, produces this **thick, slippery fluid**. **Synovial fluid** acts like oil in a machine: it lubricates the joint so the bones glide easily and also nourishes the cartilage, which has no blood supply of its own.

Because synovial joints allow a wide range of movement, they are functionally classified as **diarthroses** (freely movable joints).

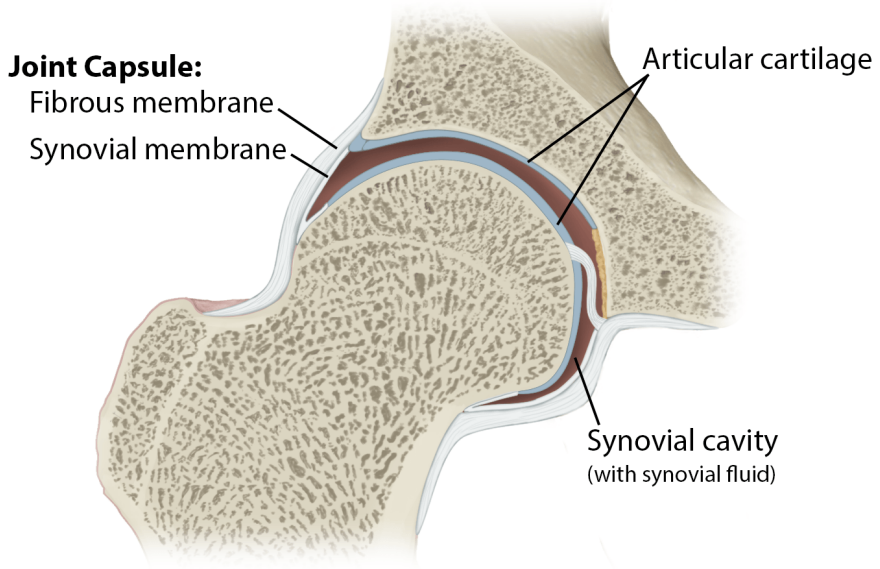


Figure 4.10.1: **Synovial Joints.** Synovial joints enable smooth movement between bones. An articular capsule surrounds the joint

cavity, which contains synovial fluid. The bone surfaces are covered with articular cartilage, and ligaments stabilize the joint by holding the bones together and limiting abnormal motion.

Ligaments: The Joint's Safety Straps

Outside of their articulating surfaces, the bones are held together by **ligaments** — strong bands of fibrous connective tissue. Ligaments stabilize the joint by anchoring the bones together and preventing their separation. They allow for normal movement while **preventing too much motion** that could cause injury. Depending on where in relationship to the joint capsule they are located, ligaments are classified as:

- **Extrinsic**: outside the capsule
- **Intrinsic**: fused to the capsule
- **Intracapsular**: located inside the capsule

Muscles and Tendons: Dynamic Joint Support

Muscles and their **tendons**, which connect muscle to bone, also help support synovial joints when the tendons cross them. When a joint is under more strain, the surrounding muscles contract more strongly, acting like "dynamic ligaments" to reinforce and protect the joint. This kind of support is especially important in joints like the **shoulder**, where the ligaments are relatively weak.

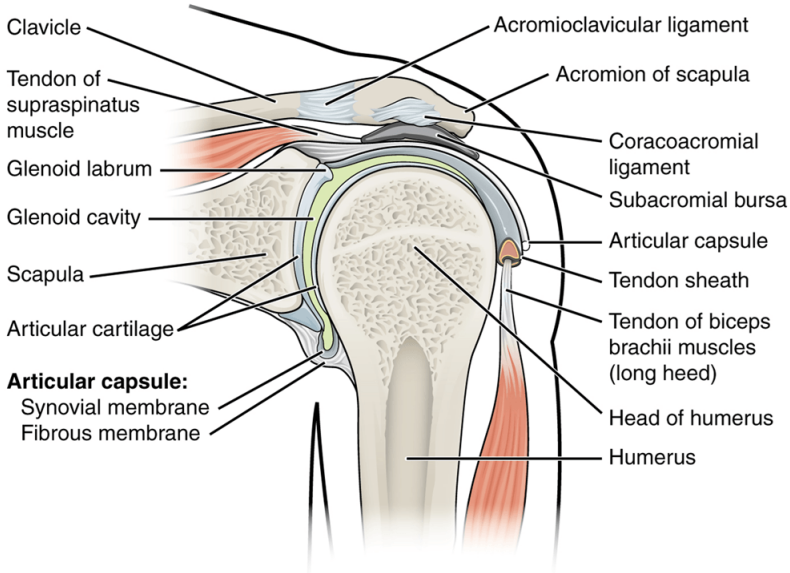


Figure 4.10.2: **Shoulder Joint (a.k.a. glenohumeral joint).** Diagram of the shoulder joint showing bones, ligaments, tendons, bursa, and articular capsule. This is a **ball-and-socket joint**, with the **rounded head of the humerus** (upper arm bone) nesting into the shallow **glenoid cavity of the scapula** (shoulder blade). This design lets you swing, lift, and rotate your arm almost anywhere you want — earning it the title of the **most flexible joint in the human body**.

The Knee's Support Team: Additional Structures That Protect and Stabilize Synovial Joints

Some synovial joints include additional "helper" structures that improve stability, reduce friction, and protect the bones during movement. The knee joint provides an excellent example of these supportive features.

- **Menisci** (singular: **meniscus**) in the knee. They are **C-shaped wedges of fibrocartilage** sitting between the femur (thigh bone) and tibia (shin bone). There are two menisci in each knee (medial and lateral). Their main function is shock absorption by cushioning the impact between the femur and tibia during walking, running, and jumping.

- **Fat pads** act as cushions inside some joints.

- **Bursae** are little fluid-filled sacs that reduce friction between bones, muscles, tendons, or skin.

    - **Subcutaneous bursae** sit between skin and bone (e.g., over the kneecap).
    - **Submuscular bursae** sit between a muscle and bone (e.g., at the hip).
    - **Subtendinous bursae** sit between tendon and bone (e.g., under the shoulder's acromion).

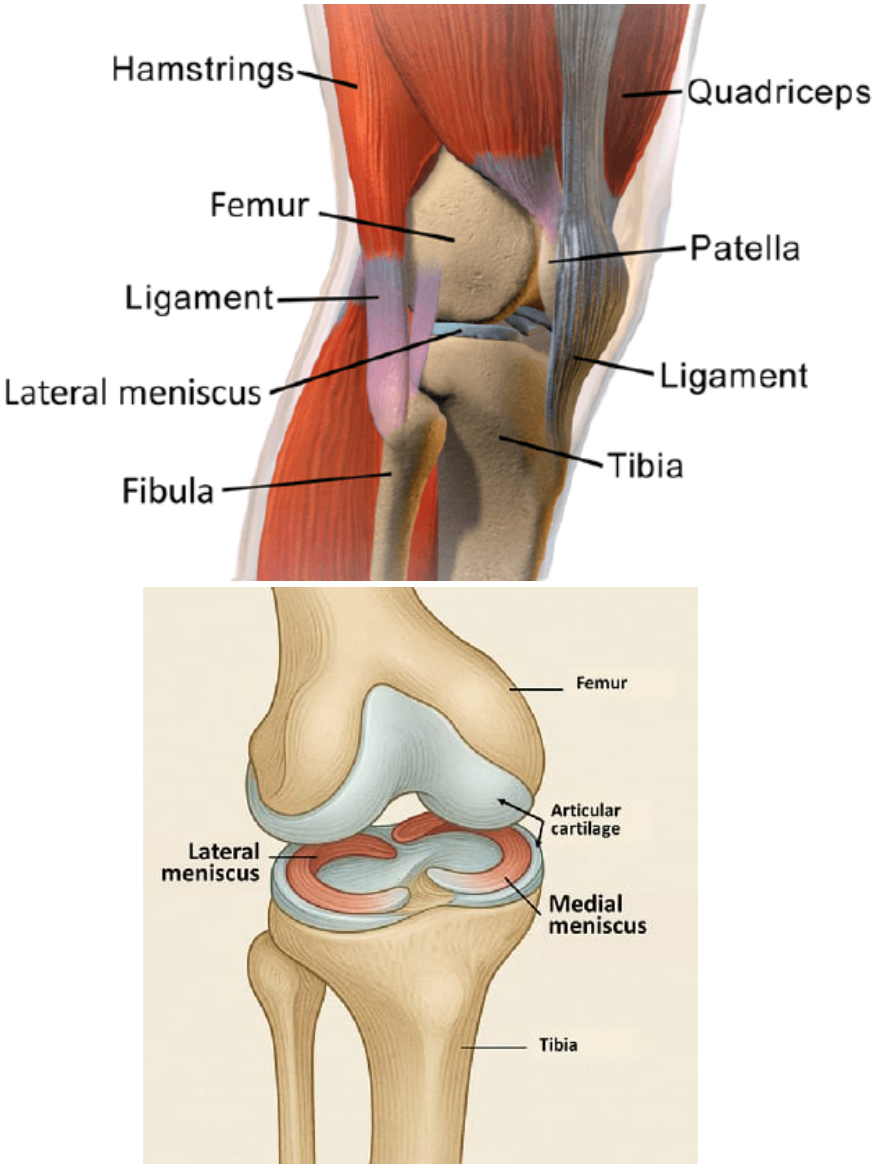


Figure 4.10.3: **Knee Joint.** *Image on the left:* Lateral view shows the femur articulating with the tibia to form a hinge joint. The patella sits anteriorly and improves leverage for the quadriceps muscle during extension. Ligaments stabilize the joint, and the lateral meniscus acts as a shock absorber between the bones. *Image on the right:* Simplified drawing of the crescent-shaped menisci; the patella is missing.

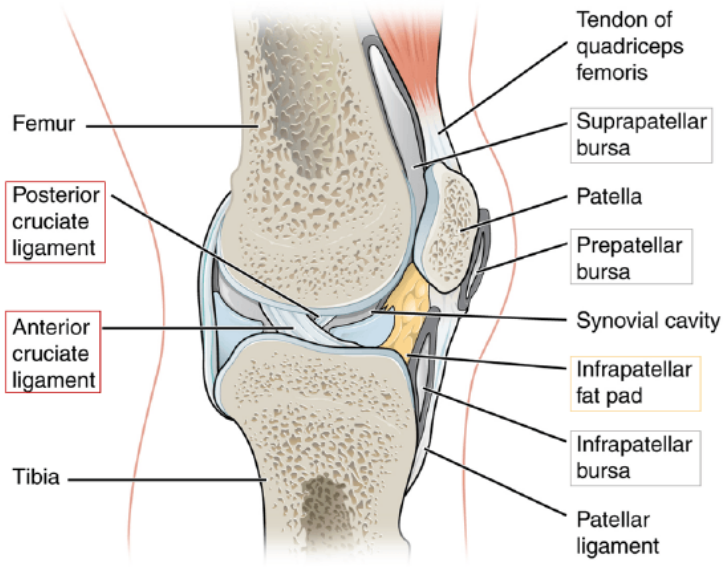


Figure 4.10.4: **Sagittal Section of the Knee Joint.** The femur (thigh bone) articulates with the tibia (shin bone), and the patella (kneecap) lies anteriorly within the quadriceps tendon. The anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) cross within the joint to stabilize the knee and prevent excessive forward or backward movement of the tibia. Several bursae and the synovial cavity are shown, which reduce friction and allow smooth movement during flexion and extension of the knee.

Types of Synovial Joints

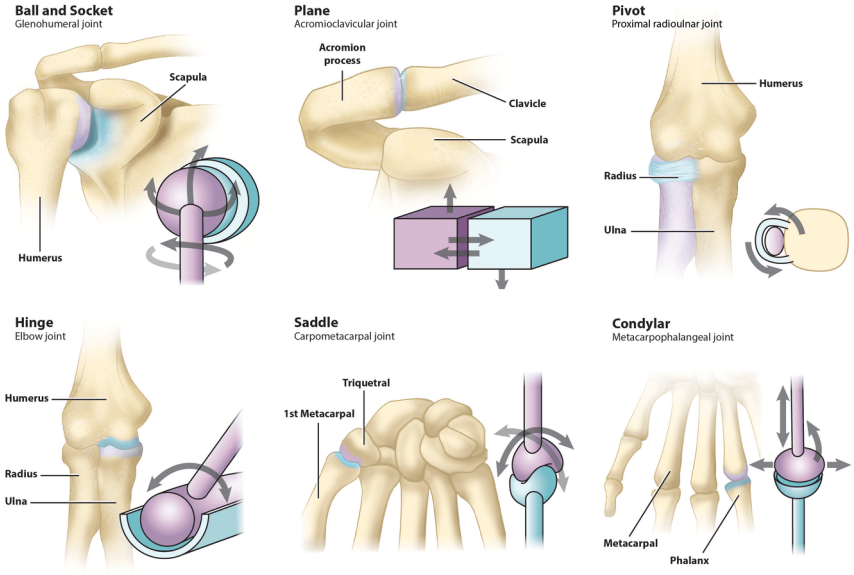


Figure 4.10.4: **Types of Synovial Joints.** The six types of synovial joints allow the body to move in a variety of ways that are determined by the fit (shape) of the two articulating bones.

Ball-and-Socket Joint

The joint with the **greatest range of motion** is the **ball-and-socket joint**, the champion of flexibility in the human body. In these joints, the **rounded head** of one bone (the “ball”) fits into the **cup-shaped socket** of another bone.

There are only **two** in the body:

- **Hip joint:** the head of the femur fits into the acetabulum of the hip bone
- **Shoulder joint:** the head of the humerus fits into the glenoid cavity of the scapula

Functionally, ball-and-socket joints are **multiaxial** — they can move forward and backward (**anterior–posterior**), side-to-side (**medial–lateral**), and rotate around their long axis.

The **shoulder** has a **shallow socket**, giving it an impressive range of motion, but making it less stable. The **hip** has a **deep socket** and strong ligaments, which limit motion but provide stability for standing, walking, and supporting body weight.

Plane Joint (Gliding Joints)

A **plane joint** has flat or slightly curved bone surfaces that are about the same size. This design lets the bones **slide past each other**, but the movement is usually small and limited by nearby ligaments. In theory, the shape of the articulating surfaces could allow movement in many directions (even rotation), making them **multiaxial joints**. In reality, the exact movements depend on the specific joint and how much nearby ligaments and bones allow—some can move in several ways, others in just one.

Examples include:

- Between wrist bones (**intercarpal joints**)
- Between foot bones (**intertarsal joints**)
- Between the clavicle and acromion of the scapula (**acromioclavicular joint**)
- Between the articular processes of neighboring vertebrae (**zygapophysial joints**)

Pivot Joint

This joint works like a turning axle. One bone has a **rounded projection** that fits inside a **ring** formed partly by another bone and partly by a ligament. This setup allows the bone to **rotate** within the ring.

Because the movement happens around **one axis only**, pivot joints are **uniaxial**.

Examples include:

- **Atlantoaxial joint** (between C1 atlas and C2 axis vertebrae): The dens of the axis fits against the inside of the atlas and is secured by the transverse ligament. This joint lets you shake your head “no.”
- **Proximal radioulnar joint** (near the elbow): The head of the radius is held in place by a ligament as it rotates against the ulna’s radial notch. This rotation lets you turn your palm up (**supination**) or down (**pronation**).

Hinge Joint

A **hinge joint** works much like the hinge on a door — it allows movement in just **one direction**. At these joints, the convex surface of one bone fits into the concave surface of another, permitting bending (**flexion**) and straightening (**extension**) along a **single axis**.

Because movement occurs around **only one axis**, hinge joints are **uniaxial**.

Examples include:

- **Elbow joint** – between the humerus and ulna
- **Knee joint** – between the femur and tibia (with help from other structures for stability)
- **Ankle joint** – between the tibia, fibula, and talus

- **Interphalangeal joints** – between the finger and toe bones

Hinge joints are strong and stable, but their design limits them to forward-and-back movement — no sideways motion or rotation.

Saddle Joint

A **saddle joint** gets its name because both bone surfaces are shaped like a saddle (U-shaped) — **concave in one direction and convex in the other**. This shape allows movement in **two planes**, making them **biaxial joints**.

The best example is the **first carpometacarpal joint** at the base of the thumb, between the trapezium (a wrist bone) and the first metacarpal. This joint lets the thumb move in the same plane as the palm **and** stick out perpendicular to it — giving humans their famous **opposable thumb** for gripping and manipulating objects.

Condyloid (Condylar) Joints

A **condyloid joint** is like a ball-and-socket joint, but the surfaces are **oval** instead of round. This shape allows movement in **two planes** — making them **biaxial joints** — but it prevents twisting.

Examples include:

- **Knuckle joints** (metacarpophalangeal joints) between each metacarpal and its proximal phalanx
- **Radiocarpal joint** of the wrist, where the end of the radius meets the scaphoid, lunate, and triquetrum bones

Condyloid joints allow:

1. **Bending and straightening** (flexion and extension) – sagittal plane
2. **Side-to-side movement** (abduction and adduction) – frontal plane

Why no twisting?
Because the oval surfaces have a **long axis** and a **short axis**. When you try to rotate, the long axis bumps into the other bone's short axis, stopping the movement.

Interactive Link

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Watch this video to see an animation of synovial joints in action. Synovial joints are places where bones articulate with each other inside of a joint cavity. The different types of synovial joints are the ball-and-socket joint (shoulder joint), hinge joint (knee), pivot joint (atlantoaxial joint, between C1 and C2 vertebrae of the neck), condyloid joint (radiocarpal joint of the wrist), saddle joint (first carpometacarpal joint, between the trapezium carpal bone and the first metacarpal bone, at the base of the thumb), and plane joint (facet joints of vertebral column, between superior and inferior articular processes). Which type of synovial joint allows for the widest range of motion?

A

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4.11: Types of Body Movements

Synovial joints provide the body with a wide range of movements across different planes, creating flexibility, stability, and motion.

Master this section and you'll be able to

- Define the different types of body movements
- Identify the joints that allow for these motions

Synovial joints allow the body a tremendous range of movements. Each movement at a synovial joint results from the contraction or relaxation of the muscles that are attached to the bones on either side of the articulation. The type of movement that can be produced at a synovial joint is determined by its structural type. While the ball-and-socket joint gives the greatest range of movement at an individual joint, in other regions of the body, several joints may work together to produce a particular movement. Overall, each type of synovial joint is necessary to provide the body with its great flexibility and mobility. There are many types of movement that can occur at synovial joints (Table 4.11.1). Movement types are generally paired, with one being the opposite of the other. Body movements are always described in relation to the anatomical position of the body: upright stance, with upper limbs to the side of body and palms facing forward.

Planar Movements

The most common movements that our joints can do see that part of the body move in a motion parallel to one of the three body planes:

- sagittal plane movements - part moves in an anterior or posterior direction
- frontal plane movements - part moves in a medial or lateral direction
- transverse plane movements - a twisting movement

Sagittal Plane - Flexion and Extension

Flexion and **extension** are movements that take place within the sagittal plane and involve anterior or posterior movements of the trunk or limbs.

In the limbs, flexion decreases the angle between the bones (bending of the joint), while extension increases the angle and straightens the joint. For the upper limb, all anterior-going motions are flexion and all posterior-going motions are extension. These include anterior-posterior movements of the arm at the shoulder, the forearm at the elbow, the hand at the wrist, and the fingers at the metacarpophalangeal and interphalangeal joints. For the thumb, extension moves the thumb away from the palm of the hand, within the same plane as the palm, while flexion brings the thumb back against the index finger or into the palm. These motions take place at the first carpometacarpal joint. In the lower limb, bringing the thigh forward and upward is flexion at the hip joint, while any posterior-going motion of the thigh is extension. Note that extension of the thigh beyond the anatomical (standing) position is greatly limited by the ligaments that support the hip joint. Knee flexion is the bending of the knee to bring the foot toward the posterior thigh, and extension is the straightening of the knee. Flexion and extension movements are seen at the hinge, condyloid, saddle, and ball-and-socket joints of the limbs (Figure 4.11.1).

For the vertebral column, sagittal plane movements keep the inferior portion of the body stable and the superior portion moves in an anterior or posterior direction. Again, flexion is an anterior bending while extension involves a posterior-directed motion, such as straightening from a flexed position or bending backward (Figure 4.11.1). These movements occur in both the cervical and lumbar regions of the vertebral column and involve both the symphysis joint formed by each intervertebral disc, as well as the plane type of synovial joint formed between the inferior articular processes of one vertebra and the superior articular processes of the next lower vertebra.

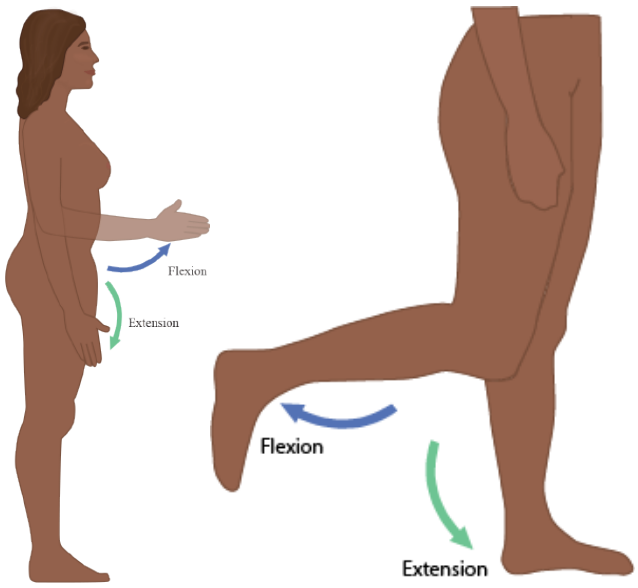


Figure 4.11.1: **Flexion and Extension.** Flexion and extension are opposing movements that are in the sagittal (anterior–posterior) plane of motion. These movements take place at the intervertebral, shoulder, hip, elbow, knee, wrist, metacarpophalangeal, metatarsophalangeal, and interphalangeal joints. *(Image credit: "Flexion and Extension" by Sophia Elizondo is licensed under CC BY-NC-SA 4.0.)*

Hyperextension is the abnormal or excessive extension of a joint beyond its normal range of motion, thus resulting in injury. Similarly, **hyperflexion** is excessive flexion at a joint. Hyperextension injuries are common at hinge joints such as the knee or elbow. In cases of “whiplash” in which the head is suddenly moved backward and then forward, a patient may experience both hyperextension and hyperflexion of the cervical region.

Frontal Plane - Lateral Flexion, Abduction and Adduction

Abduction and **adduction** motions occur within the frontal (coronal) plane and involve medial-lateral motions of the limbs. Abduction moves the limb laterally away from the midline of the body, while adduction is the opposing movement that brings the limb toward the body midline or across the midline. For example, abduction is raising the arm at the shoulder joint, moving it laterally away from the body, while adduction brings the arm down to the side of the body. Similarly, abduction and adduction at the wrist moves the hand away from or toward the midline of the body. Spreading the fingers or toes apart is also abduction, while bringing the fingers or toes together is adduction. For the thumb, abduction is the anterior movement that brings the thumb to a 90° perpendicular position, pointing straight out from the palm. Adduction moves the thumb back to the anatomical position, next to the index finger. Abduction and adduction movements are seen at joints with more than a single axis of rotation - condyloid, saddle, and ball-and-socket joints (Figure 4.11.2) .

Lateral flexion is the bending of the neck or trunk toward the right or left, moving either away from or closer to the midline. Just like with other movements, lateral flexion right and lateral flexion left are opposing movements. If you tilt your head toward your left shoulder this is lateral flexion left; moving your head back to center is lateral flexion right.

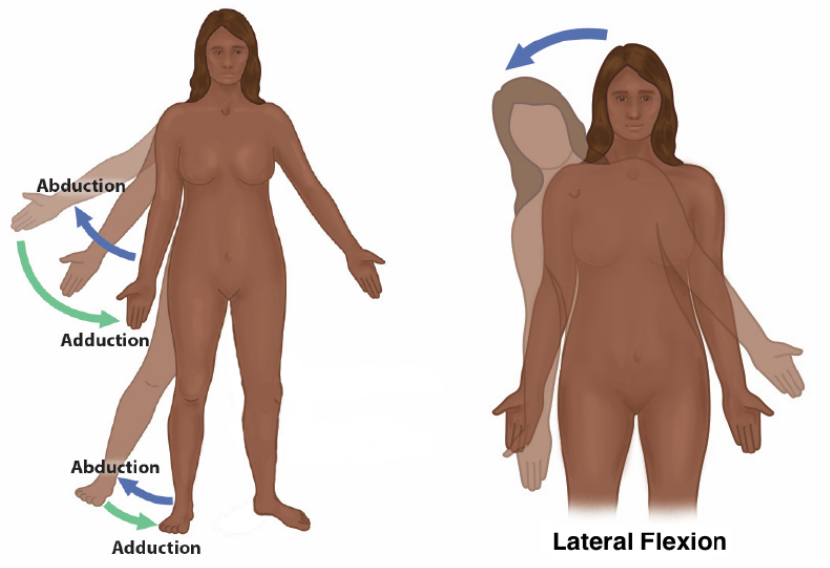


Figure 4.11.2: **Adduction, Abduction and Lateral Flexion.** Adduction and Abduction are opposing movements that are in the frontal (medial-lateral) plane of motion. These movements take place at the shoulder, hip, wrist, and metacarpophalangeal joints. When the motion is occurring at the intervertebral joints this movement is called lateral flexion to the right or to the left. *(Image credit: "Movements" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors, modifications by Jennifer Lange.)*

Rotation

Rotation can occur within the vertebral column, at a pivot joint, or at a ball-and-socket joint. Rotation of the neck or body is the twisting movement produced by the summation of the small rotational movements available between adjacent vertebrae. At a pivot joint, one bone rotates in relation to another bone. This is a uniaxial joint, and thus rotation is the only motion allowed at a pivot joint. For example, at the atlantoaxial joint, the first cervical (C1) vertebra (atlas) rotates around the dens, the upward projection from the second cervical (C2) vertebra (axis). This allows the head to rotate from side to side as when shaking the head "no." The proximal radioulnar joint is a pivot joint formed by the head of the radius and its articulation with the ulna. This joint allows for the radius to rotate along its length during pronation and supination movements of the forearm (Figure 4.11.3).

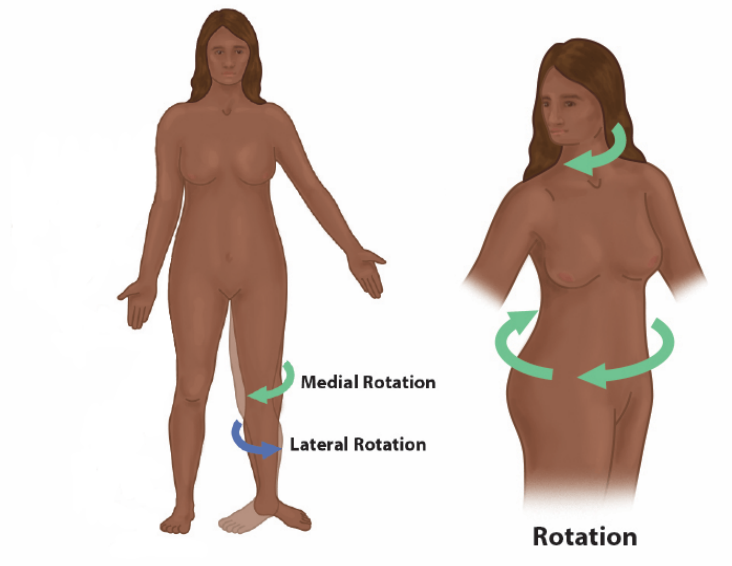


Figure 4.11.3: **Rotations.** Medial rotation and lateral rotation are opposing movements that are in the transverse plane of motion. These movements are twisting motions that take place at the shoulder and hip joints. When the motion is occurring at the intervertebral joints this movement is called lateral rotation to the right or to the left. *(Image credit: "Movements" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors, modifications by Jennifer Lange.)*

Rotation can also occur at the ball-and-socket joints of the shoulder and hip. Here, the humerus and femur rotate around their long axis, which moves the anterior surface of the arm or thigh either toward or away from the midline of the body. Movement that brings the anterior surface of the limb toward the midline of the body is called **medial (internal) rotation**. Conversely, rotation of the limb so that the anterior surface moves away from the midline is **lateral (external) rotation** (Figure 4.11.3). Be sure to distinguish medial and lateral rotation, which can only occur at the multiaxial shoulder and hip joints, from circumduction, which can occur at either biaxial or multiaxial joints.

Non-planar or Special Movements

Circumduction

Circumduction is the movement of a body region in a circular manner, in which one end of the body region being moved stays relatively stationary while the other end describes a circle. It involves the sequential combination of flexion, adduction, extension, and abduction at a joint. This type of motion is found at biaxial condyloid and saddle joints, and at multiaxial ball-and-sockets joints (Figure 4.11.4).

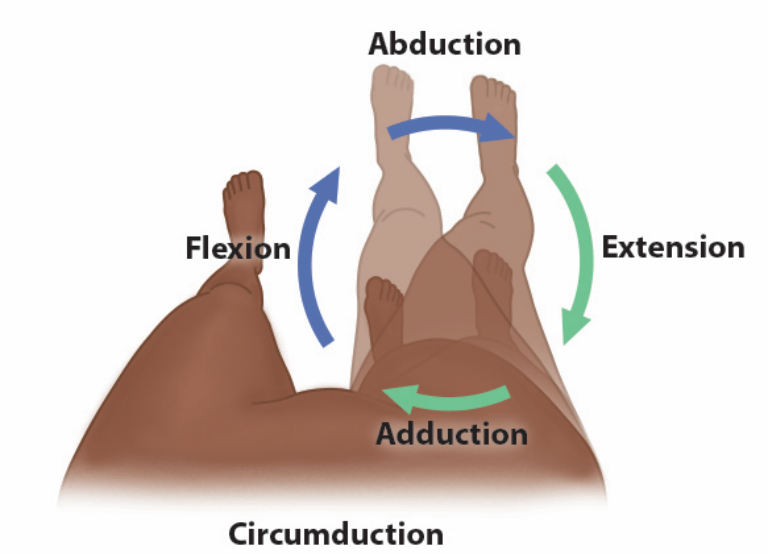


Figure 4.11.4: **Circumduction.** Circumduction is actually a combination of movements that cross multiple planes. This motion can only take place at multiaxial joints - the shoulder, wrist, metacarpophalangeal, and hip joints. *(Image credit: "Movements" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Supination and Pronation

Supination and pronation are movements of the forearm. In the anatomical position, the upper limb is held next to the body with the palm facing forward. This is the **supinated position** of the forearm. In this position, the radius and ulna are parallel to each other. When the palm of the hand faces backward, the forearm is in the **pronated position**, and the radius and ulna form an X-shape.

Supination and pronation are the movements of the forearm that go between these two positions. **Pronation** is the motion that moves the forearm from the supinated (anatomical) position to the pronated (palm backward) position. This motion is produced by rotation of the radius at the proximal radioulnar joint, accompanied by movement of the radius at the distal radioulnar joint. The proximal radioulnar joint is a pivot joint that allows for rotation of the head of the radius. Because of the slight curvature of the shaft of the radius, this rotation causes the distal end of the radius to cross over the distal ulna at the distal radioulnar joint. This crossing over brings the radius and ulna into an X-shape position. **Supination** is the opposite motion, in which rotation of the radius returns the bones to their parallel positions and moves the palm to the anterior facing (supinated) position (Figure 4.11.5).

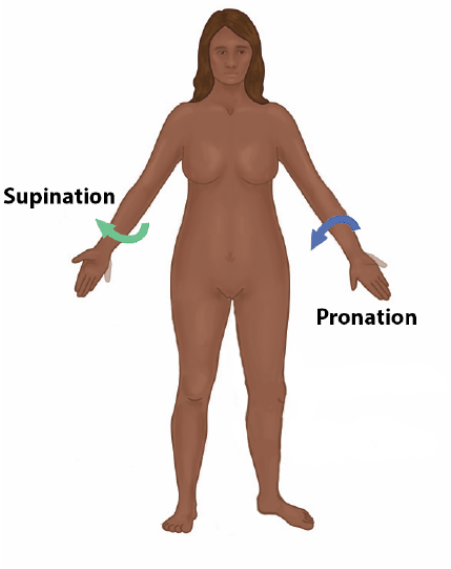


Figure 4.11.5: **Pronation and Supination.** In anatomical position your forearms are supinated (supine) and the palms are anterior. Pronation twists the forearm so the palm is facing posterior. *(Image credit: "Pronation-Supination" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by BlueLink .)*

Dorsiflexion and Plantar Flexion

Dorsiflexion and **plantar flexion** are movements at the ankle joint, which is a hinge joint. Lifting the front of the foot, so that the top of the foot moves toward the anterior leg is dorsiflexion, while lifting the heel of the foot from the ground or pointing the toes downward is plantar flexion. These are the only movements available at the ankle joint (Figure 4.11.6.A).

Inversion and Eversion

Inversion and eversion are complex movements that involve the multiple plane joints among the tarsal bones of the posterior foot (intertarsal joints) and thus are not motions that take place at the ankle joint. **Inversion** is the turning of the foot to angle the bottom of the foot toward the midline, while **eversion** turns the bottom of the foot away from the midline. The foot has a greater range of inversion than eversion motion. These are important motions that help to stabilize the foot when walking or running on an uneven surface and aid in the quick side-to-side changes in direction used during active sports such as basketball, racquetball, or soccer (Figure 4.11.6.B) .

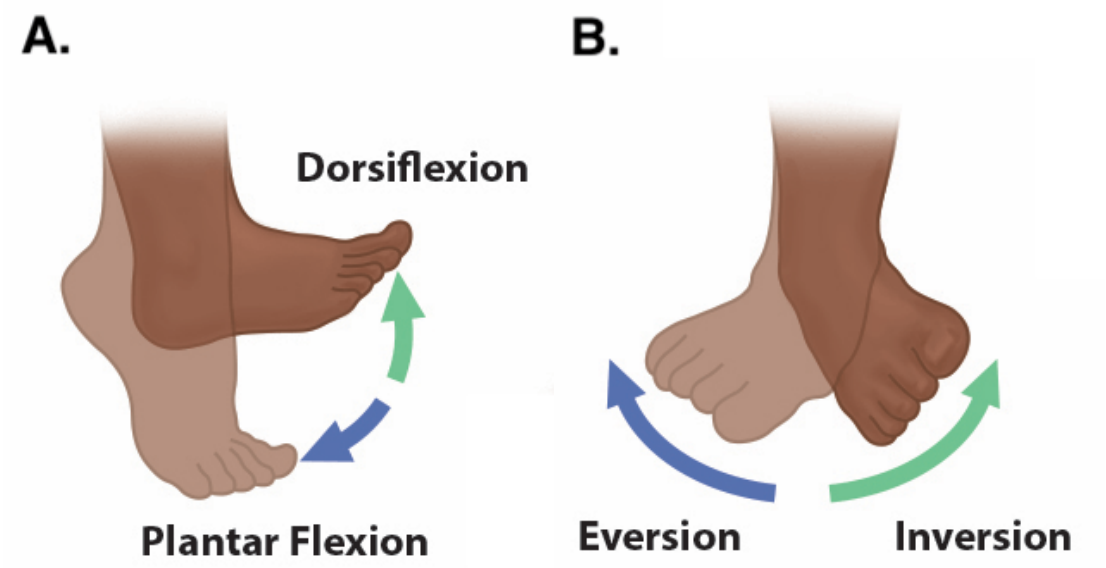


Figure 4.11.6: **Ankle and Foot.** A) When the foot is moving in the sagittal plane, dorsiflexion of the foot at the ankle joint moves the top of the foot toward the leg, while plantar flexion lifts the heel and points the toes. B) When the foot is moving in the frontal plane, eversion of the foot at the intertarsal joints moves the bottom (sole) of the foot away from the midline of the body, while foot inversion faces the sole toward the midline. *(Image credit: "Movements" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Protraction and Retraction

Protraction and **retraction** are anterior-posterior movements of the pectoral girdle or the mandible. Protraction of the pectoral girdle occurs when the shoulder is moved forward, as when pushing against something or throwing a ball. Retraction is the opposite motion, with the scapula being pulled posteriorly and medially, toward the vertebral column. For the mandible, protraction occurs when the lower jaw is pushed forward, to stick out the chin, while retraction pulls the lower jaw backward. (Figure 4.11.7).

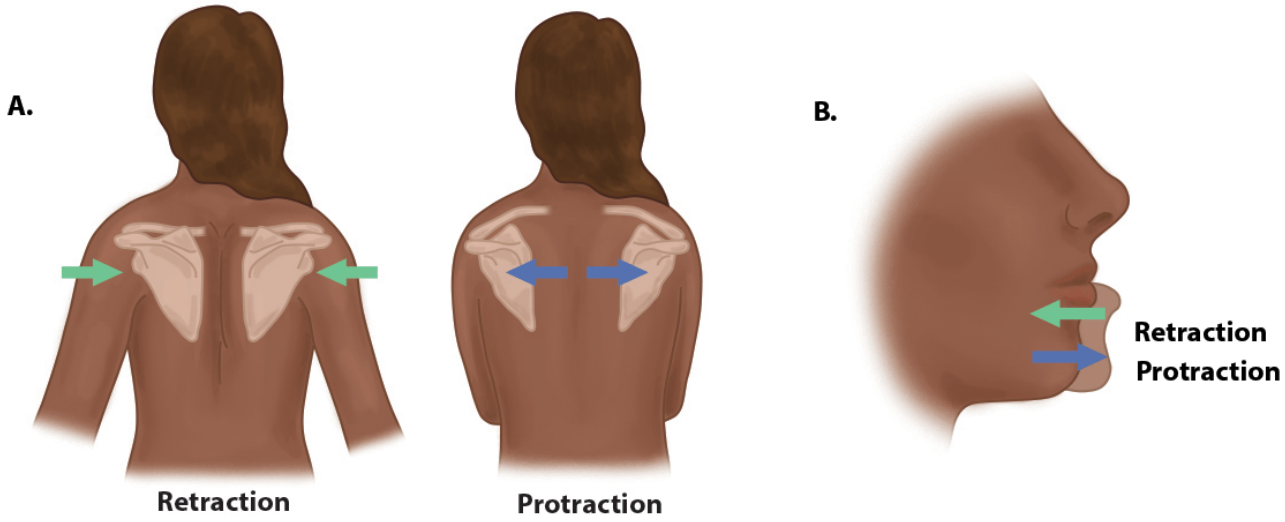


Figure 4.11.7: **Protraction and Retraction.** These moments occur at the sternoclavicular (A) and temporomandibular (B) joints. *(Image credit: "Movements" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Depression and Elevation

Depression and **elevation** are downward and upward movements of the pectoral girdle or the mandible. The upward movement

of the pectoral girdle is elevation, while a downward movement is depression. These movements are used to shrug your shoulders. Similarly, elevation of the mandible is the upward movement of the lower jaw used to close the mouth or bite on something, and depression is the downward movement that produces opening of the mouth (Figure 4.11.8) .

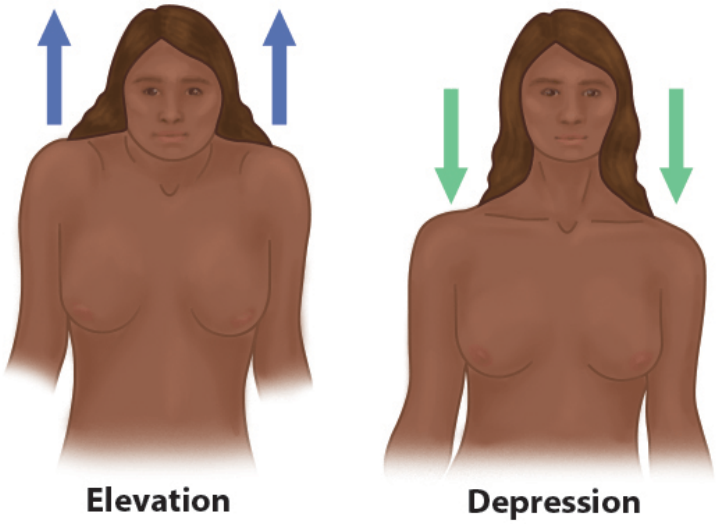


Figure 4.11.8: **Elevation and Depression.** The movements of elevation and depression also occur at the sternoclavicular joint and the temporomandibular joint (not shown). *(Image credit: "Movements" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Opposition and Reposition

Opposition is the thumb movement that brings the tip of the thumb in contact with the tip of a finger. This movement is produced at the first carpometacarpal joint, which is a saddle joint formed between the trapezium carpal bone and the first metacarpal bone. Thumb opposition is produced by a combination of flexion and abduction of the thumb at this joint. Returning the thumb to its anatomical position next to the index finger is called **reposition**. View these movements in the following video:

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Concept Review

The variety of movements provided by the different types of synovial joints allows for a large range of body motions and gives you tremendous mobility. These movements allow you to flex or extend your body or limbs, medially rotate and adduct your arms and flex your elbows to hold a heavy object against your chest, raise your arms above your head, rotate or shake your head, and bend to touch the toes (with or without bending your knees).

Each of the different structural types of synovial joints also allow for specific motions. The atlantoaxial pivot joint provides side-to-side rotation of the head, while the proximal radioulnar articulation allows for rotation of the radius during pronation and supination of the forearm. Hinge joints, such as at the knee and elbow, allow only for flexion and extension. Similarly, the hinge joint of the ankle only allows for dorsiflexion and plantar flexion of the foot.

Condyloid and saddle joints are biaxial. These allow for flexion and extension, and abduction and adduction. The sequential combination of flexion, adduction, extension, and abduction produces circumduction. Multiaxial plane joints provide for only small motions, but these can add together over several adjacent joints to produce body movement, such as inversion and eversion of the foot. Similarly, plane joints allow for flexion, extension, and lateral flexion movements of the vertebral column. The multiaxial ball and socket joints allow for flexion-extension, abduction-adduction, and circumduction. In addition, these also allow for medial (internal) and lateral (external) rotation. Ball-and-socket joints have the greatest range of motion of all synovial joints.

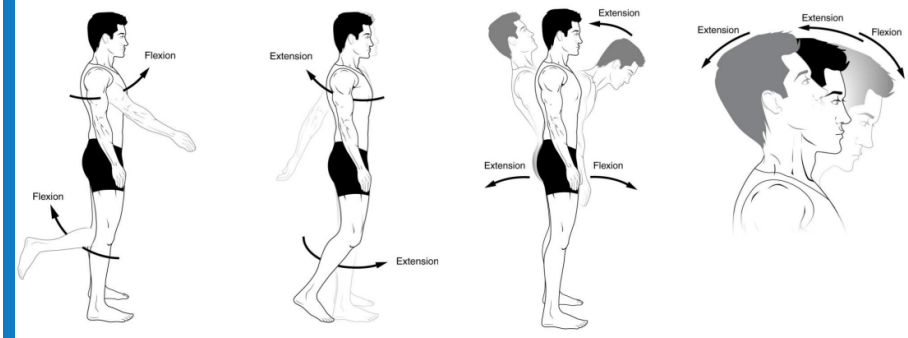
Synovial Joint Summary

Type of Joint	Movement	Example
Pivot	Uniaxial joint; allows rotational movement	Atlantoaxial joint (C1–C2 vertebrae articulation); proximal radioulnar joint
Hinge	Uniaxial joint; allows flexion/extension movements	Knee; elbow; ankle; interphalangeal joints of fingers and toes
Condyloid	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	Metacarpophalangeal (knuckle) joints of fingers; radiocarpal joint of wrist; metatarsophalangeal joints for toes
Saddle	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	First carpometacarpal joint of the thumb; sternoclavicular joint
Plane	Multiaxial joint; allows inversion and eversion of foot, or flexion, extension, and lateral flexion of the vertebral column	Intertarsal joints of foot; superior-inferior articular process articulations between vertebrae
Ball-and-socket	Multiaxial joint; allows flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation movements	Shoulder and hip joints

Table 4.11.2: Synovial Joint Movements Summary

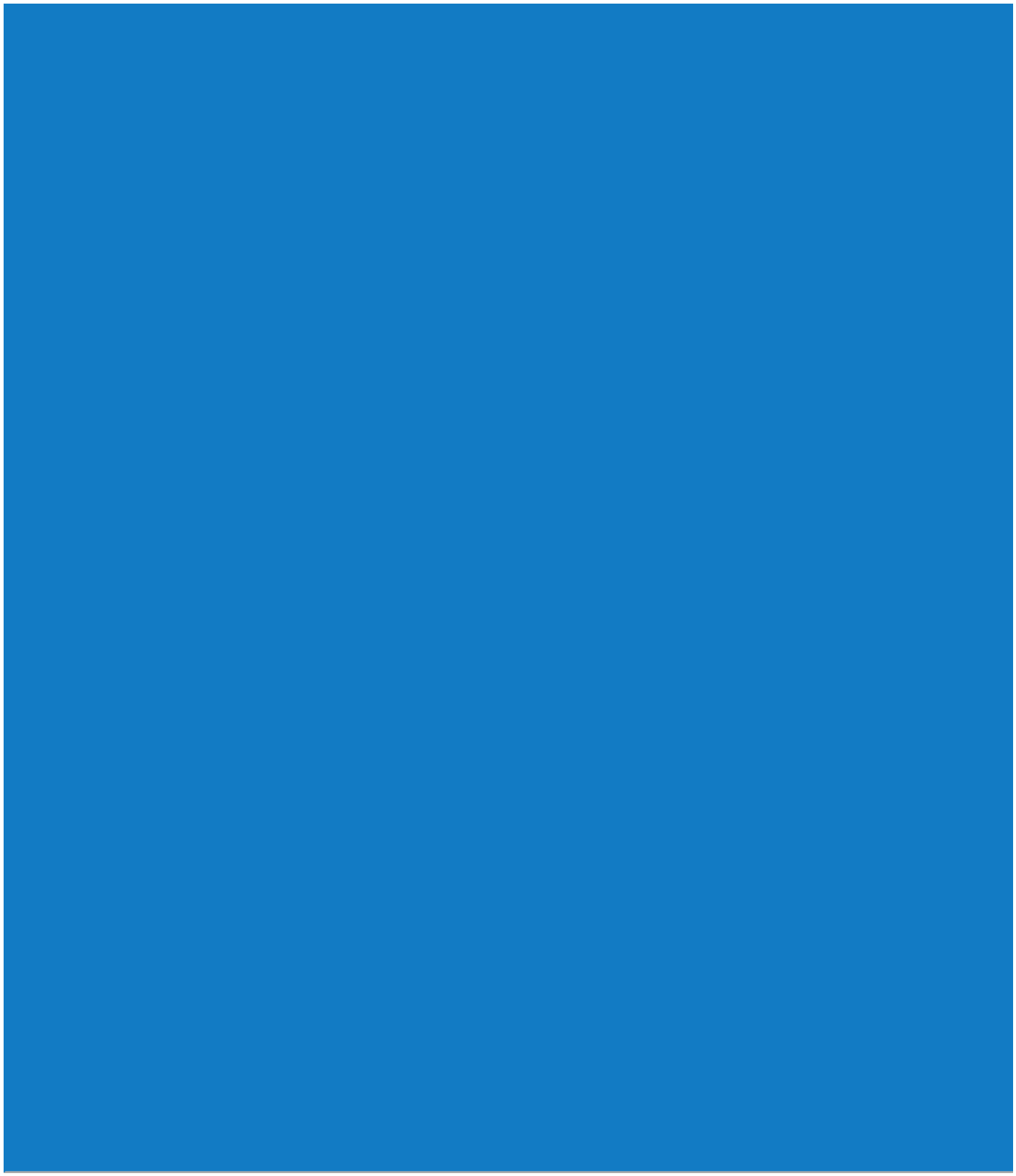
Flexion: Movement that ***decreases*** the angle between two bones or two parts of the body

Extension: Movement that ***increases*** the angle between two bones or two parts of the body



Plane of movement: ***Sagittal plane***

Where it happens: Neck, arm at the shoulder, forearm at the elbow, hand at the wrist, digits, spine, thigh at the hip, leg at the knee



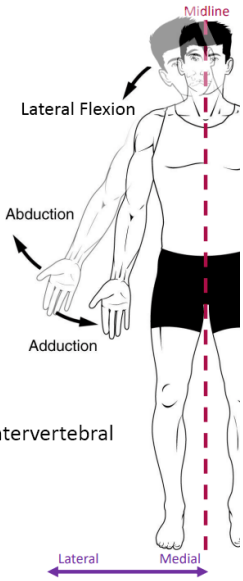
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Abduction: Movement of the limb/digit ***away*** from the midline ***(laterally)***

Adduction: Movement of the limb/digit ***towards*** the midline ***(medially)***

Plane of movement: ***Frontal plane***

Where it happens: Arm at the shoulder, digits, thigh at the hip



Lateral Flexion: Movement of the trunk in a lateral/medial direction

Plane of movement: ***Frontal plane***

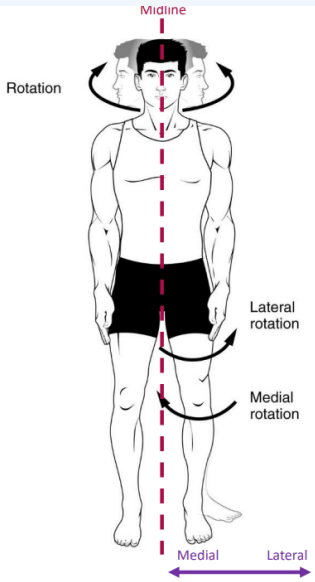
Where it happens: Trunk at the lumbar intervertebral joints, cervical intervertebral joints, and atlanto-occiptal joints.

Rotation: ***Turning*** around a central longitudinal axis

The head can be rotated to the ***left*** and the ***right*** (i.e., shaking the head "no")

Rotation of the limbs occurs when the forward-facing (anterior) surface is turned ***internally (medially)*** towards the midline, or ***externally (laterally)***, away from the midline

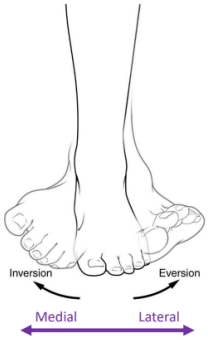
Where it happens: Head, arm at the shoulder, thigh at the hip



Plantar Flexion: Pushing or pointing the toes and the ball of the foot ***down*** towards the ground (i.e., standing on "tip toes")

Dorsiflexion: Standing on the heel of the foot, with the toes ***pointing up*** towards the sky



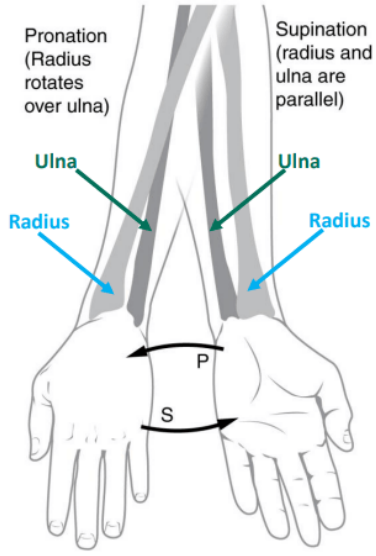


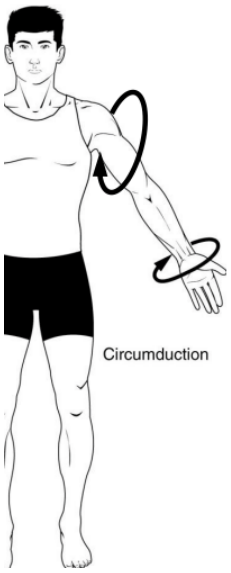
Inversion: Moving the foot to turn the sole ***inwards (medially)***

Eversion: Moving the foot to turn the sole ***outwards (laterally)***

Pronation: ***Rotation*** of the forearm (radius bone) ***inwards (medially)***, causing the palm to face ***downwards***

Supination: ***Rotation*** of the forearm (radius bone) ***outwards (laterally)***, causing the palm to face ***upwards***





Circumduction: Movement ***at the joint*** that causes the limb to ***move in a circle***

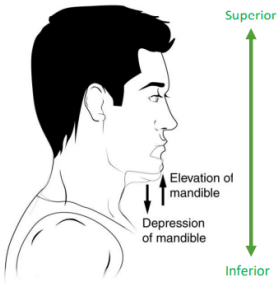
Note: Circumduction is a compound movement that involves abduction, adduction, extension, and flexion

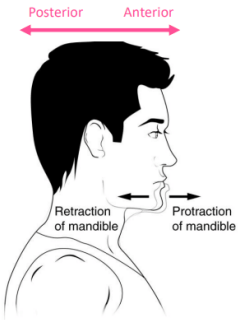
Where it happens: Ball-and-socket joints (e.g., shoulder, hip)

Elevation: Moving a body part ***upwards (superiorly)***

Depression: Moving a body part ***downwards (inferiorly)***

Where it happens: Eyelid, jaw (mandible), shoulder





Protraction: Moving a body part ***forwards (anteriorly)***

Retraction: Moving a body part ***backwards (posteriorly)***

Where it happens: Jaw (mandible), scapula



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4.12: Diseases and Injuries of Joints

Common musculoskeletal problems such as bursitis, sprains, strains, and arthritis show how inflammation, tissue injury, and joint wear can disrupt movement, cause pain, and shape treatment approaches.

Master this section and you'll be able to:

- Define and differentiate bursitis, sprains, and strains based on the tissues affected, causes, and common locations in the body.
- Distinguish sprains and strains.
- Explain the role of bursae in joint function and outline how inflammation affects their protective function.
- Compare and contrast osteoarthritis, rheumatoid arthritis, and gout in terms of causes, pathophysiology, symptoms and treatment strategies.
- Explain the suffix "-itis"

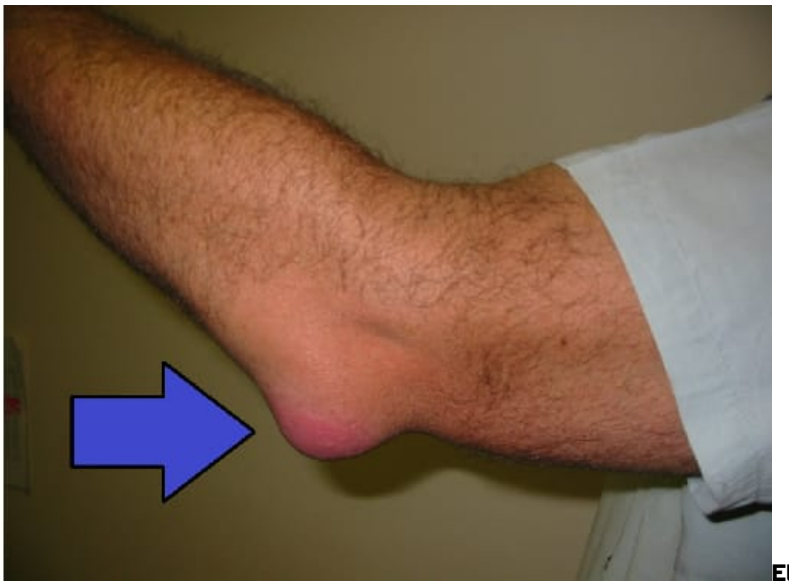
Bursitis



Bursitis is the inflammation of a **bursa** — the small, fluid-filled sac that cushions and reduces friction between bones, tendons, and muscles near joints. When a bursa gets inflamed, it can cause **pain, swelling, tenderness**, and sometimes **joint stiffness**.

Although bursae are found all over the body, bursitis most often strikes at the **shoulder, hip, knee, or elbow joints**:

- **Shoulder** – *Subacromial bursitis* affects the bursa between the acromion of the scapula and a shoulder tendon passing beneath it.
- **Hip** – *Trochanteric bursitis* involves the bursa over the greater trochanter of the femur, just below the hip's outer side.
- **Hip (sitting pressure)** – *Ischial bursitis* occurs in the bursa between the skin and the ischial tuberosity, the bony part you sit on.
- **Knee** – *Prepatellar bursitis* ("housemaid's knee") affects the bursa between the skin and the kneecap. It is now more often seen in roofers, carpet layers, or floor installers who kneel without knee pads.

-  **Elbow** – *Olecranon bursitis* (“student’s elbow”) inflames the bursa between the skin and the tip of the ulna at the back of the elbow.

Bursitis can be **acute** (lasting just a few days), or **chronic** (lingering). Repeated acute episodes of bursitis can result in a chronic condition.

Causes include overuse of a muscle, trauma, prolonged pressure, rheumatoid arthritis, gout, or infection. Repeated acute episodes can turn into a chronic problem.

Treatment depends on the cause. Treatments for the disorder include antibiotics if the bursitis is caused by an infection, or anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids if the bursitis is due to trauma or overuse. Chronic bursitis may require that fluid be drained, but additional surgery is usually not required. *In summary*

- **Infection** – antibiotics.
- **Inflammation from trauma or overuse** – anti-inflammatory drugs (NSAIDs) or corticosteroid injections.
- **Chronic bursitis** – fluid drainage, with surgery (rarely needed).

Bursitis is your body's way of saying, "Ease up! I am tired of the friction"!

💡***Note:***

In medical terminology, the suffix **“-itis”** means **inflammation**. It comes from **Greek** and has been used in medicine for centuries to describe a body part that is red, swollen, painful, and often warm due to irritation or infection.

Examples other than bursitis are **arthritis** – inflammation of a joint (*arthro-* = joint); **tonsillitis** – inflammation of the tonsils; **dermatitis** – inflammation of the skin (*derma-* = skin).

Key tip:
When you see or hear “-itis” in a medical term, your brain should think: *“Something here is inflamed.”* That means there is likely pain, swelling, and often heat and redness.

Sprains

A **sprain** is an acute **injury to a ligament** — the strong, **fibrous tissue that connects bone to bone** — usually caused by a sudden or forceful movement that pushes a joint beyond its normal range of motion. Ligaments are tough, but they are not indestructible. Their collagen fibers have just a hint of give, stretching only about **4% of their length** before reaching their limit. Go past that, and those fibers begin to tear.

Sprains can happen in any joint, but the **ankle, knee, and wrist** are the usual trouble spots. Many sprains are mild, producing some swelling and bruising that respond well to the classic first-aid formula **RICE**:

- **Rest**
- **Ice**
- **Compression**
- **Elevation**

On the other end of the spectrum are severe sprains involving **complete ligament tears or ruptures,** accompanied by bone fractures. These can cause significant instability, sharp pain, and limited mobility — and may require weeks of immobilization, surgical repair, and physical therapy.

Sprains are classified by severity:

First-degree sprain (mild) – Only a small portion of the ligament's collagen fibers are overstretched or damaged on a microscopic level. There is mild swelling or bruising, but the joint remains stable with normal range of motion. Most people recover in **4 days to 4 weeks**.

Second-degree sprain (moderate) – The ligament is **partially torn**, causing more noticeable swelling, tenderness, bruising, and some joint instability. Weight-bearing may be painful, and range of motion is often limited. Recovery can take **4 weeks to 4 months**, depending on the extent of damage.

Third-degree sprain (severe) – The ligament is **completely torn or ruptured**, and in some cases, it pulls away a small piece of bone (avulsion fracture). These injuries often cause major swelling, bruising, instability, and an inability to bear weight. Interestingly, some patients feel **no pain at all** if the injury also severs nearby nerve endings. Recovery may take **3 to 6 months**, and surgery is sometimes required.

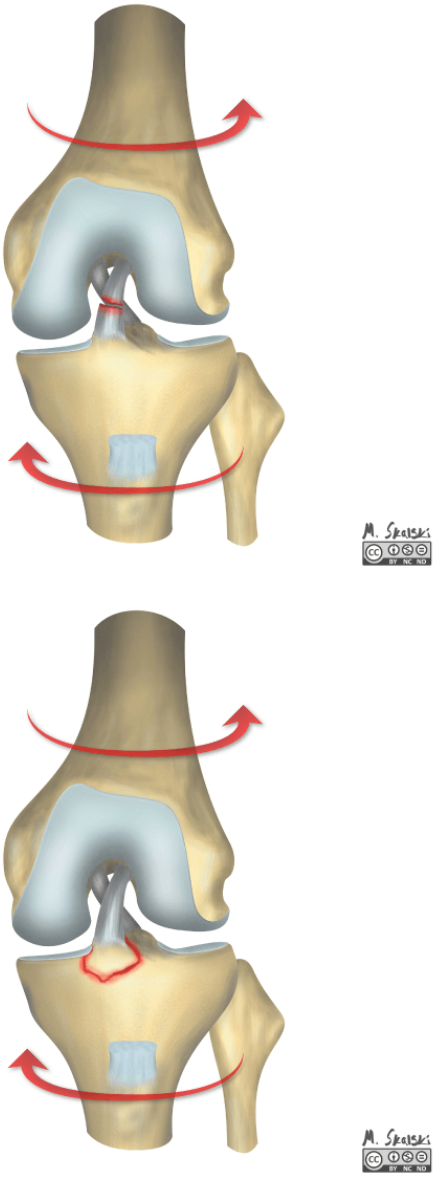


Figure 4.12.1: **Third Degree Sprains.** Excessive twisting of the knee joint can cause two different types of third degree sprains: the anterior cruciate ligament may tear completely or it may pull out of its attachment site on the tibia causing an avulsion. *(Image credit: "ACL Tear and ACL Avulsion Illustrations" are based on original case courtesy of Dr. Matt Skalski, Radiopaedia.org. From the case rID: 21443)*

Strains

A **strain** is an acute injury to a **muscle or its tendon** (the strong cord that connects muscle to bone). Strains are sometimes called “pulled muscles” — and for good reason. They are often caused by **sudden, forceful contractions** or **overstretching** that push the muscle-tendon unit past its limits.

Muscle fibers, like ligaments, can only stretch so far before they start to tear. These injuries are common in the **lower back, hamstrings, and calf muscles**, especially during sports or heavy lifting. Mild strains can cause discomfort but heal quickly with **RICE** (Rest, Ice, Compression, Elevation) and gentle stretching, while severe strains can sideline someone for months and may even require surgery.

Strains are classified by severity:

First-degree strain (mild) – A small number of muscle or tendon fibers are overstretched or slightly torn. There may be mild pain, tenderness, and stiffness, but no significant loss of strength or range of motion. Recovery typically takes **a few days to 3**

weeks.

Second-degree strain (moderate) – There is a **partial tear** in the muscle or tendon. Symptoms include moderate pain, swelling, bruising, and noticeable loss of strength or flexibility. Everyday activities and sports are often painful. Recovery can take **3 to 12 weeks** depending on the location and severity.

Third-degree strain (severe) – The muscle or tendon is **completely ruptured**, sometimes with a visible gap or deformity where the tear occurred. There is usually sudden, sharp pain (sometimes accompanied by a "popping" sound), severe swelling, bruising, and total loss of function in the affected area. Recovery can take **3 to 6 months** and often requires surgical repair followed by physical therapy.

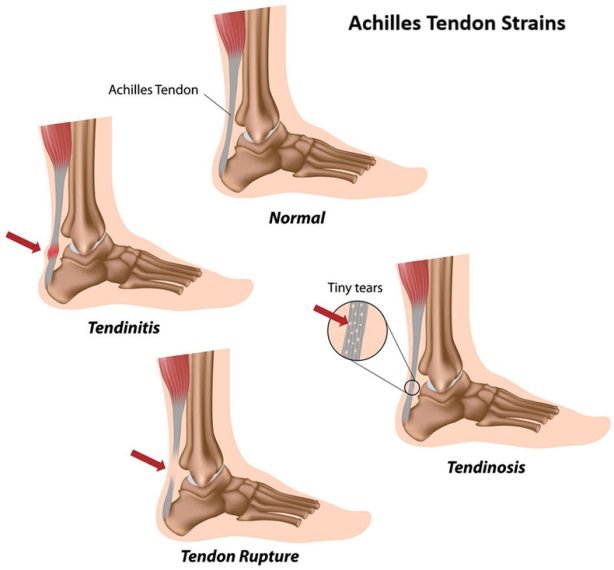


Figure 4.12.2: **Achilles Tendon Injuries.** **Acute rupture** is a complete or partial tear of the tendon that happens when it is overstretched, often feeling like a sudden kick to the back of the ankle and making it hard to walk. **Achilles tendinopathy** is a chronic condition in which repeated small tears (tendinosis) weaken and degenerate the tendon, often from increasing activity too quickly without proper preparation. Partial tears can mimic its symptoms, while complete ruptures cause sudden, more severe impairment.

Comparing Sprains and Strains

Feature	Sprain	Strain
Tissue Affected	Ligament (connects bone to bone)	Muscle or tendon (connects muscle to bone)
Common Causes	Sudden twist, fall, or force pushing a joint beyond its normal range of motion	Sudden, forceful muscle contraction or overstretching
Common Locations	Ankle, knee, wrist	Lower back, hamstrings, calf muscles
Key Symptoms	Swelling, bruising, pain, possible joint instability	Pain, muscle spasm, weakness, swelling, bruising
First-degree (Mild)	Minor stretching or microscopic tears; mild swelling/bruising; joint stable; recovery in **4 days–4 weeks**	Few fibers overstretched; mild pain/stiffness; recovery in **few days–3 weeks**
Second-degree (Moderate)	Partial tear; moderate swelling/bruising; some instability; pain with weight-bearing; recovery in **4 weeks–4 months**	Partial tear; moderate pain/swelling/bruising; loss of strength/flexibility; recovery in **3–12 weeks**

Feature	Sprain	Strain
Third-degree (Severe)	Complete tear or rupture (sometimes with avulsion fracture); severe instability; may have no pain if nerves damaged; recovery in **3–6 months**, often with surgery	Complete rupture; severe pain, swelling, bruising, loss of function; recovery in **3–6 months**, often with surgery
Treatment	RICE, immobilization, possible surgery/physical therapy	RICE, gradual stretching/strengthening, possible surgery/physical therapy

Arthritis

Arthritis is a common problem that affects **synovial joints**, causing inflammation inside the joint. This inflammation can lead to **pain**, **swelling**, **stiffness**, and **reduced movement**. There are over 100 different types of arthritis. It can be triggered by **aging**, **damage to the articular cartilage**, **autoimmune disorders**, **infections**, or even **genetic factors**.

Osteoarthritis

The most common form is **osteoarthritis** — often called the “wear-and-tear” arthritis — which becomes more likely as we age. **Risk factors** include:

- Previous joint injuries
- Jobs with heavy physical labor
- Sports with repeated running, twisting, or throwing
- Carrying excess body weight

All of these put extra stress on the **articular cartilage** that normally cushions the ends of bones in synovial joints. Over time, this cartilage becomes **thinner** and less able to protect the bone.

When cartilage wears down:

1. **More stress** is placed on the underlying bone.
2. The joint produces extra **synovial fluid** in an attempt to protect itself, which can cause **swelling** and stretch the **articular capsule**, leading to stiffness and pain.
3. The bone beneath the damaged cartilage may **thicken** and develop **rough or bumpy surfaces**, making movement painful and promoting more inflammation.

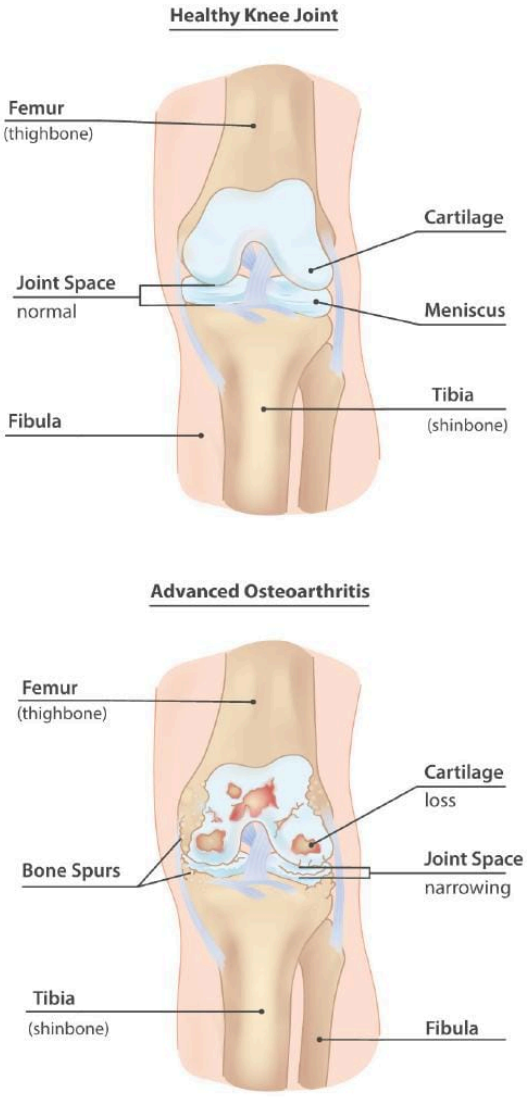


Figure 4.12.3: **Osteoarthritis**. Osteoarthritis of a synovial joint results from aging or prolonged joint wear and tear. These cause erosion and loss of the articular cartilage covering the surfaces of the bones, resulting in inflammation that causes joint stiffness and pain. In more advanced stages of osteoarthritis bone spurs (small sharp nodules) develop on the bones, which then accelerates further cartilage damage. *(Image credits: "Healthy Knee Joint" and "Advanced Osteoarthritis" by Injury Map are licensed under CC BY 4.0.)*

Progression and Treatment of Osteoarthritis

In the **early stages** of osteoarthritis, symptoms can sometimes improve with gentle activity that “warms up” the joint. However, symptoms may return — and even worsen — after exercise.

In **advanced osteoarthritis**, the affected joints often become so painful that movement is limited, leading to **reduced mobility** and more stiffness.

There is **no cure** for osteoarthritis, but several treatments can reduce pain and help maintain mobility:

- **Lifestyle changes** such as weight loss and low-impact exercises (like swimming or cycling)
- **Medications**, both over-the-counter and prescription, to reduce pain and inflammation

For **severe cases**, doctors may recommend **joint replacement surgery** (***arthroplasty***). This is a major procedure, so other options are always tried first. When performed, arthroplasty can significantly **reduce chronic pain** and **restore mobility** within months.

Examples (see the image below):

Total hip arthroplasty:

1. Damaged parts of the hip — including the **head and neck of the femur** and the **acetabulum** (hip socket) — are removed.
2. A **prosthetic femoral head** (a rounded ball on a shaft) is inserted into the femur's shaft.
3. The acetabulum is reshaped, and a **replacement socket** is fitted in.

Total knee arthroplasty:

1. Damaged parts of the knee — including the **ends of the femur** and **tibia** — are removed, along with any degraded cartilage and sometimes the underside of the patella.
2. The exposed surfaces of the femur and tibia are precisely shaped and resurfaced.
3. **Metal components are fitted over** the ends of the femur and tibia to create new joint surfaces. A **plastic (polyethylene) liner** is inserted between these components to serve as the new cartilage.
4. The underside of the patella may also be resurfaced and fitted with a plastic button, depending on the patient's needs and the surgeon's approach.

The prosthetic parts are pre-made (and occasionally custom-designed) for optimal fit and function.

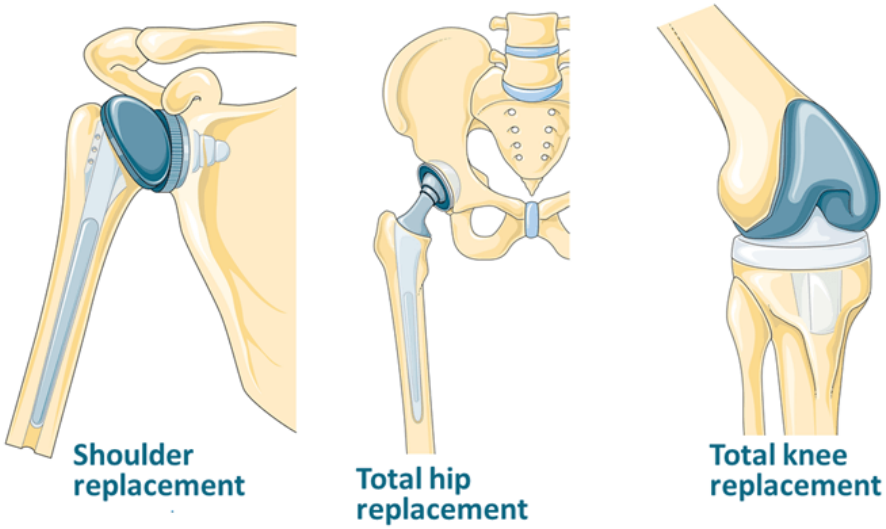


Figure 4.12.4: **Shoulder, Hip, and Knee Arthroplasty.** Illustration of prosthetic implants for shoulder, hip, and knee joint replacements.

Here is what this looks like in real life:



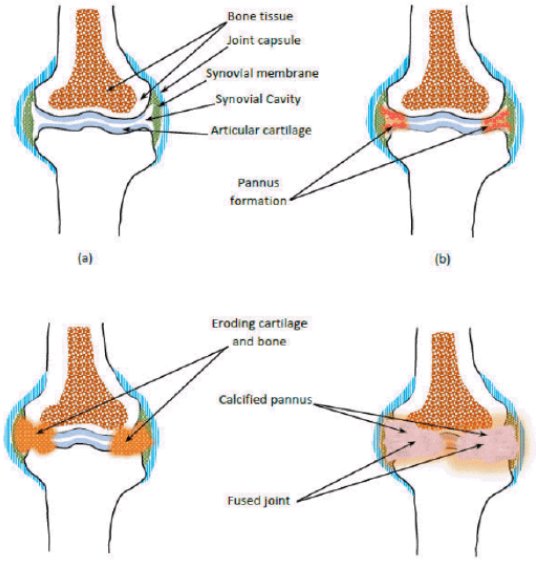
Figure 4.12.5: **Hip** (left) **and Knee Replacements** (right). Damaged cartilage and bone have been replaced with metal and plastic components. Left: AP X-ray of the pelvis after hip arthroplasty. Right: Lateral and AP X-rays of the knee three months after arthroplasty.

Rheumatoid Arthritis (RA)

Rheumatoid arthritis is a troublemaker that prefers freely movable joints, especially in **the wrists, hands, ankles, and feet** — though it can also affect the shoulders, elbows, and knees. Like osteoarthritis, RA causes pain and stiffness, but it does not stop there. It often brings along extra baggage: weakness, fatigue, and even damage to organs like the heart, blood vessels, lungs, nerves, skin, and eyes. This is because RA can attack connective tissues throughout the body. Interestingly, RA sometimes goes into periods of **temporary remission**, where symptoms improve.

The exact cause is still a mystery, but scientists know the *how*. RA is an **autoimmune disease**, meaning the immune system — our body's defense team — mistakes healthy connective tissues for dangerous invaders. In a misguided attempt to "help," it attacks normal connective tissue, treating it as if it were harmful.

In joints, this immune attack destroys cartilage, which is replaced by an unusual scar tissue called a **pannus**. The pannus releases enzymes that damage even more cartilage, bone, and the synovial membrane. As the pannus spreads, it replaces normal joint structures. This leads to pain, swelling, and eventually loss of joint function.

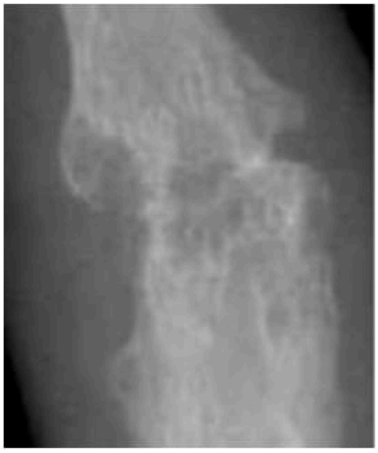




Normal hand



RA - Damaged finger joints



RA - Fused finger joint





RA – Damaged fingers and wrist



RA – Fused wrist bones



RA - Damaged hand

Figure 4.12.6: **Effects of Rheumatoid Arthritis on Joint Structure.** As the joint weakens, the bones shift out of position. Sometimes, the pannus becomes calcified and stiff. Progressive calcification sometimes results in fusion of the bones. In addition, the ordinary scar tissue produced at the joint shrinks as time passes, pulling the bones farther out of alignment and locking them into abnormal positions. Thus, the joint becomes distorted and immovable — often producing crippling deformities most noticeable in the hands and feet.
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There is **no way to prevent or cure RA**. The goals of treatment are the same as those for osteoarthritis: slowing the progress of the disease and minimizing pain and disability. Various medications may be prescribed to inhibit the immune system and relieve pain. Mild exercise helps maintain joint mobility. A variety of other treatment modalities may be initiated. Unfortunately, not all individuals respond well to these treatments.

Gout

Gout (pronounced *gowt*) is a form of inflammatory arthritis that is often very painful. It usually affects one joint at a time—most often the big toe joint. Like other forms of arthritis, it causes pain and swelling in the affected joint(s). Gout is a **chronic condition** with alternating periods of **flares** (when symptoms worsen) and **remission** (when there are no symptoms).

Gout flares tend to start suddenly and can last for days or weeks. They are often followed by long symptom-free periods—sometimes lasting weeks, months, or even years—before another flare begins. While the big toe is the most common site, gout can also affect other toe joints, the ankle, or the knee.

Typical signs and symptoms of a gout flare include:

- Intense pain
- Swelling
- Redness
- Warmth (heat) in the joint



Repeated flares can lead to **gouty arthritis**, a more persistent form of arthritis that can last for one to two weeks before improving. Severe cases may be complicated by **tophi** — firm, often visible lumps under the skin caused by uric acid crystal deposits. Tophi usually develop after years of repeated gout attacks and can appear around joints, along tendons, or in other tissues. If the skin over a tophus (singular) breaks, a whitish, paste-like material made of uric acid crystals may ooze out.

Where does the uric acid come from?

Uric acid forms when the body breaks down **purines**, natural substances found in our cells and in many foods. Normally, excess uric acid is filtered by the kidneys and removed in urine. However, if uric acid levels become too high, they can build up in the blood (**hyperuricemia**) and form needle-shaped crystals in and around joints. These crystals trigger inflammation, causing the sudden pain, swelling, and redness of a gout flare.

Foods especially high in purines—such as organ meats (liver, kidney), certain seafood (sardines, anchovies), some red meats, and beer—can raise uric acid levels and increase the risk of gout attacks. People with gout are often advised to limit these foods to help prevent flares.

Diagnosis and treatment

Gout is usually diagnosed with a blood test measuring uric acid levels. Treatment often includes medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) or colchicine to relieve pain and inflammation. While there is no cure for gout, it can be effectively managed with medication, lifestyle changes, and self-care strategies.

Interestingly, **hyperuricemia does not always cause gout**, and people with high uric acid levels but no symptoms generally do not need treatment.

Risk factors for hyperuricemia (and gout)

- Being male
- Being overweight or obese
- Having certain health conditions, such as:
  - High blood pressure (hypertension)
  - Insulin resistance or diabetes
  - Poor kidney function

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5: MUSCULAR SYSTEM

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5.2: Microscopic Anatomy of Skeletal Muscle Fibers

5.3: Connective Tissue Wrappings — The Layers That Hold It All Together

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5.1: The Three Types of Muscle Tissue

Muscle tissue allows movement and exists in three types: skeletal, cardiac, and smooth.

Master this section and you'll be able to

- Identify and compare the three types of muscle tissue (skeletal, cardiac, and smooth) based on structure, function, and location in the body.
- List the four functional properties of muscle tissue and explain how they contribute to muscle movement.
- Differentiate between voluntary and involuntary muscle control, providing examples of each from everyday body functions.

Muscle is one of the four primary tissue types of the body. There are three types of muscle tissue: **skeletal** muscle, **cardiac** muscle, and **smooth** muscle. Muscle tissue is characterized by properties that allow movement. All muscle tissue have four functional properties in common which include **excitability**, **contractility**, **extensibility**, and **elasticity**.

- **Excitability:** Muscle cells can respond to a stimulus. The plasma membrane can change electrical states and send an electrical wave called an **action potential** along the entire surface of each cell.
- **Contractility:** Muscle cells can shorten and generate a pulling force. When attached between two movable objects — bones — contractions of the muscles cause the bones to move.
- **Extensibility:** Muscle cells can stretch or elongate.
- **Elasticity:** Following contraction or extension, a muscle can recoil to its original length when relaxed due to elastic proteins.

Some muscle movements are **voluntary**, meaning you control them consciously. Think of it like choosing to open a book and read a chapter on anatomy (😉) — your brain gives the command, and your muscles follow. Other movements are **involuntary**, happening automatically without you even thinking about them. A good example is your pupil shrinking in bright light. You cannot "tell" your eye to do that — it just happens.

The Three Muscle Tissue Types

Muscle tissue is divided into three types based on structure and function: **skeletal, cardiac, and smooth**One of the easiest ways to tell the three muscle types apart is by looking at them under a microscope. Inside each muscle cell (or **myofiber**) are the contractile proteins **actin** and **myosin**, which slide past each other to make the cell contract.

- **Skeletal and cardiac muscle** keep things very organized. Their actin and myosin are stacked in a repeating, brick-like pattern. This arrangement produces visible **stripes called striations**. Under a light microscope, you can actually see these as alternating light–dark bands. (*See figure below.)* The stripes stand out more clearly in skeletal muscle than in cardiac muscle.

- **Smooth muscle**, on the other hand, is less of a perfectionist. Its actin and myosin are arranged irregularly, so the cells look uniform rather than striped. This smooth look is the reason for the name **smooth muscle**.

Comparison of Structure and Properties of the Three Muscle Tissue Types

Tissue	Histology	Function	Location
Skeletal	Long cylindrical fiber, striated, many peripherally located nuclei	Voluntary movement, produces heat, protects organs	Attached to bones and around entrance points to body (e.g., mouth, anus)
Cardiac	Short, branched, striated, single central nucleus	Contracts to pump blood	Heart

Tissue	Histology	Function	Location
Smooth	Short, spindle-shaped, no evident striation, single nucleus in each fiber	Involuntary movement, moves food, involuntary control of respiration, moves secretions, regulates flow of blood in arteries by contraction	Walls of major organs and passageways

1) Skeletal Muscle Tissue

Skeletal **myofibers** (muscle cells) are **long, cylindrically-shaped, and striated**. They can be just a few millimeters or stretch out to many centimeters — often extending beyond the sides of a microscope image.

➡️ **Record holder:** The **sartorius**, the longest muscle in the body, has myofibers that average about **42 cm (16.5 in)** in length!

Skeletal muscle makes up about **40% of your body weight**. It contains **50–75% of all body proteins** — a reminder of how "protein-rich" muscle tissue really is.

Skeletal muscle cells have **multiple nuclei** — the longer the myofiber, the more nuclei. This helps efficiently manage the cell's activities across this length, because each nucleus controls the metabolism and protein production for the area of cytoplasm near it.

How do skeletal muscle cells end up with so many nuclei?

During development, skeletal muscle fibers form through the **fusion of myoblasts**. Myoblasts are small precursor cells, each containing its own nucleus. When many myoblasts join together to create one long skeletal muscle fiber, all their nuclei remain inside. This is why skeletal muscle fibers are *multinucleated* — they are essentially a team of cells that merged into one giant cell.

Unlike in most cells, the nuclei in skeletal muscle fibers are **pushed to the cell's edges** *(see arrows in the image below)*. This makes room in the center for the thousands of contractile proteins packed inside.

Skeletal muscle is the **"voluntary" muscle type**. Anytime you consciously choose to contract or relax a muscle, you are using skeletal muscle. Examples include:

- **Moving the skeleton:** arms, legs, back, neck, etc.
- **Skin movement:** facial expressions.
- **Breathing:** muscles of respiration, including the diaphragm.
- **Specialized control of openings:** external anal and external urethral sphincters.
- **Speech and eating:** your tongue is skeletal muscle, too!

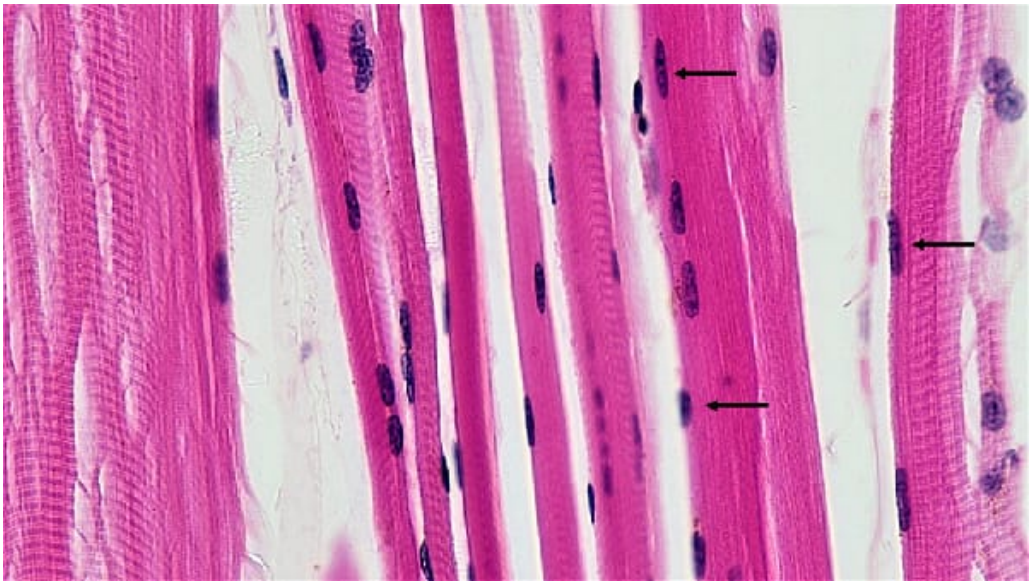


Figure 5.1.1: **Skeletal muscle fibers** at 200x (longitudinal section). Long, pink striated skeletal muscle fibers with dark oval

nuclei along the edges, marked by arrows.

2) Cardiac Muscle Tissue

Cardiac muscle tissue is **found only in the heart**. The heart's highly coordinated contractions keep blood moving through the vessels of the circulatory system.

The structure of cardiac muscle fibers differs from the skeletal muscle fibers by size and nuclei: cardiac muscle fibers are **shorter** than skeletal muscle fibers, and most have **a single nucleus**, located in the center of the cell.

The **energy demand** of the heart muscle cells is huge because the heart never gets a break. The cardiac myofibers therefore contain **many mitochondria** and a lot ot of **myoglobin**, producing ATP mainly through **aerobic metabolism**.

Unlike skeletal muscle cells, cardiac muscle cells are **branching.** This **extensive branching** gives the tissue a strong, interwoven structure.

Cardiac muscle cells are joined at their ends by **intercalated disks** *(see image below)*. These specialized junctions are part of the sarcolemma (cell membrane) and have two special structures which serve two main purposes:

- **Gap Junctions**
  - Form channels that connect neighboring cells.
  - Allow electrical signals to pass rapidly from one fiber to the next.
  - This ensures the **entire heart contracts in a coordinated way** (not like a crowd clapping out of sync at a concert).

- **Desmosomes**
  - Act like **spot welds**, anchoring cells together.
  - Prevent fibers from pulling apart when the heart contracts forcefully, beat after beat.

✅ **Key Takeaway**: Cardiac muscle is built for **endurance and teamwork**. It has energy-rich cells, a branching structure, and intercalated disks that keep all fibers contracting in sync without tearing apart.

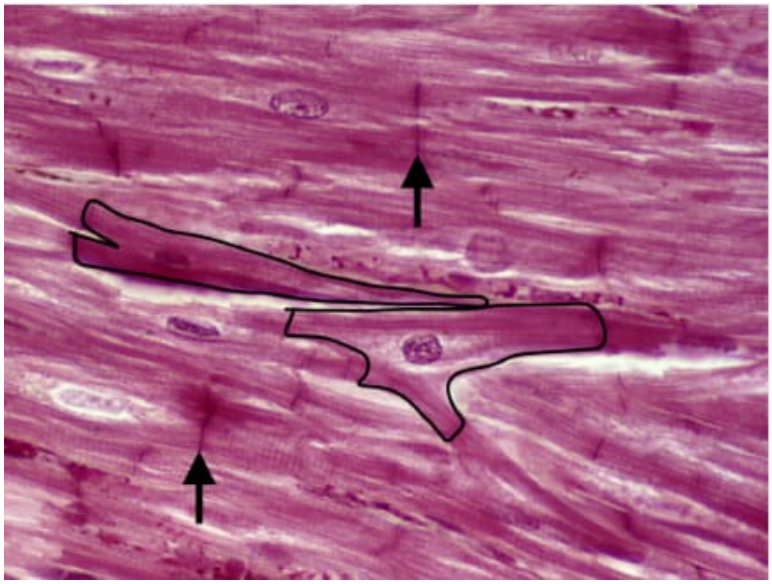


Figure 5.1.2: **Cardiac Muscle Fibers** at 400x (longitudinal section). Indicated by arrows are the intercalated discs. The outlines show the branching fibers. *(Image credits: Types of Muscle Tissue by Jennifer Lange are licensed under CC-BY-SA-NC 4.0. Micrographs A1, A2, and C1 provided by the Regents of University of Michigan Medical School, micrographs B1, B2, and C2 provided by Virginia Commonwealth University.)*

3) Smooth Muscle Tissue

Smooth muscle is found throughout the body, lining the walls of hollow organs and passageways. It is called s*mooth* because,

unlike skeletal and cardiac muscle, its cells do not have visible striations under the microscope.

Smooth muscle fibers are **spindle-shaped** (wide in the middle, tapered at both ends, like a football). Each fiber has **a single, centrally located nucleus** *(see image below)*. Smooth muscle cells are much shorter than skeletal muscle fibers, ranging from **30–200 µm** in length.

Each fiber produces its own thin layer of connective tissue called the **endomysium**.

Unlike skeletal muscle, both smooth muscle and cardiac muscle are **involuntary**, meaning they contract automatically without conscious control. Smooth muscle is found in the**:**

- **Digestive system:** stomach and intestines
- **Urinary system:** urinary bladder, ureters
- **Reproductive system:** uterus and related structures
- **Circulatory system:** walls of arteries and veins
- **Respiratory system:** tracts that carry air to and from the lungs
- **Eyes:** controls the size of the iris and the shape of the lens
- **Skin:** attached to hair follicles; contraction causes “goosebumps” in response to cold or fear

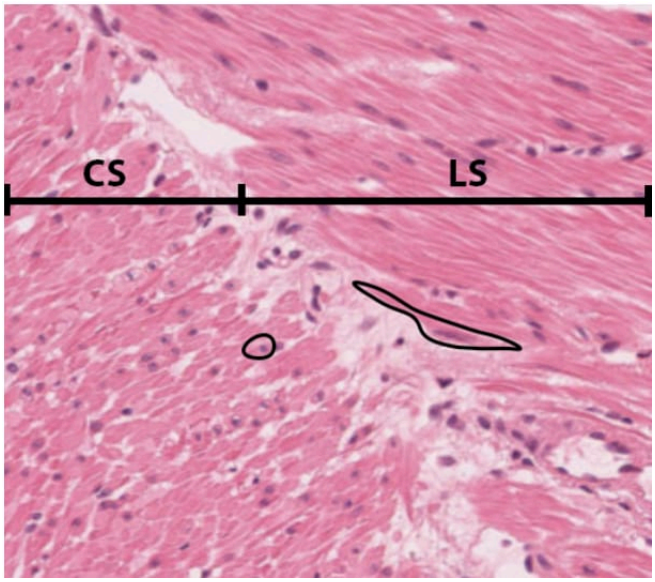


Figure 5.1.3: **Smooth Muscle Fibers** at 400x. Histology image of smooth muscle tissue with cross section (CS) and longitudinal section (LS). Outlined is a single cell in each section. Smooth muscle cells are spindle shaped and taper to points at the ends. They have a centrally located nucleus. Because of this shape, when viewed in CS the myofibers will appear to have different diameters and only those cut through the center will show the nucleus.
(Image credit: "Smooth Muscle Fibers" by Jennifer Lange is licensed under CC-BY-SA-NC 4.0. Micrographs from Virginia Commonwealth University.)

Interactive Element

Watch this video and learn more about muscle tissue:

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

In looking through a microscope how could you distinguish skeletal muscle tissue from smooth muscle?

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- 9.2: Overview of Muscle Tissues by Whitney Menefee, Julie Jenks, Chiara Mazzasette, and Kim-Leiloni Nguyen is licensed CC BY 4.0.

5.2: Microscopic Anatomy of Skeletal Muscle Fibers

Skeletal muscles are composed of striated subunits called sarcomeres, which are composed of the myofilaments actin and myosin.

Master this section and you'll be able to

- Describe the structural organization of skeletal muscle, from myofiber to myofibril to sarcomere to myofilaments.
- Define and briefly explain the function of sarcoplasm, sarcolemma, sarcoplasmic reticulum, and transverse tubules.

Myofiber Structure

Myocytes, or in the case of skeletal muscle often called muscle fibers or **myofibers**, are the cells that form the bulk of muscle tissue. These cells are bound together by **perimysium**, a sheath of connective tissue, into bundles called **fascicles**, which are in turn bundled together to form muscle tissue. Myocytes in general contain numerous specialized cellular structures which facilitate their contraction and therefore that of the muscle as a whole.

The highly specialized structure of myocytes has led to the creation of terminology which differentiates them from generic animal cells. Specific terms are:

- Generic muscle cell = **Myocyte**
- Skeletal muscle cell = **Myofiber**
- Cytoplasm = **Sarcoplasm**
- Cell membrane = **Sarcolemma**
- Smooth endoplasmic reticulum = **Sarcoplasmic reticulum**

Myofibers can be very large, with diameters up to 100 micrometers and lengths exceeding 40 centimeters. Remember from the previous section, the longest muscle in the human body is the sartorius, a long, thin, strap-like muscle that runs diagonally across the front of the thigh.

The sarcoplasm of a myofiber is rich in glycogen (a storage form of glucose) and myoglobin (an oxygen-binding protein), which provide the energy resources needed for contraction. Most of the space inside the cell is filled with **myofibrils**, long organelles composed of **myofilaments** that are responsible for muscle contraction.

The sarcolemma of myocytes contains numerous invaginations (pits) called **transverse tubules** which are usually perpendicular to the length of the myofiber. Transverse tubules play an important role in supplying the myocyte with **Ca^{+} ions**, which are key for muscle contraction.

As you know, each myofiber contains multiple nuclei due to their derivation from multiple myoblasts, progenitor cells that give rise to mature muscle cells.

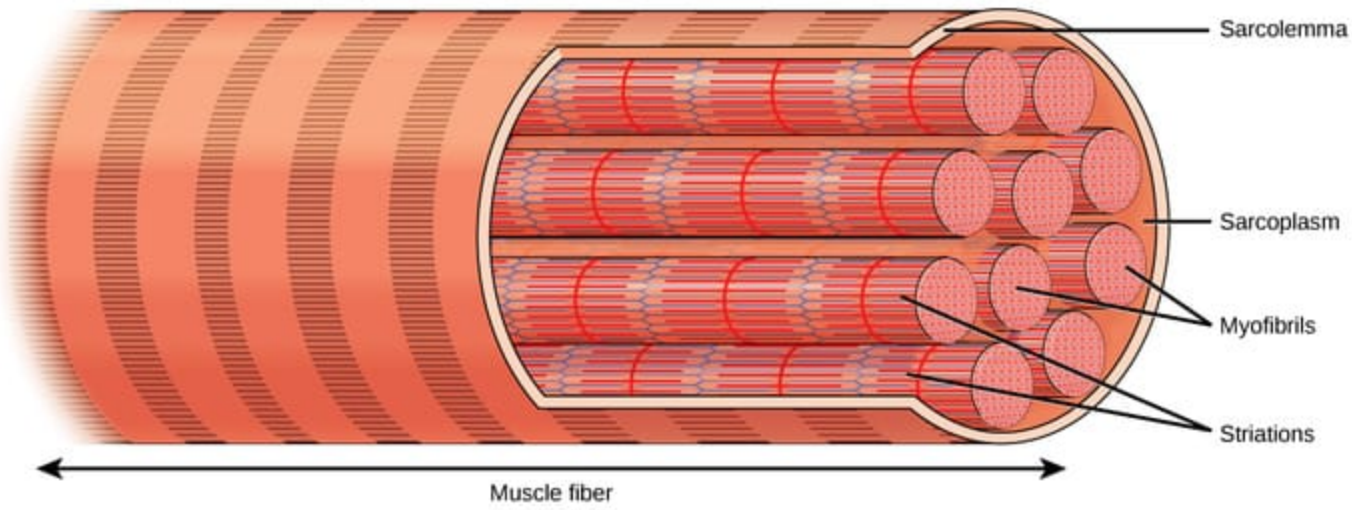


Figure 5.2.1: **Myofiber = Skeletal muscle cell.** A skeletal muscle cell is surrounded by a plasma membrane called the sarcolemma with a cytoplasm called the sarcoplasm. A muscle fiber is composed of many myofibrils, packaged into orderly units.

Myofibril Structure

Each myofiber can contain many thousands of myofibrils. Myofibrils run parallel to the myocyte and typically run for its entire length, attaching to the sarcolemma at either end. Each myofibril is surrounded by the **sarcoplasmic reticulum**, which is closely associated with the transverse tubules. The sarcoplasmic reticulum acts as a sink of Ca^{+} ions, which are released upon signaling from the transverse tubules.

Myofibrils are composed of long **myofilaments** of **actin**, **myosin**, and **other associated proteins.** These proteins are organized into regions termed **sarcomeres**, the functional contractile unit of the myofiber. Within the sarcomere actin and myosin, myofilaments are interlaced with each other and slide over each other via the **sliding filament model of contraction**. The regular organization of these sarcomeres gives skeletal and cardiac muscle their distinctive striated appearance.

Sarcomeres

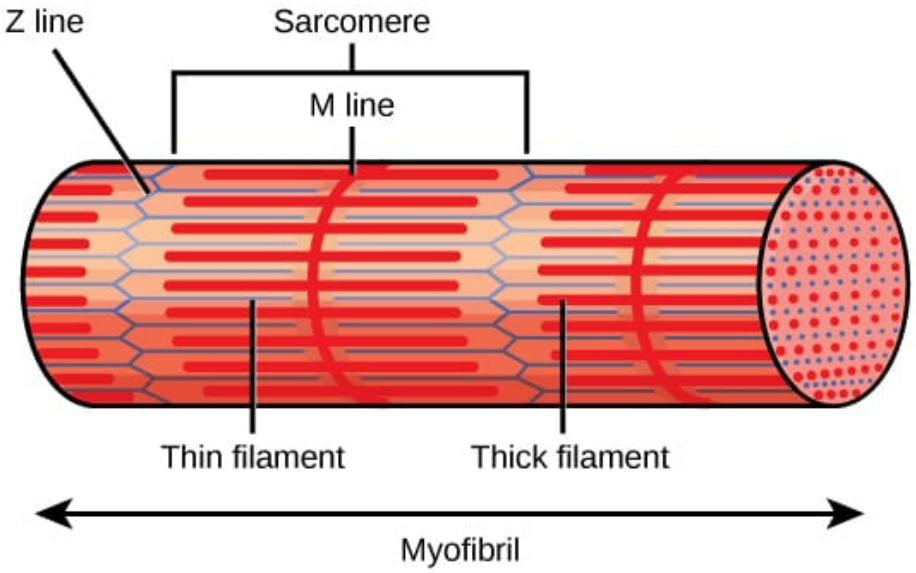


Figure 5.2.2: **Sarcomere.** The sarcomere is the functional unit of the muscle cell. It defines the region of interaction between a set of thick (myosin) and thin (active) filaments.

Myofilament (Thick and Thin Filament) Structure

Myofibrils are composed of smaller subunits called myofilaments. There are two main types of myofilaments: thick filaments and thin filaments.

- **Thick filaments** are composed primarily of **myosin proteins**, the tails of which bind together leaving the heads exposed to the interlaced thin filaments.
- **Thin filaments** are composed of **actin protein** subunits, as well as **tropomyosin** and **troponin** proteins.

The molecular model of contraction which describes the interaction between actin and myosin myofilaments is called the **cross-bridge cycle**.

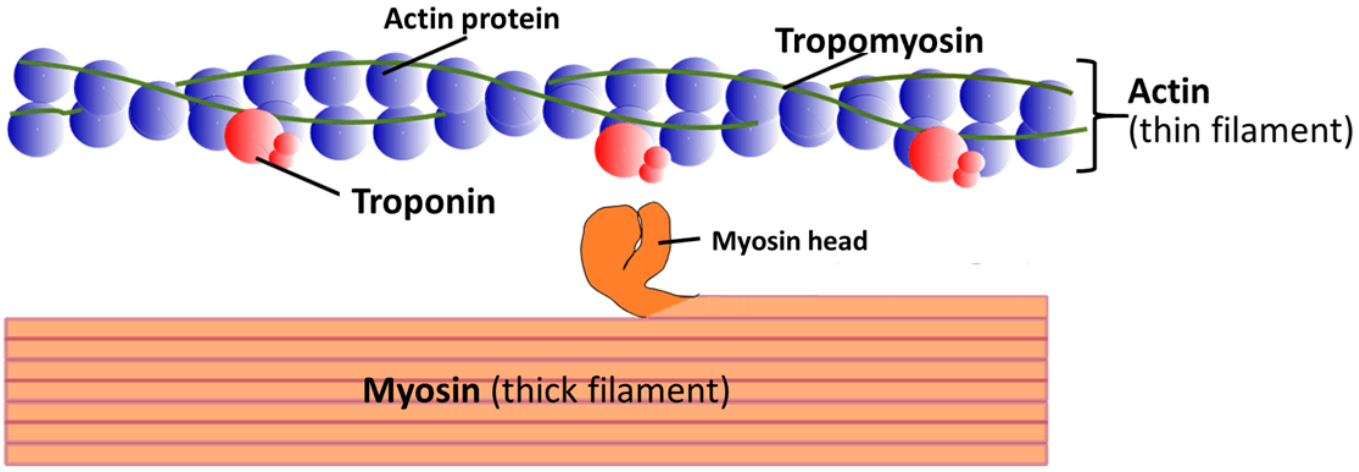


Figure 5.2.3: **The two myofilaments.** Interaction of the thin filament (actin, tropomyosin, and troponin) with the thick filament (myosin) leads to muscle contraction. The myosin head attaches to actin to generate force. More details to come.

Key Point Summary

- Muscles are composed of long bundles of myofibers.
- Myofibers contain thousands of myofibrils.
- Each myofibril is composed of numerous sarcomeres, the functional contractile region of a striated muscle. Sarcomeres are composed of myofilaments of myosin and actin, which interact using the sliding filament theory (model) and cross-bridge cycle to contract.

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5.3: Connective Tissue Wrappings — The Layers That Hold It All Together

Skeletal muscles are organs made of muscle fibers and connective tissue layers that organize the fibers and transmit force to produce movement.

Master this section and you'll be able to

- Identify the three connective tissue layers of skeletal muscle and explain how they organize skeletal muscle.
- Outline how the mysia, tendons/aponeuroses, and periosteum work together to transmit the force of muscle contraction into skeletal movement.
- Differentiate between a tendon and an aponeurosis, and give an example for each.

Muscles are not just made up of muscle fibers — they are carefully organized and supported by connective tissue layers that give them structure, strength, and protection.

Remember the definition of an organ?

An **organ** is a structure made up of two or more tissue types working together for a specific function.

Skeletal muscles qualify as organs because they contain **muscle tissue, connective tissue, blood vessels, and nerves** — all cooperating to produce movement.

So the next time you flex your biceps, you are looking at an *organ at work* (just one you do not usually think of as an organ).

The Mysia: Connective Tissue Layers of Skeletal Muscle

The three connective tissue layers in skeletal muscle are collectively called the **mysia**. They provide structure for the whole muscle and organize the fibers inside it.

Epimysium (Outermost Layer)

- A sheath of **dense irregular connective tissue**.
- Surrounds the entire muscle.
- Keeps the muscle strong while it contracts.
- Separates the muscle from surrounding tissues so it can move independently.

Perimysium (Middle Layer)

- Wraps groups of muscle fibers into bundles called **fascicles**.
- Also made of **dense irregular connective tissue**.
- Important in limb muscles, where fascicles allow the nervous system to recruit smaller groups of fibers for **precise control** of movement (think about the difference between lifting a pencil vs. a dumbbell).

Endomysium (Innermost Layer)

- A thin layer of **areolar connective tissue**.
- Surrounds each individual muscle fiber.
- Houses **capillaries and extracellular fluid** that deliver nutrients and oxygen directly to each fiber.

Beyond the Mysia: Tendons and Aponeuroses

In addition to the mysia, a couple of other connective tissue structures play key roles in muscle function:

Tendon

The three connective tissue layers of muscle (the mysia) do more than just organize the fibers — their **collagen fibers blend together** and **continue into the tendon.**

In the tendon, these collagen fibers are arranged in straight, parallel bundles, forming **dense regular connective tissue** (perfect for handling pulling forces).

At the other end of the tendon, where it attaches to bone, the collagen fibers merge with the **periosteum** (the connective tissue covering the bone). Here, the collagen becomes part of **dense irregular connective tissue** again as it was in the epi- and perimysium.

📌 **Key idea:**

When a muscle contracts, the tension is passed along from the muscle fiber to the bone in a continuous chain of connective tissues, transmitting the force of contraction into movement of parts of the skeleton.

> Muscle fiber --> Mysia --> Tendon --> Periosteum --> Bone

Famous example: The **Achilles tendon** — the largest and strongest tendon in the human body — connects the **gastrocnemius and soleus muscles** of the calf to the **calcaneus (heel bone)**. Its function is to transmits the powerful contraction of the calf muscles into the push-off force at your heel. Without it, you could not walk, run, or jump, nor could you stand on your toes. Despite its strength, the Achilles tendon is also prone to injury. A complete rupture often feels like being “kicked in the back of the ankle” and can make walking very difficult. The name comes from Greek mythology: the warrior **Achilles** was invincible except for his heel, where he was ultimately fatally wounded.

Aponeurosis

In some places, instead of merging into a cord-like tendon, the mysia form a broad sheet of dense regular connective tissue called an **aponeurosis**.

📌 **Quick tip:** A tendon looks like a **rope**, while an aponeurosis looks like a **flat sheet**.

Example: The **rectus sheath** (also called the abdominal aponeurosis). This is a broad, flat tendon in the abdominal wall that encloses the **rectus abdominis muscles** (the “six-pack” muscles). It is formed by the aponeuroses of the three flat abdominal muscles: the **external oblique, internal oblique, and transversus abdominis**.

Function: The abdominal aponeurosis holds the rectus abdominis in place, protects the abdominal organs, and allows the abdominal muscles to work together for **bending, twisting, and stabilizing the trunk**.

So, the next time you hear someone brag about their “six-pack abs,” you can impress them by pointing out that what they are really showing off is the **rectus abdominis muscles wrapped and outlined by the abdominal aponeurosis**!

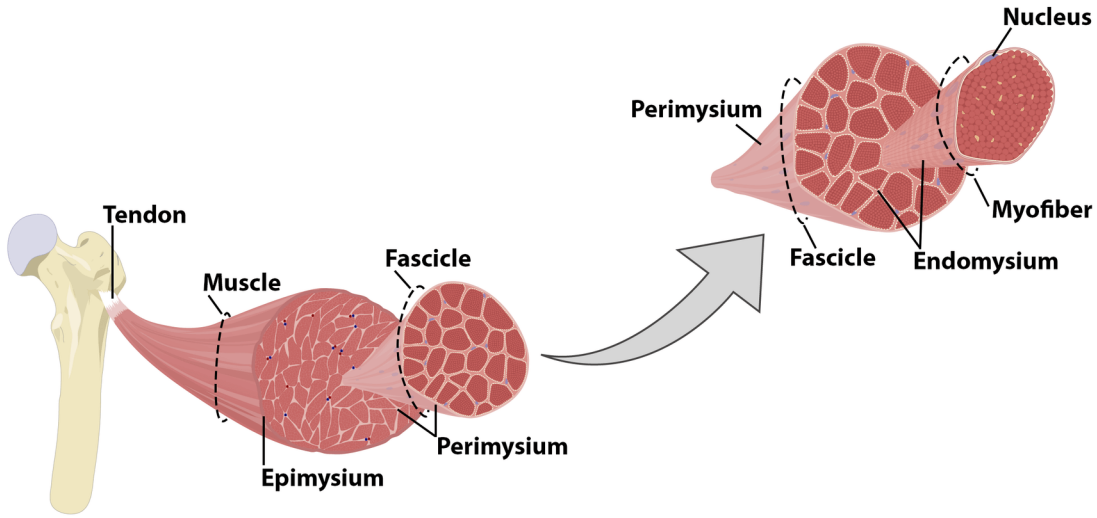
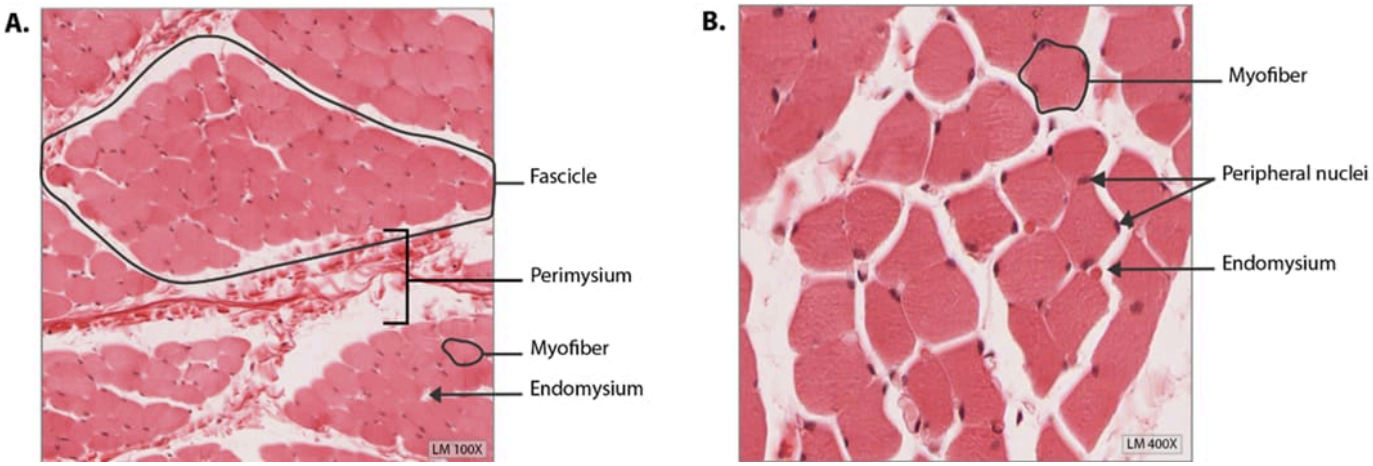


Figure 5.3.1: **Skeletal Muscle Organ Structure.** Each level of the organization of a skeletal muscle is wrapped in a connective tissue layer: the cell (myofiber) is surrounded by the endomysium, the bundle of cells (muscle fascicle) is surrounded by the perimysium, and the organ (muscle) is surrounded by the epimysium.

(Image credit: "Skeletal Muscle Organ Structure" by Justin Greene is licensed under CC BY-NC-SA 4.0).



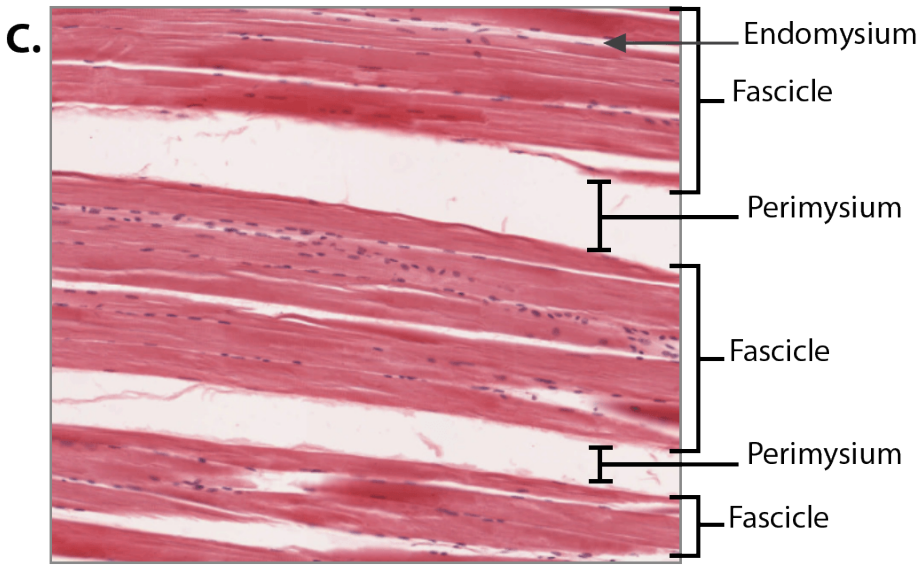


Figure 5.3.2: **Histology of Skeletal Muscles in Cross and Longitudinal Sections.** Muscles are held together by and transfer force through their connective tissue layers. The perimysium surround the fascicles and can be seen between them. The endomysium surrounds the myofibers and appears thinner than the perimysium. A. Slide of cross section at 100x, B. Slide of cross section at 400x, C. Slide of longitudinal section at 100x. *(Image credit: "Histology of Skeletal Muscle" by Jennifer Lange, based on micrographs provided by the Regents of the University of Michigan under CC-BY-NC-SA 3.0)*

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5.4: The Sarcomere — Functional Unit of Muscle

The sarcomere is the functional unit of skeletal muscle, where actin and myosin filaments interact to produce contraction.

Master this section and you'll be able to

- Identify areas of the skeletal muscle fibers
- Describe excitation-contraction coupling

The Sarcomere

As you have learned already, skeletal muscle fibers look **striped (striated)** under the microscope. This striped pattern comes from the precise arrangement of two types of protein filaments: **actin (thin filaments)** and **myosin (thick filaments)**. These filaments, along with regulatory proteins like **troponin** and **tropomyosin**, are organized into repeating units called **sarcomeres**.

Functional Unit of Muscle

- The **sarcomere** is the **functional unit** of a muscle fiber.
- Sarcomeres are linked end to end along the length of structures called **myofibrils**. Myofibrils are rod-like **organelles** inside the long, tubular muscle cells, also known as myofibers.
- Each myofibril runs the entire length of the muscle cell and is anchored to the cell membrane (**sarcolemma**) at its ends.
- When the sarcomeres in a myofibril contract, the entire myofibril shortens — causing the whole muscle fiber to contract.

Size and Arrangement

- Myofibrils are very thin, only about **1.2 micrometers** in diameter, but each fiber contains **hundreds to thousands of myofibrils**, and each myofibril contains **thousands of sarcomeres**.
- A typical sarcomere is about **2 micrometers long** and has a **cylindrical, three-dimensional arrangement**.
- Each sarcomere is bordered by **Z-discs (or Z-lines)**, which anchor the thin filaments (actin).

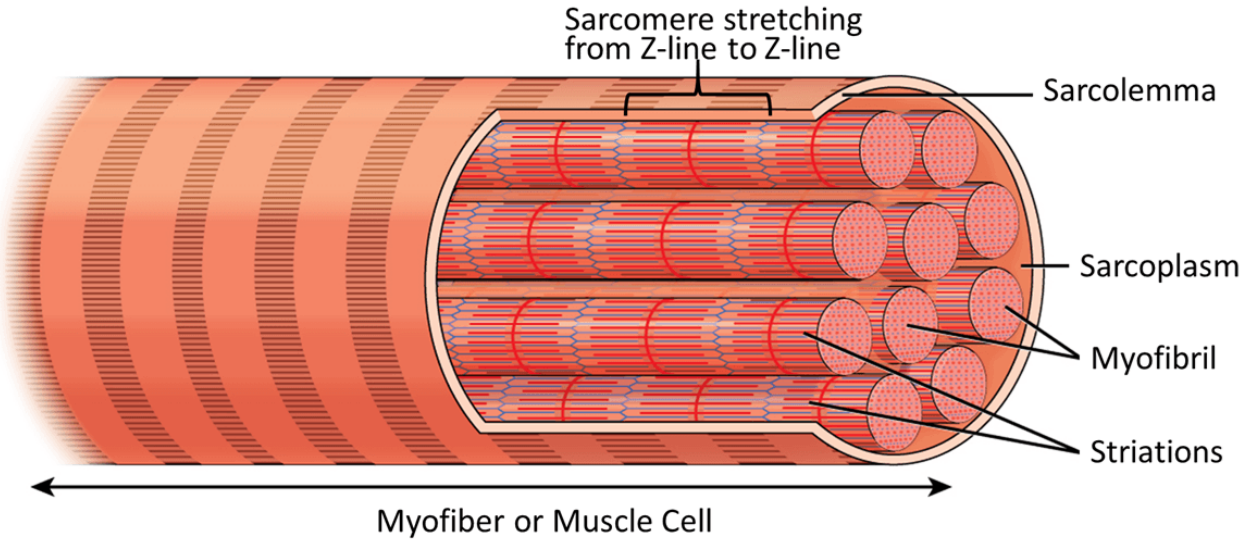


Figure 5.4.1: **Sarcomere Structure.** Cross-section of a muscle fiber showing sarcomere, sarcolemma, sarcoplasm, myofibrils, and striations.

Thin vs. Thick Filaments

- **Thin filaments**: made mostly of actin, with troponin and tropomyosin as regulatory proteins. These filaments extend **from the Z-discs toward the center** of the sarcomere.
- **Thick filaments**: made of myosin, with many projecting "heads." These extend **from the center of the sarcomere outward**, but they do not reach all the way to the Z-discs.
- The overlap of thin and thick filaments gives muscle its striated appearance and is key to contraction.

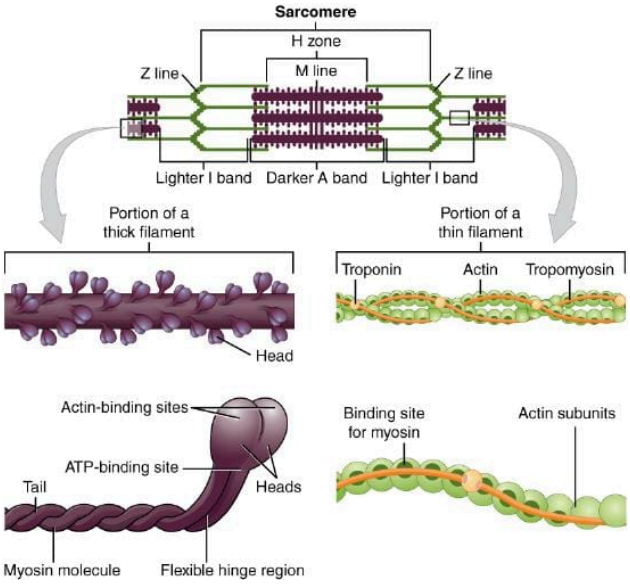


Figure 5.4.2: **The sarcomere.** The sarcomere, the region from one Z-line to the next Z-line, is the functional unit of a skeletal muscle fiber.

The Sarcomere

The striated appearance of skeletal muscle fibers is due to the arrangement of the myofilaments of actin and myosin in sequential order from one end of the muscle fiber to the other. Each packet of these microfilaments and their regulatory

proteins, **troponin** and **tropomyosin** (along with other proteins) is called a **sarcomere**.

The sarcomere is the functional unit of the muscle fiber. The sarcomere itself is bundled within the myofibril that runs the entire length of the muscle fiber and attaches to the sarcolemma at its end. As myofibrils contract, the entire muscle cell contracts. Because myofibrils are only approximately 1.2 μm in diameter, hundreds to thousands (each with thousands of sarcomeres) can be found inside one muscle fiber. Each sarcomere is approximately 2 μm in length with a three-dimensional cylinder-like arrangement and is bordered by structures called Z-discs (also called Z-lines, because pictures are two-dimensional), to which the actin myofilaments are anchored. Because the actin and its troponin-tropomyosin complex (projecting from the Z-discs toward the center of the sarcomere) form strands that are thinner than the myosin, it is called the **thin filament** of the sarcomere. Likewise, because the myosin strands and their multiple heads (projecting from the center of the sarcomere, toward but not all to way to, the Z-discs) have more mass and are thicker, they are called the **thick filament** of the sarcomere.

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5.5: Skeletal Muscle Motor Units

The motor unit is the functional unit of muscle contraction and includes the motor nerve fiber and the muscle fibers it innervates.

Master this section and you'll be able to

- Define and describe a motor unit and explain its role as the basic functional unit of muscle contraction.
- Differentiate between small and large motor units and relate their size to precision versus strength of movement.
- Explain how motor unit recruitment and summation (spatial and temporal) allow the nervous system to control the force and endurance of muscle contractions.

What is a Motor Unit?

A motor unit is the **basic functional team of muscle contraction**. It consists of:

- **One motor neuron** – a nerve cell that carries signals from the spinal cord to the muscle.
- **All the skeletal muscle fibers it innervates** – the fibers that receive input from that neuron.

When the motor neuron fires an electrical signal (called an **action potential**), **all the muscle fibers in that motor unit contract together**.

💡 **Analogy:** Think of motor units like light switches. Each switch (motor neuron) controls a set of light bulbs (muscle fibers).

- Flip on one switch, and a few bulbs light up (a weak contraction).
- Flip on many switches, and the room lights up brightly (a strong contraction).

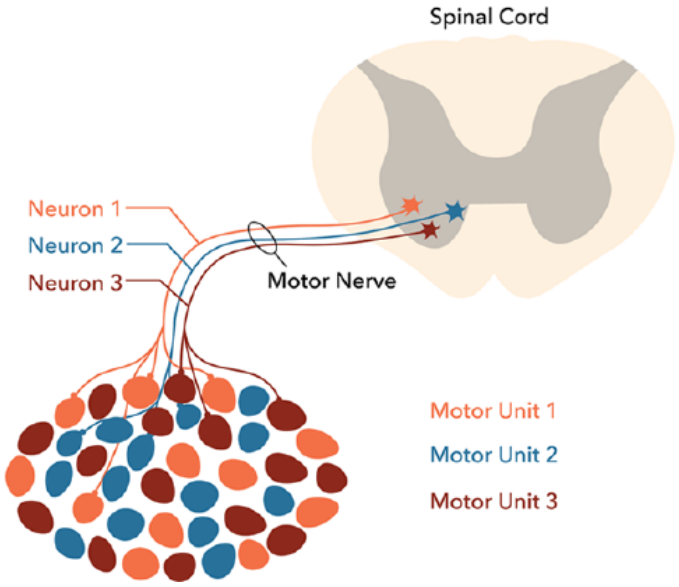


Figure 5.5.1: **Motor Unit.** The motor unit is the motor neuron and all of the myofibers it innervates. Note that a certain myofiber is innervated by only one motor neuron, but a motor neuron will innervate many myofibers.

Motor Unit Size

The number of muscle fibers in a motor unit varies depending on the **type of movement the muscle performs**. Precision is **inversely related** to the size of the motor unit. In other words, the smaller the motor unit, the finer the control.

- **Small motor units** allow for very precise movements because one motor neuron controls only a few muscle fibers. These are found in muscles that require delicate control, such as the eye muscles or the fingers.
- **Large motor units** allow for powerful but less precise movements because one motor neuron controls hundreds (or even thousands) of fibers. These are found in muscles that need strength, such as the quadriceps or calf muscles.

For example, the quadriceps, which generate large, powerful movements, may have motor units containing over a thousand fibers. By contrast, eye muscles, which perform tiny, accurate motions, may have motor units with as few as ten fibers.

To produce movement, **groups of motor units are activated together**, coordinating to contract the whole muscle with the right balance of strength and precision.

Comparison of Small vs. Large Motor Units

Feature	Small Motor Units	Large Motor Units
Number of fibers per motor neuron	Few (as few as 10)	Many (hundreds to thousands)
Location	Muscles requiring fine control (eyes, fingers)	Muscles requiring strength (quadriceps, calves)
Precision of movement	Very high (delicate, accurate movements)	Low (powerful, gross movements)
Strength of contraction	Weak, but finely graded	Strong, but less precise

Recruitment of Motor Units

Muscles can contract with different strengths depending on how many motor units are active. This is called **motor unit recruitment**.

- **Few motor units activated** → weak contraction.
- **Many motor units activated** → strong contraction.

This is how you can lift a feather gently or lift a heavy box with much more force, using the same muscle.

Motor Unit Alternation (Asynchronous Recruitment)

Muscles can "take turns" to avoid fatigue.

- While some motor units are active, others rest.
- They switch roles, so the muscle as a whole can keep contracting for longer without tiring as quickly.
- Example: holding your head upright for a long time.

Why It Matters

Understanding motor units helps explain:

- Why we can make both delicate and powerful movements.
- How muscles prevent fatigue during posture and endurance activities.
- Why damage to a motor neuron can weaken or paralyze the muscle fibers it controls.

Motor Pools and Force

All of the motor units within a single muscle are collectively known as a **motor pool**.

Within a motor pool, motor units vary in size. This range allows a muscle to adjust both the **precision** and the **force** of its contractions. For example, in the biceps, a small motor unit may be activated for fine, precise movements, while larger motor units are recruited for stronger, more powerful actions.

Because motor pools contain motor units of different sizes, the nervous system can finely control muscle force in two main ways:

- **Spatial summation:** Increasing force by recruiting more motor units or larger motor units.
- **Temporal summation:** Increasing force by stimulating a motor unit repeatedly so that the individual contractions add together (summation).

Through these mechanisms, the nervous system can smoothly scale muscle contractions from delicate movements to powerful actions.

Spatial vs. Temporal Summation

Type of Summation	What It Means	How Force Increases	Example
Spatial summation	Recruiting additional motor units (small to large)	More muscle fibers contract at once	Lifting a heavier object by activating more motor units in the biceps
Temporal summation	Repeated stimulation of the same motor unit	Contractions add together (summation) to produce greater force	Rapid signals cause a stronger, sustained contraction when holding a weight steady

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5.6: Neuromuscular Junction

A neuromuscular junction exists between the axon terminal and the motor end plate of a muscle fiber where neurotransmitters are released.

Master this section and you'll be able to

- Identify and describe the structure and function of the neuromuscular junction (NMJ) as a special type of synapse.
- Sequence the events that occur at the NMJ, from arrival of a motor neuron action potential to contraction of a skeletal muscle fiber.
- Summarize the pathophysiology of myasthenia gravis (MG), including how autoimmune cause damage.
- Recognize common symptoms of MG and explain how they relate to disrupted neuromuscular communication.

The Neuromuscular Junction: A Special Kind of Synapse

A **neuromuscular junction (NMJ)** is the connection between the axon terminal of a motor neuron and the plasma membrane of the **motor end plate** of a muscle fiber.

The motor end plate is a specialized region of the muscle fiber's plasma membrane (**sarcolemma**) that lies directly beneath the axon terminal. This so called "**synapse**" is the spot where the nervous system communicates directly with the skeletal muscle.

In general, the point of communication between a neuron and another cell is called a **synapse**. The NMJ is a **special type of synapse**, because here the target cell is a **muscle fiber** instead of another neuron or a gland cell. *(We will revisit synapses in more detail when we cover the nervous system.)*

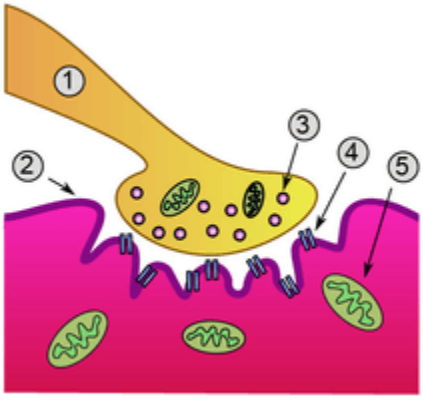


Figure 5.6.1: **Detailed view of a neuromuscular junction.** 1) Presynaptic axon terminal; 2) Sarcolemma at motor end plate; 3) Synaptic vesicle filled with ACh; 4) Acetylcholine receptor; 5) Mitochondrion.

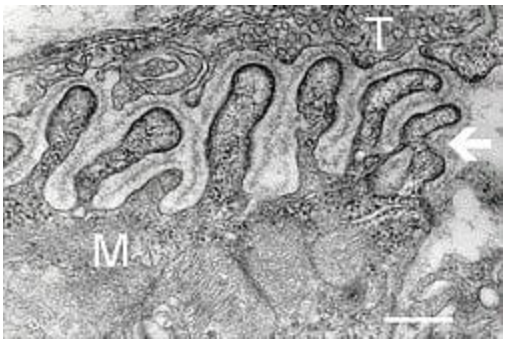


Figure 5.6.2: **Electron micrograph of a neuromuscular junction cross section.** T is the axon terminal and M is the muscle fiber. Scale is 0.3 µm.

Sequence of Events at the Neuromuscular Junction (NMJ)

1) Arrival of the Signal

- An **action potential** reaches the axon terminal of a motor neuron.
- **Voltage-gated calcium channels** in the axon terminal open, and **Ca^{2+} enters** the neuron from the extracellular fluid.
- The influx of Ca^{2+} causes **synaptic vesicles** in the axon terminal — filled with **acetylcholine (ACh)** — to fuse with the presynaptic membrane.

2) Neurotransmitter Release

- The motor neuron's terminal releases **ACh** (via **exocytosis**) into the tiny gap between neuron and muscle fiber (the **synaptic cleft**).

3) Binding to Receptors

- ACh diffuses across the cleft and binds to **ACh receptors** on the motor end plate of the muscle fiber.
- The receptors open ion channels: **Na^{+} enters** and **K^{+} exits**, creating a local depolarization called the **end-plate potential (EPP)**.

4) Muscle Action Potential

- If the EPP is strong enough, it triggers an **action potential** in the muscle fiber.
- This action potential spreads along the **sarcolemma** and travels down into the muscle through the **T-tubules**.

5) Calcium Release

- Depolarization of the T-tubules activates channels linked to the **sarcoplasmic reticulum (SR)**.
- The SR releases a flood of **Ca^{2+} into the cytosol** of the muscle fiber.

6) Contraction Begins

- The rise in Ca^{2+} allows **actin and myosin** to interact.
- Cross-bridges form, filaments slide, and the muscle fiber contracts.

📌 **Key idea:** The NMJ converts an **electrical signal in a neuron** into a **chemical signal (ACh)**, which then becomes a new

electrical signal in the muscle — leading to contraction.

CLINICAL EXAMPLE: Myasthenia Gravis (MG)



Myasthenia gravis (MG) is a **chronic autoimmune disorder** that messes with the way our nerves talk to our muscles. Normally, nerves release the chemical messenger **acetylcholine (ACh)** at the neuromuscular junction, which binds to receptors on muscle fibers and tells them to contract.

In autoimmune disorders, the **immune system gets confused,** and instead of only attacking the "bad guys," it accidentally attacks parts of your own body. It is like the guards mistaking your friendly neighbors for burglars. When a person has MG, their immune system produces **antibodies that block or destroy the ACh receptors on the muscle end plate.** This blockage causes muscle weakness, often first exhibiting drooping eyelids *(see image on the right)* and expanding to include overall muscle weakness and fatigue. Imagine trying to text a friend but their phone screen is shattered — your message is sent, but they cannot "read" it. As a result, the muscle does not get the signal properly, leading to weakness.

The effects of myasthenia gravis highlight the importance of a properly functioning neuromuscular junction, where communication between neurons and muscle fibers enables normal muscle contraction and relaxation.
✨ Bottom line: MG is all about a miscommunication at the neuromuscular junction. The nerves are "talking," but the muscles cannot fully "hear" the message.

MG is considered **rare**. It can affect anyone, but it most often shows up in **women under 40** and **men over 60**. While there might be a genetic predisposition for people to get MG, it is not typically considered a hereditary disorder.

Key Symptoms

- **Eyes and face:** drooping eyelids, double vision, difficulty with facial expressions
- **Swallowing and speech:** trouble chewing, swallowing, or talking clearly
- **Neck and limbs:** weakness that gets worse the more the muscle is used
- **Breathing:** in severe cases, the muscles used for breathing can fail — this is called a **myasthenic crisis** and is a true medical emergency

A classic feature is that weakness **worsens with activity** but **improves with rest** (kind of like your muscles are running on a bad battery that only recharges when you stop moving).

The good news: with today's treatments — which may include medications to boost acetylcholine, therapies that calm down the immune system, and supportive care — many people with MG can manage their symptoms and live active, fulfilling lives.

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5.7: Sliding Filament Theory of Contraction

In the sliding filament model, the thick and thin filaments pass each other, shortening the sarcomere.

Master this section and you'll be able to

- Identify the main parts of a sarcomere: Z-line, A-band, I-band, H-band, and M-line, and describe what each represents.
- Explain the sliding filament model of muscle contraction, including how the various bands change or stay the same.

Sarcomere Structure Review

To understand the sliding filament model requires an understanding of sarcomere structure. Remember from page 5.4 of the study guide that a sarcomere is the **basic contractile unit** of striated muscle, meaning it's the smallest segment of muscle fiber capable of contracting and generating force. Sarcomeres are arranged end-to-end along myofibrils, which are long thread-like organelles found inside muscle fibers. Each sarcomere sits between **two Z-discs (or Z-lines)**, which define its boundaries.

Within each sarcomere, there are two main kinds of protein filaments:

- **Thin filaments** made mostly of actin.
- **Thick filaments** made mostly of myosin.

These filaments are organized in a precise, overlapping pattern, giving skeletal and cardiac muscles their striped (striated) appearance under the microscope. When a muscle contracts, the filaments slide past one another, pulling the Z-discs closer together and shortening the sarcomere, which shortens the entire muscle.

The sarcomere also contains:

- **I bands** (light bands) — with only thin filaments,
- **A bands** (dark bands) — where thick and thin filaments overlap,
- **H band** (or zone) — a lighter area in the center of the A band with only thick filaments,
- **M line** (the central point of the sarcomere).

This careful arrangement allows muscle contraction to be powerful, coordinated, and efficient.

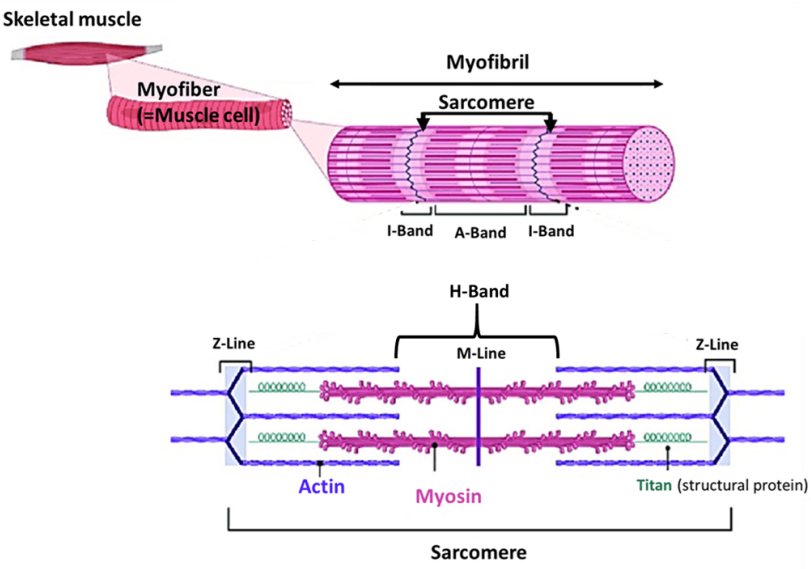


Figure 5.7.1: **Sarcomere Structure.** Diagram of skeletal muscle showing myofiber (muscle cell) —> myofibril (organelle) —> sarcomere with overlapping actin (microfilament) and myosin (motor protein).

Sliding Filament Model and Band Changes

The **sliding filament model** (aka theory) of contraction describes how — when signaled by a motor neuron — **thin filaments (actin)** slide past **thick filaments (myosin)** to shorten the sarcomere. You can see the structural changes under a light microscope. Specifically during contraction:

- The **Z lines move closer together.**
- The **I-Band shortens.**
- The **H-Zone (or H-band) shortens/disappears.**
- The **A-Band stays the same width.**
- At full contraction, the thin and thick filaments overlap completely.

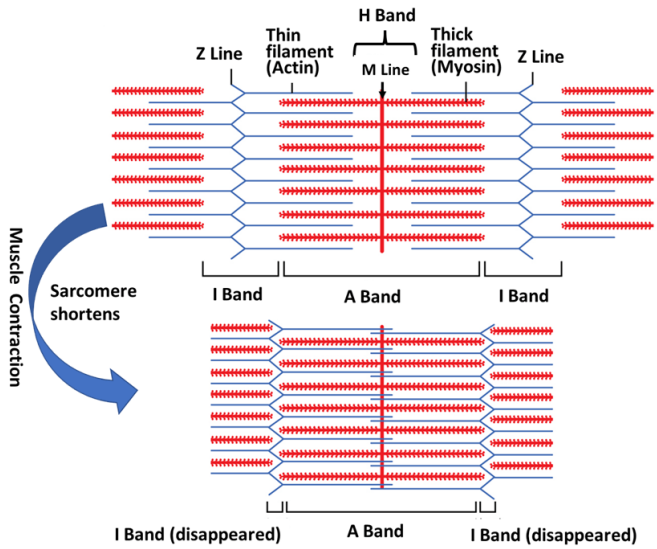


Figure 5.7.2: **Band Shortening During Muscle Contraction.** As the sarcomere shortens, the Z lines move closer together and the I Band (actin only) gets smaller or disappears. The A band (containing actin and myosin filaments) stays the same.

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5.8: Detailed Mechanism of Cross-bridge Formation

A neuromuscular junction exists between the axon terminal and the motor end plate of a muscle fiber where neurotransmitters are released.

Master this section and you'll be able to

- Outline the steps of the cross-bridge cycle.
- Identify the roles of calcium ions and ATP in regulating cross-bridge cycling and muscle fiber shortening.
- Explain the anatomical limit of shortening.

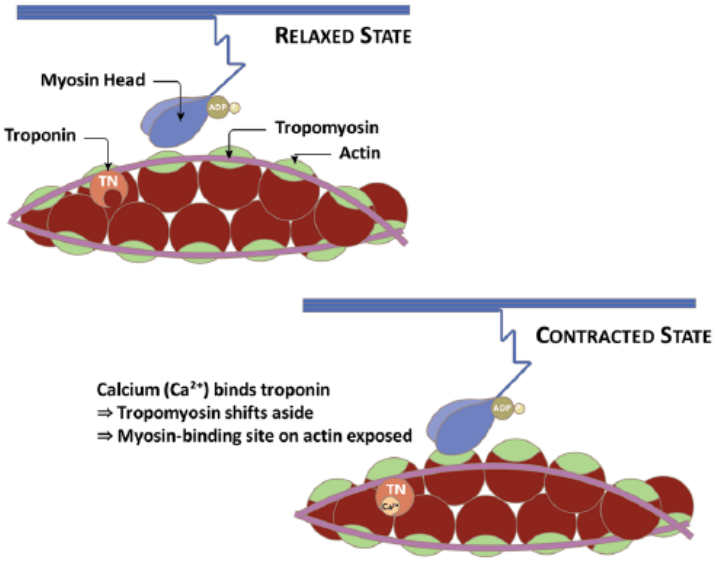
Cross-Bridge Formation is a key event in the molecular mechanism of the sliding filament model of muscle contraction. It occurs when the head of a myosin molecule temporarily attaches to a binding site on an actin filament within a sarcomere. This attachment forms a “cross-bridge” between the thick (myosin) and thin (actin) filaments, creating a physical link that allows the muscle to contract.

Cross-Bridge Cycle: The Molecular Mechanism of Sarcomere Shortening

Cross-bridge formation is essential, but it does not occur automatically. The binding sites on actin must first be “unlocked.” This regulation is controlled by two proteins:

- **Tropomyosin**: a long protein that wraps around actin filaments, covering the myosin-binding sites.
- **Troponin**: a protein attached to tropomyosin that acts as a calcium sensor.

Together, they form the **troponin–tropomyosin complex,** which prevents myosin from binding to actin when the muscle is relaxed.



Step 1: Calcium Unlocks the Binding Sites

When a motor neuron stimulates a muscle fiber, calcium ions (Ca^{2+}) flood into the sarcoplasm. Then:

- **Ca^{2+} binds to troponin**.
- **Troponin changes shape** and shifts tropomyosin away from the binding sites on actin.
- Once the **binding site is exposed**, myosin heads can attach to actin, forming **cross-bridges**.

Step 2: The Cross-Bridge Cycle (The Pulling Action)

Myosin heads then go through a repeated cycle of binding, pulling, releasing, and resetting — like tiny oars rowing a boat. Each cycle involves four main steps:

1. **Cross-bridge formation**: A myosin head binds to an exposed binding site on actin (only possible when Ca^{2+} is present).
2. **Power stroke**: The myosin head pivots, pulling the actin filament toward the M-line (the center of the sarcomere).
3. **Cross-bridge detachment**: ATP binds to the myosin head, causing it to release from actin.
4. **Reactivation**: ATP is hydrolyzed into ADP and Pi, releasing energy that re-cocks the myosin head into its high-energy position, ready for another cycle.

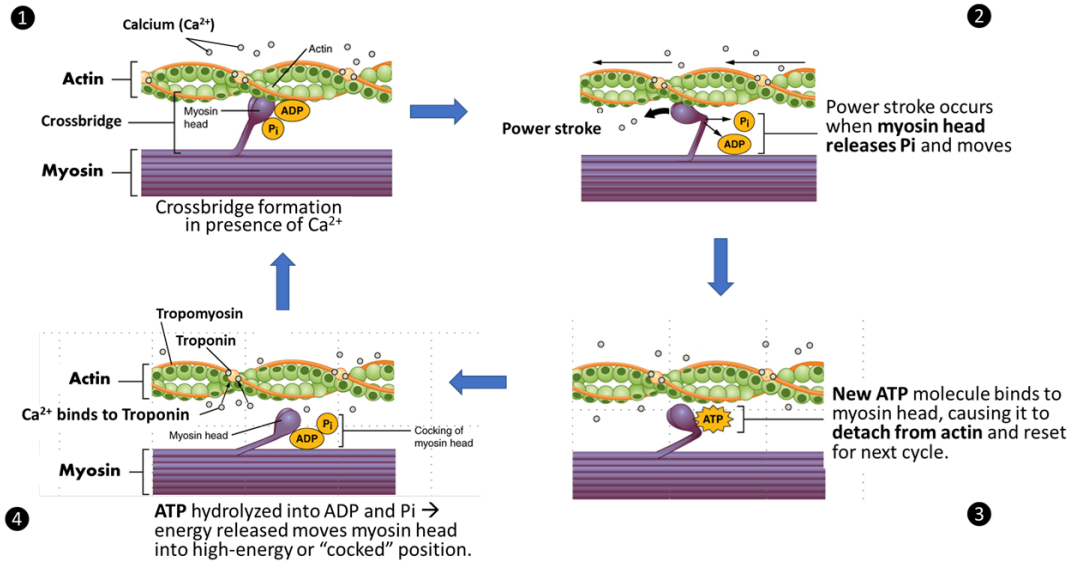
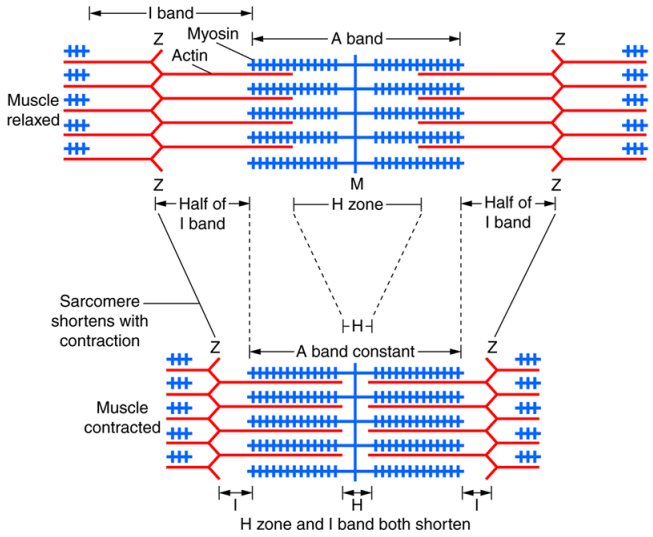


Figure 5.8.1: **Steps of the Cross-Bridge Cycle.** Compare to the description above.

Because each pull is brief, the cycle must repeat many times in rapid succession. The repeated attachment, pivoting, and release of myosin heads slide the thin (actin) filaments past the thick (myosin) filaments, shortening the sarcomere. The force produced by one sarcomere is small, but when multiplied across all sarcomeres within a myofibril, all myofibrils within a muscle fiber, and all fibers within a muscle, the total force and movement generated become significant. The coordinated **action of millions of myosin heads working together generates a strong, steady contraction** of the entire muscle.



A muscle (or more specifically: a sarcomere) keeps shortening as long as

- **Calcium is present** to bind to troponin and uncover the binding sites on actin; and
- **ATP is available** to fuel the pulling action of myosin; or
- **Until the thick filaments (myosin) bump up against the Z-lines**, which is the built-in stop point (see image on the right).

Expansion and contraction of the sarcomere occur only within the I band and H zone (both shortening or disappearing). The myofilaments themselves do not change in length, so the A band remains constant.

👉 **In summary:** The **sliding filament theory** is the conceptual framework that explains how sarcomeres shorten through changes in the H and I bands. The **cross-bridge cycle** is the microscopic engine — the molecular mechanism — by which myosin and actin filaments slide over each other.

Watch this short video to review the mechanism of muscle contraction:

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

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5.9: Energy (ATP) for Muscle Contraction

Muscle contraction requires ATP, and because stored ATP is minimal, muscle fibers must continually regenerate it using creatine phosphate, anaerobic glycolysis, and aerobic respiration.

Master this section and you'll be able to

- Compare and contrast the three ATP regeneration pathways in muscle cells in terms of oxygen requirement, speed, efficiency, and duration of energy supply.
- Apply knowledge of ATP regeneration pathways to different forms of physical activity, predicting which energy system predominates during short bursts (e.g., sprinting), intermediate efforts (e.g., 400-meter run), and long-duration exercise (e.g., marathon running).

ATP and Muscle Contraction

Muscle contraction is an energy-demanding process, and the "fuel" that powers it is **adenosine triphosphate (ATP)**. Each myosin head in a contracting muscle fiber needs ATP to grab onto actin, pull, and then reset for the next cycle. In addition to its direct role in the **cross-bridge cycle**, ATP also provides the energy for the **active-transport Ca^{2+} pumps in the SR**. Without a steady supply of ATP, contraction quickly stops. However, muscles store only a tiny amount of ATP — just enough for a second or two of intense activity — so the cell must constantly regenerate it.

Think of ATP as the rechargeable battery that keeps your muscles running. The problem is, muscles do not keep a big battery pack on reserve — they only have a very small charge ready to go. To keep moving, muscle fibers need to recharge that battery continuously **using three different pathways**, each with its own speed, power, and endurance:

1. Creatine Phosphate Metabolism: The Quick Reserve

Creatine phosphate — also called **phosphocreatine** — serves as a short-term energy buffer. In a resting muscle, extra ATP transfers a phosphate group to creatine, forming ADP and creatine phosphate. When contraction begins, creatine phosphate donates its phosphate back to ADP to regenerate ATP in a reaction catalyzed by the enzyme **creatine kinase**. This reaction happens very quickly and provides energy for the first 10–15 seconds of activity. Once creatine phosphate stores are depleted, the muscle must switch to other ATP sources.

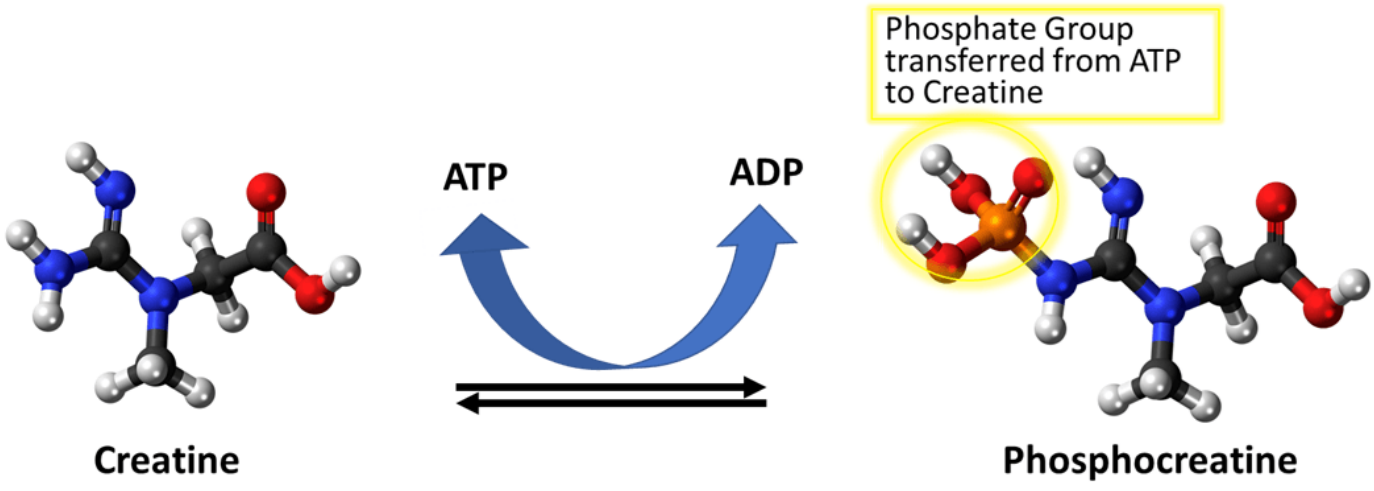


Figure 5.9.1: **Conversion of Creatine to Phosphocreatine**. Ball-and-stick models illustrate how a creatine molecule gains a phosphate group from ATP, forming creatine phosphate (phosphocreatine) and ADP.

2. Anaerobic Glycolysis: The Short Burst System

As creatine phosphate runs out, muscles turn to glycolysis, an **anaerobic pathway** that breaks down glucose without oxygen. Glycolysis produces **two ATP molecules per glucose**, along with **pyruvic acid**.

- If oxygen is available, pyruvic acid can move into aerobic respiration.
- If oxygen is lacking (as in intense exercise), pyruvic acid is converted into **lactic acid**, which helps regenerate NAD+ so glycolysis can continue.

This pathway is less efficient than aerobic respiration and produces ATP more slowly than creatine phosphate, but it allows for about a minute of high-intensity muscle activity. The buildup of lactic acid may contribute to muscle fatigue as pH drops inside the muscle fiber.

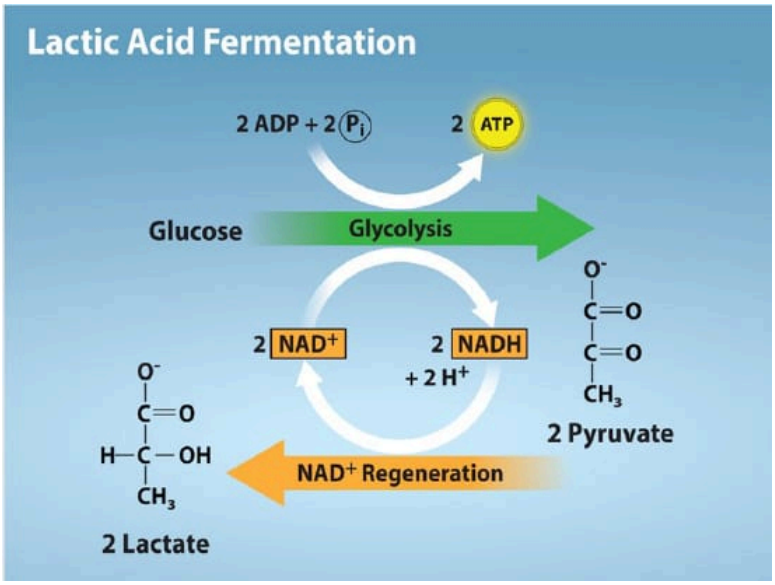


Figure 5.9.2: **Glycolysis.** Glucose breakdown in anaerobic conditions: glycolysis makes 2 ATP, pyruvate is reduced to lactate.

3. Aerobic Respiration: The Endurance System

For long-lasting activity, muscles rely on **aerobic respiration**, which requires oxygen and takes place in the mitochondria. Aerobic respiration can use multiple fuels: glucose, pyruvic acid, and fatty acids. It is **highly efficient**, generating about **36 ATP per glucose molecule** (compared to 2 from glycolysis).

Although slower to ramp up, aerobic respiration provides about **95% of the ATP** used by resting or moderately active muscles. Muscles store some oxygen in the protein **myoglobin**, which helps delay fatigue. Endurance training also improves the delivery of oxygen by strengthening the circulatory and respiratory systems.

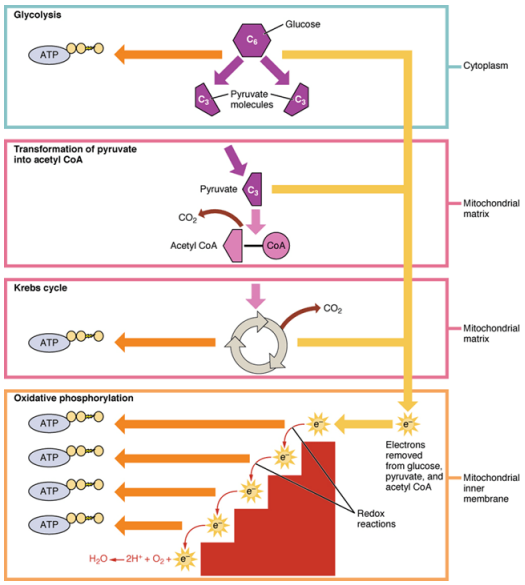


Figure 5.9.3: **Aerobic Respiration.** Diagram of cellular respiration: glycolysis in cytoplasm, pyruvate to acetyl-CoA, Krebs cycle, oxidative phosphorylation in mitochondria.

Comparison of ATP Regeneration Pathways in Muscle Cells

Pathway	Oxygen Required?	Speed of ATP Production	ATP Yield (per glucose or equivalent)	Duration of Energy Supply	Key Features
Creatine Phosphate System	No	Very fast (immediate)	1 ATP per creatine phosphate	~10–15 seconds	Uses stored creatine phosphate; provides quick "backup battery" for short bursts
Anaerobic Glycolysis	No	Fast	2 ATP per glucose	~30–60 seconds	Breaks down glucose without O_2; produces lactic acid, useful for short, high-intensity activity
Aerobic Respiration	Yes	Slower	~36 ATP per glucose (plus ATP from fatty acids)	Minutes to hours	Highly efficient, sustained energy; depends on O_2 and mitochondria; fuels endurance

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5.10: Muscle Fatigue

Muscle fatigue occurs following a period of sustained activity.

Master this section and you'll be able to

- Identify and outline the major causes of muscle fatigue.
- Differentiate between peripheral fatigue and central fatigue, and describe the physiological and psychological mechanisms involved in each.
- Analyze the effects of exercise and aging on muscle performance.

Muscle fatigue is the decline in the ability of a muscle to generate force or power during sustained or repeated activity or due to pathological issues. Muscle fatigue has a number of possible causes including impaired blood flow, ion imbalance within the muscle, nervous fatigue, loss of desire to continue, and most importantly, the accumulation of lactic acid in the muscle.

Fatigue can originate **at different levels** in the neuromuscular system and is typically classified in two main types: **peripheral fatigue** and **central fatigue.**

Peripheral Fatigue

Peripheral fatigue occurs at or beyond the neuromuscular junction. Let's take a closer look at a couple of causes:

2) Ion Imbalance

For a muscle to contract, **calcium ions (Ca^{2+})** must bind to **troponin**, which pushes tropomyosin out of the way and exposes the actin binding sites to the myosin heads. Without calcium, the cross-bridge cycle cannot begin.

During **prolonged exercise**, the body loses water and electrolytes (such as sodium, potassium, and chloride) through sweat. These electrolytes are **osmotically active molecules** that normally help maintain the balance of fluids inside and outside the muscle cell. When too many are lost, the **osmotic gradient** shifts, making it harder for calcium to move efficiently into the muscle fiber.

As a result, the precise balance of ions needed for contraction and relaxation is disrupted. In mild cases, this contributes to **muscle fatigue**. In more severe cases, it can cause painful, involuntary, and prolonged contractions known as **muscle cramps**.

👉 In short: without enough ions to keep signals firing smoothly, your muscles can “lock up” instead of working in their normal rhythm.

3) Depletion of Energy Stores

Muscle contraction depends heavily on a continuous supply of **ATP**. Every step of the cross-bridge cycle, calcium pumping, and sodium–potassium gradient maintenance requires energy. At the start of exercise, ATP is replenished rapidly through **creatine phosphate** and then through **glycolysis** and **aerobic respiration**. However, during prolonged or intense activity, these energy reserves become strained:

- **ATP levels** may drop if the rate of use exceeds the rate of regeneration.
- **Glycogen stores**, the muscle’s main reservoir of glucose, gradually diminish. Once glycogen is depleted, muscles rely more on blood glucose and fat oxidation, which are slower pathways and cannot meet sudden high-intensity demands.

👉This energy shortage means myosin heads cannot cycle efficiently, ion pumps fail to fully restore gradients, and contraction

weakens — a classic picture of **muscle fatigue**.

4) Metabolite Accumulation

Fatigue is not only about “running out of fuel.” By-products of metabolism also interfere with normal contraction:

- **Magnesium ions (Mg^{2+}):** Released as ATP is broken down (ATP is normally bound to Mg^{2+}), excess free Mg^{2+} can compete with calcium, reducing calcium release from the **sarcoplasmic reticulum (SR)**.
- **Reactive oxygen species (ROS):** Produced in the mitochondria during intense aerobic activity, ROS can damage proteins involved in excitation–contraction coupling, including calcium channels.
- **Inorganic phosphate (Pi):** Built up from rapid ATP hydrolysis, Pi can combine with calcium inside the SR, lowering the free Ca^{2+} available for release.
- **Hydrogen ions (H^{+}):** While lactic acid often gets the spotlight, the real issue is H^{+} accumulation, which lowers pH and reduces **troponin’s sensitivity to Ca^{2+}**, further impairing contraction.

5) Lactic Acid Accumulation

Last, but not least, let's look at a specific metabolite a bit closer: Lactic acid (also know as lactate). For long-term muscle activity, fibers rely on a steady supply of **oxygen** and **glucose** so that **aerobic respiration** can occur. This process happens inside the mitochondria and produces large amounts of ATP, the fuel needed for contraction.

This system is much less efficient and provides only a fraction of the ATP.

But if the **respiratory** or **circulatory** systems cannot deliver enough oxygen, such as during high-intensity or anaerobic exercise, the body shifts to the **glycolytic (anaerobic) system**. This results in lactic acid accumulation. Lactic acid was once believed to be the direct cause of muscle fatigue because it leads to acidosis, disrupting muscle contraction processes. However, more recent research indicates its role is less direct — acidosis may not impair muscle function at physiological temperatures as much as previously thought, and other metabolites, like inorganic phosphate, may play bigger roles.

👉 You can think of anaerobic glycolysis like using a **credit card for energy**: It lets you keep going when oxygen is scarce, but eventually you have to "pay back" the debt with extra oxygen during recovery. The extra oxygen needed to process lactic acid and restore normal balance after exercise is called the **oxygen debt**.

Central Fatigue and Loss of Desire

Not all fatigue originates in the muscle itself. **Central fatigue** arises from the **central nervous system (CNS)** — the brain and spinal cord — which governs how strongly and how often motor neurons stimulate skeletal muscles.

Central fatigue may involve:

- A **reduction in neural drive**, meaning fewer or weaker signals are sent from the motor cortex and spinal cord to motor units.
- **Altered neurotransmitter balance** (for example, changes in serotonin, dopamine, or acetylcholine) that can reduce excitability of motor neurons.
- **Psychological factors**, such as reduced motivation or perception of effort, which influence how much voluntary drive the brain sends to the muscle.

It is important to note that most daily activities and even moderate exercise require muscle forces **well below maximal capacity**. Thus, in healthy individuals, central fatigue usually does not prevent contraction altogether. However, as **metabolic stress builds**

in working muscles (lactate accumulation, ion imbalances, low oxygen, and rising temperature), the brain receives **sensory feedback** signaling discomfort and potential danger.

This feedback, combined with psychological perception of effort, can diminish the **desire to continue exercising**. In other words, the body is physically capable of generating more force, but the brain essentially "turns down the dial" to protect the organism from overexertion or damage.

👉 Central fatigue is therefore a blend of **neurophysiological mechanisms** (changes in neurotransmitter signaling and motor unit recruitment) and **psychological regulation** (motivation, pain tolerance, perceived effort).

The Combined Effect

You have seen that muscle fatigue is not caused by just one factor like "low oxygen", "low energy", or "too much lactic acid". Rather, it is a **multifactorial process** involving many different players. The combination of **substrate depletion** (ATP and glycogen running low) plus **metabolite accumulation** (Mg^{2+}, ROS, Pi, H^+) gradually weakens contraction. This makes it harder to sustain force, slows relaxation, and eventually forces the muscle to stop working until balance is restored.

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5.11: When Muscles Fall Silent — Understanding Paralysis

Paralysis is the loss of voluntary movement caused by disrupted nerve signals to muscles, resulting in either limp weakness (flaccid paralysis) or stiff, overactive muscles (spastic paralysis).

Master this section and you'll be able to

- Differentiate between flaccid and spastic paralysis by describing their mechanisms, clinical features, and example conditions.

Introduction to Paralysis

Now that you know how muscles normally contract and relax to produce movement, let's look at what happens when this system **fails**.

Paralysis is the **loss of voluntary muscle function**, meaning a muscle (or group of muscles) cannot contract when you want it to. It occurs when the carefully coordinated teamwork between the nervous system and the muscles breaks down. Paralysis does not mean the muscle tissue has disappeared — rather, the signal from the nervous system fails to properly activate the muscle.

Paralysis can be:

- **Partial (paresis):** some movement is possible, but it is weak or limited.
- **Complete:** no voluntary movement at all.
- **Temporary or permanent,** depending on the cause.

Causes include damage to the **brain, spinal cord, peripheral nerves, or neuromuscular junctions**, as well as diseases that affect the **muscle fibers themselves**.

Flaccid Paralysis

- **Definition:**
  Flaccid paralysis is marked by weakness or paralysis with a dramatic ***loss of muscle tone*** **(hypotonia)**. The affected muscles are limp, soft, and cannot contract, leading to an absence of reflexes (areflexia).
- **Mechanism:**
  This occurs when the lower motor neurons, their axons, the neuromuscular junction, or the muscle fibers themselves are damaged. In each case, nerve impulses fail to effectively reach or activate the muscle, so the muscles cannot contract, resulting in hypotonia (limpness).

Example Conditions Causing Flaccid Paralysis:

- **Guillain-Barré Syndrome (GBS):** An autoimmune attack on peripheral nerves, often leading to sudden onset flaccid paralysis. Often triggered by infection (e.g., *Campylobacter jejuni, various Herpes viruses, and even the flue virus*).
- **Myasthenia Gravis (neuromuscular junction disorder):** Impaired signal transmission at the NMJ). Not as common as GBS, but an important chronic cause of muscle weakness. Produces fluctuating weakness rather than the sudden, complete flaccid paralysis seen in GBS.

- **Botulism:** Toxin from *Clostridium botulinum* bacteria blocks acetylcholine release at the neuromuscular junction. Very rare in the U.S. (~200 cases per year, mostly infant botulism). Still medically significant because of severity. Also the "classic example" of flaccid paralysis.

Clinical Features:

- Muscle weakness
- Loss of muscle tone (soft, floppy limbs)
- Absent reflexes
- Over time: muscle wasting

Clinical Case: A Family Dinner Gone Wrong

Last weekend, Maria, a 34-year-old woman, and her 14 year old son attended a family gathering where everyone enjoyed home-canned green beans her aunt had prepared. About 24 hours later, Maria's son began to feel dizzy and complained of double vision.  By the next morning, his eyelids were drooping, and he had trouble speaking clearly. His arms felt weak, and he had difficulty swallowing water.

Alarmed, Maria took him to the emergency department. On exam, doctors noticed he was alert and fully conscious, but his pupils were dilated and unresponsive to light, and he had weakness in his face and upper limbs. His breathing was becoming shallow.

Because Maria and other family members had also eaten the same beans and some were developing similar symptoms, doctors suspected **foodborne botulism**. The public health department was notified immediately. Maria's son was placed in intensive care, where he received **botulinum antitoxin** and supportive care, including a ventilator to help him breathe.

Over the next two weeks, Maria's son slowly recovered as his nerve endings regenerated. His family was advised to always follow pressure-cooking guidelines when canning foods, and to never taste the home-canned food if it smells odd.

Spastic Paralysis

- **Definition:**
  Spastic paralysis features ***increased muscle tone*** **(hypertonia)**, stiffness, and muscle spasms, often with exaggerated reflexes.

- **Mechanism:**
  Due to damage to the *upper motor neurons* in the brain or spinal cord, there is a loss of inhibitory input to the muscles. This imbalance means the muscles contract involuntarily or become resistant to movement.

Example Conditions Causing Spastic Paralysis:

- **Stroke**: The most common cause of long-term disability in adults in the United States. A stroke often damages upper motor neurons in the brain. This can produce **spastic hemiplegia** or **hemiparesis** — stiff and weak muscles, usually on one side of the body.
- **Tetanus**: Caused by a toxin released by *Clostridium tetani* bacteria. The toxin blocks the inhibitory signals that normally tell muscles to relax, leading to uncontrolled spasms and rigidity. Thankfully, tetanus is **rare in the U.S.** today because of effective vaccination programs!
- **Cerebral Palsy (CP)**: The **leading cause of spastic paralysis in children.** It results from abnormal development or damage to the motor areas of the brain. Most cases are **congenital**, meaning the condition develops before birth during pregnancy.

Clinical Features:

- Stiff, tight muscles
- Hyperactive or exaggerated reflexes
- Difficulty with voluntary movement (muscle contracts when stretched)
- May lead to muscle/joint deformities over time

Case Study: The Farmyard Accident

Miguel, a 27-year-old ranch worker, was fixing a broken fence when he accidentally stepped on an old nail hidden in the dirt. He brushed it off at the time, cleaned the wound with water, and went back to work.

Five days later, Miguel began to feel restless and irritable. That evening, he noticed that swallowing water was difficult and his jaw felt stiff. The next morning, his family rushed him to the emergency department after he collapsed during a sudden, painful back spasm that arched his whole body.

Doctors quickly suspected **tetanus**, based on his symptoms and the story of the puncture wound. A “spatula test” confirmed their suspicions when Miguel’s jaw clamped down instead of triggering a gag reflex.

He was treated with wound care, antibiotics to kill *Clostridium tetani* bacteria, and an injection of **tetanus immune globulin (TIG)** to neutralize toxin that had not yet bound to his motor neurons. Miguel recovered slowly but required weeks of hospital care.



Figure 5.11.1: **Tetanus.** This historical image shows a person with **opisthotonos**, a severe arching of the back caused by uncontrolled muscle spasms. The condition is most often linked to tetanus, in which a bacterial toxin blocks inhibitory nerve signals, leaving muscles locked in contraction. Before the tetanus vaccine was available and modern treatment, such dramatic symptoms were a common hallmark of the disease.

Key Distinctions Between Flaccid and Spastic Paralysis

	Flaccid Paralysis	Spastic Paralysis
Cause	Lower motor neuron, peripheral nerve, or neuromuscular junction damage	Upper motor neuron, CNS (brain/spinal cord) damage
Muscle Tone	Decreased, limp, soft	Increased, stiff, rigid
Reflexes	Absent or reduced	Exaggerated or increased
Examples	Polio, Guillain-Barré, botulism, nerve injury	Stroke, MS, cerebral palsy, TBI

Summary:
Flaccid paralysis usually indicates a problem with the nerve or junction directly connecting to the muscle, leading to weakness and limpness. Spastic paralysis points to a problem higher up in the nervous system (brain or spinal cord), causing increased tone and muscle stiffness. The specific features help clinicians both diagnose the underlying problem and target treatments.

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5.12: Exercise and Muscle Performance

Physical training alters skeletal muscle by increasing endurance or strength through cellular adaptation, while inactivity and aging lead to muscle atrophy.

Master this section and you'll be able to

- Describe and compare the structural and cellular adaptations that occur in skeletal muscle in response to endurance versus resistance training how resistance exercise builds muscle.
- Distinguish between muscle hypertrophy and atrophy, and sarcopenia and analyze how lifestyle factors and age influence changes in muscle mass and performance.
- Explain how performance-enhancing substances affect muscle.

Muscle Training and Changes in Muscle Size

Physical training can change both the **appearance** of skeletal muscles and their **performance**. With regular exercise, muscles become stronger and often look larger and more defined. On the other hand, lack of activity causes muscles to weaken and shrink. Key terms:

- Muscle **hypertrophy:** growing without new cells.
  When muscles grow, they do not make brand-new muscle cells. Instead, existing muscle fibers add more **structural proteins** (like actin and myosin). This makes each fiber thicker, which increases the overall diameter of the muscle. This growth process is called hypertrophy.

- Muscle **atrophy**: use it or lose it.
  This is the opposite of muscle hypertrophy. In atrophy, **structural proteins inside the muscle fibers are lost, so the fibers get smaller.** This leads to a visible decrease in muscle mass and weaker performance.

- **Sarcopenia**: Age-Related Atrophy
  When atrophy happens as a natural part of aging, it is called **sarcopenia**. This condition often starts slowly but can have big impacts on strength, balance, and independence if not addressed with regular physical activity.

Muscle fibers are highly adaptable. Their **cellular components** (aspecifically mitochondria, enzymes, and protein content) can change in response to how much, and in what way, the muscle is used. For example, endurance training increases mitochondria for better energy production, while resistance training boosts contractile proteins for strength.

Cellular Adaptations to Endurance Training

Slow-twitch oxidative (SO) fibers — also known as **Type 1 fibers** — are the “marathoners” of the muscle world. These muscle cells are not built for heavy lifting, but for long-lasting, repeated contractions. They rely mainly on **aerobic metabolism**, which allows them to keep working without fatiguing quickly.

Regular endurance training enhances stamina rather than bulk and makes the slow-twitch fibers even more efficient:

- **Mitochondria multiply** → more sites for aerobic metabolism, so more ATP can be made.

- **Myoglobin increases** → this oxygen-binding protein, stored in the sarcoplasm, acts like an oxygen reserve tank for mitochondria.

- **Angiogenesis occurs** → new capillaries form around the fibers, improving oxygen delivery and removal of waste.

Because oxygen and nutrients need to diffuse into the fibers, **muscle mass does not increase dramatically** with endurance training. This keeps the diffusion distance short and efficient.

The percentage of SO fibers in a muscle helps determine its role:

- **Postural muscles** (like those in the back) have many SO fibers to keep us upright.
- **Endurance athletes** (such as marathon runners) benefit from a higher proportion of SO fibers.

While endurance training has many benefits, it can also lead to **overuse injuries,** such as stress fractures and tendon and joint inflammation.



Figure 5.12.1: **Elite marathon runners.** Marathon runners and top athletes in other endurance sports, often show muscle biopsies with **up to 80% slow-twitch fibers in key leg muscles** (such as the soleus), compared to a more balanced mix in the general population. Whether this distribution is primarily genetically determined or the result of years of endurance training-induced adaptations remains a debated topic in exercise physiology.

Cellular Adaptations to Strength (Resistance) Training

Resistance exercises, unlike endurance training, rely heavily on **fast-twitch glycolytic (FG)** — also known as **Type 2** — fibers. These muscle cells are designed for short bursts of powerful movements rather than long, repeated activity. Type 2 fibers contract strongly because they hydrolyze ATP rapidly and form many cross-bridges in a short amount of time.

Analogous to the marathon runners containing a much higher proportion of type 1 fibers, muscles specialized for power contain a higher proportion of glycolytic type 2 fibers.

Regular resistance training enhances muscle bulk through hypertrophy. Hypertrophy occurs when **additional myofibrils and sarcomeres are added** to existing fibers, and as a consequence, each **muscle fiber gets thicker.** Unlike endurance training, resistance training usually does **not** increase the number of mitochondria or capillary networks. Instead, it primarily builds **structural proteins** and **connective tissue**. Tendons also strengthen, so they can safely transmit the powerful force produced by muscles to bones.



Figure 5.12.2: **Visible muscle enlargement in Bodybuilder.** Top resistance training athletes generally have a large number of type 2 fibers and relatively few type 1 fibers. Because this muscular enlargement is achieved by the addition of structural proteins, people trying to build muscle mass often ingest large amounts of protein.

Progressive Overload: Why Lifting Gets Harder

For muscles to continue growing, the training load must increase over time — a principle known as **progressive overload**. Lifting the same weight over and over will only maintain existing muscle mass. To stimulate further growth, the load must become heavier, forcing muscles to adapt to the new challenge. This is why strength athletes gradually add weight to their workouts.

Risks of Improper Resistance Training

While resistance training can be highly beneficial, it carries risks if done incorrectly.

- **Overuse injuries** can affect muscles, tendons, or bones.
- Damage often occurs if the load is too heavy, if recovery time is too short, or if joint alignment is poor during exercise.
- At the cellular level, intense training can damage the sarcolemma and myofibrils, contributing to the **soreness** felt after workouts.

Interestingly, this very repair process — where new structural proteins replace damaged ones — leads to stronger, larger muscles over time. However, overtraining without rest can result in tendon injuries or even skeletal damage.

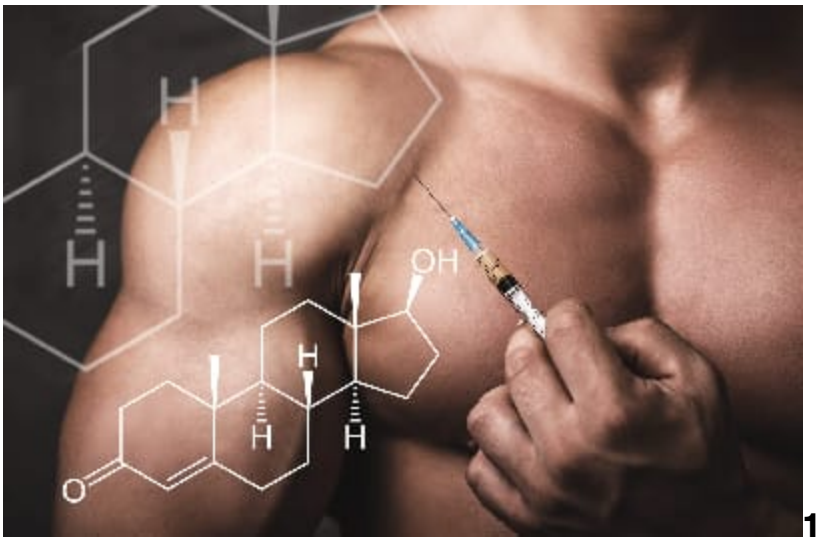
Comparison of Endurance Training and Resistance Training Effects on Skeletal Muscle

Feature	Endurance Training (e.g., marathon running, cycling)	Resistance Training (e.g., weightlifting, sprinting)
Main Fiber Type Used	Slow Oxidative (SO) fibers	Fast Glycolytic (FG) fibers
Contraction Style	Low force, sustained over long periods	High force, short bursts

Feature	Endurance Training (e.g., marathon running, cycling)	Resistance Training (e.g., weightlifting, sprinting)
Energy Pathway	Aerobic metabolism (lots of O_2, many mitochondria)	Anaerobic glycolysis (less O_2, quick ATP use)
Adaptations in Muscle	↑ mitochondria, ↑ myoglobin, ↑ capillaries (angiogenesis)	↑ myofibrils and sarcomeres (hypertrophy)
Effect on Muscle Size	Little change in size (fibers stay lean for oxygen diffusion)	Significant increase in fiber thickness (bulky muscles)
Effect on Connective Tissue	Small changes	↑ connective tissue and tendon strength
Oxygen Storage & Delivery	Improved (more myoglobin + capillary networks)	No major increase
Performance Outcome	Better endurance and fatigue resistance	Greater strength and power
Injury Risks	Usually low (unless extreme overuse)	Higher risk if load is too heavy or technique poor (muscle tears, tendon damage, joint stress)

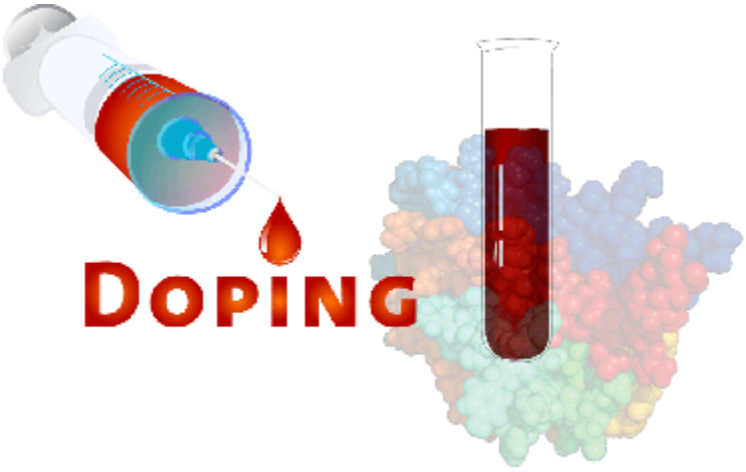
Performance-Enhancing Substances in Sports

Some athletes look for ways to boost their performance beyond what training and nutrition alone can provide. These performance-enhancing substances can affect muscle strength, recovery, and endurance, but they also carry major risks.



1) Anabolic Steroids: Muscle Builders

- **What they are**: Synthetic forms of testosterone, the primary male sex hormone.
- **How they work**: Stimulate muscle protein synthesis, leading to bigger and stronger muscles.
- **Why athletes use them**: To increase muscle mass and power output.
- **Risks**: Infertility, aggressive behavior (“roid rage”), cardiovascular disease, and even brain cancer. Many side effects are irreversible.



2) Erythropoietin (EPO): The Oxygen Booster

- **What it is**: A hormone normally produced by the kidneys that increases red blood cell production.
- **How it helps**: More red blood cells = more oxygen carried to working muscles = more aerobic respiration.
- **Why endurance athletes use it**: To delay fatigue and improve stamina in sports like cycling and distance running.
- **Risks**: Thickened blood, which increases the risk of dangerous blood clots, strokes, or heart attacks.



3) Human Growth Hormone (hGH): The Recovery Aid

- **What it is**: A hormone naturally made by the pituitary gland that promotes growth and tissue repair.
- **How athletes misuse it**: To speed up healing of muscle and connective tissues after intense training, so they can return to competition faster.
- **Risks**: Abnormal bone growth, joint pain, swelling, and increased risk of certain cancers.



4) Creatine: The Legal Edge?

- **What it is**: A compound stored in muscles as creatine phosphate, used to quickly regenerate ATP in the first seconds of contraction.
- **How it may help**: Provides a quick energy boost for short, explosive activities like sprinting or weightlifting.
- **Controversy**: Some studies suggest modest benefits, while others find little to no effect.
- **Risks**: Generally considered safer than steroids or hormones, but high doses may stress the kidneys.

The Bigger Picture: Ethics and Safety

- Most of these substances are **banned in competitive sports** because they give an unfair advantage. Using them without medical supervision is **illegal** and can cause **serious, sometimes permanent health damage**. The bottom line: training, nutrition, and rest remain the safest and most effective ways to improve performance.

Everyday Connection

Aging and Muscle Tissue

Sarcopenia (muscle atrophy with age) is inevitable and the primary reason why even highly trained athletes succumb to declining performance with age. This decline is especially noticeable in athletes whose sports require strength and powerful movements, such as sprinting, whereas the effects of age are less noticeable in endurance athletes such as marathon runners or long-distance cyclists.

The decline in muscle mass is significantly accelerated through a sedentary lifestyle and causes a loss of strength, including the strength required for posture and mobility.

The good news is that sarcopenia can be significantly slowed, halted, and, in many aspects, reversed through lifestyle interventions:

- **Physical activity is the most effective treatment.** Progressive resistance training, which includes lifting weights, using resistance bands, or doing bodyweight exercises, has been shown to increase muscle mass and strength in older adults. Multimodal exercise programs that combine resistance, aerobic, and balance training are especially effective.
- **A protein-rich diet supports muscle growth.** Experts recommend that older adults, especially those with sarcopenia, increase their daily protein intake. The goal is to provide the body with the amino acids needed to build and repair muscle tissue, particularly when combined with strength training.

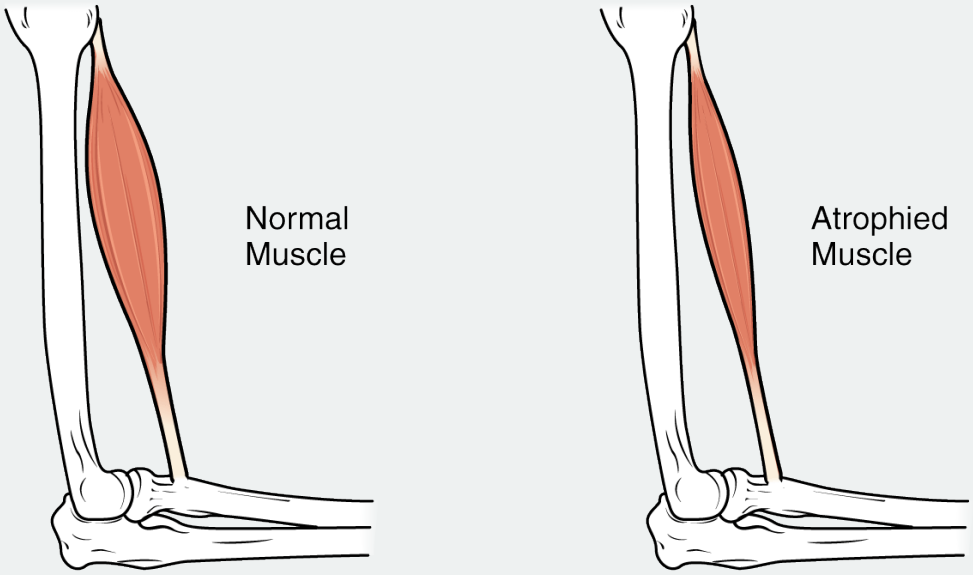


Figure 5.12.3: **Muscle Atrophy.** Muscle mass is reduced with disuse!

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6: NERVOUS SYSTEM

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6.1: Functions of the Nervous System

The primary function of the nervous system is to coordinate and control the various body functions.

Master this sectdion and you'll be able to

- Distinguish the major functions of the nervous system: sensation, integration, and response
- List the sequence of events in a simple sensory receptor–motor response pathway

The **nervous system** is the organ system that coordinates the activities of muscles, monitors organs, constructs and processes data received from the senses, and initiates both voluntary and involuntary actions. Let's break it down with a real-life scenario:

Testing the Shower Water: A Nervous System Story

Imagine this: it is early morning, and you stumble toward the shower, still half-asleep. You expect the water to be warm and cozy. You stick your hand into the spray... but wait — is it too hot? too cold? just right?

What happens next is a lightning-fast conversation inside your body. Your **nervous system** goes into action, linking your skin, spinal cord, brain, and muscles in one continuous relay.

Step 1: Detecting the Stimulus

In your skin are **thermoreceptors** — tiny sensors that act like "temperature detectives." When hot (or cold) water hits your skin, their cell membranes change voltage. If the stimulus is strong enough, the receptor fires an **action potential** — an electrical signal that zips up the sensory neuron.

Think of this as the moment when the *"ouch!"* message starts its journey.

Step 2: Passing the Message Along

The sensory neuron's axon carries that action potential into the **spinal cord**, where it passes the signal across a **synapse** (with the help of neurotransmitters) to another neuron.

From here, the message keeps traveling — like a baton in a relay race — eventually reaching the **thalamus** (the brain's relay station) and then the **cerebral cortex**, where you consciously register: *"Whoa — that water is HOT!"*

Step 3: Deciding What To Do

Your **cerebral cortex** is now buzzing. It integrates this sensory input with your memories ("Last time I got burned, it was not fun"), your emotions ("I'm too tired for surprises"), and your current goals ("I just want a comfy shower before class").

The result? A decision: **turn down the faucet.**

Step 4: Sending Out the Command

To make that decision a reality, your brain activates an **upper motor neuron** in the frontal cortex. That neuron sends an action potential all the way down to the spinal cord, where it talks to a **lower motor neuron**.

The lower motor neuron sends the final signal down your arm, ending at the **neuromuscular junction** with your hand muscles. Remember this from the last module? There, acetylcholine is released, your muscle fibers contract, and — presto — your hand twists the faucet knob.

All of this happens in fractions of a second, faster than you can say “too hot!”

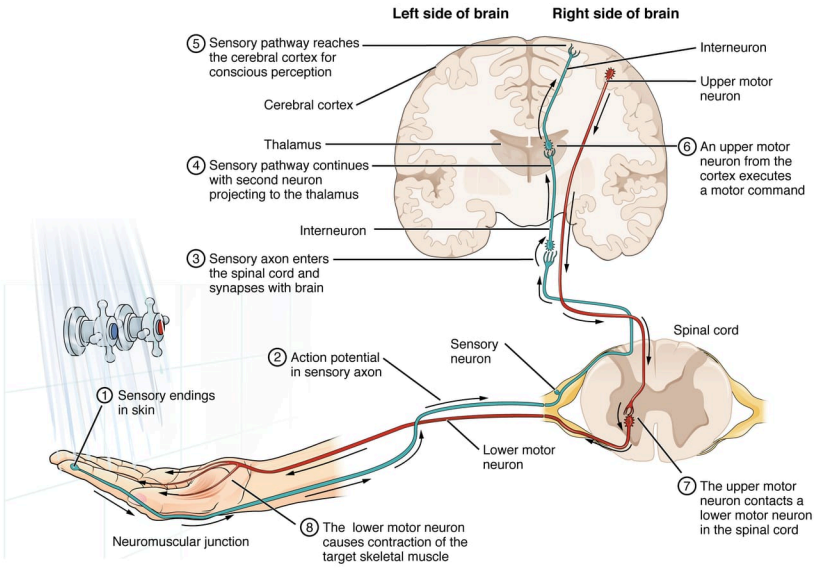


Figure 6.1.1: **Testing the Water.**
This diagram traces the full “conversation” between your finger and your brain when you test shower water:

1. **Sensory Neuron Begins the Story** – Specialized endings in the skin detect the stimulus (like water temperature). The stronger the stimulus, the stronger the signal that starts here.
2. **First Spark** – If that local graded potential is strong enough, it launches an **action potential** at the initial segment of the axon, right near the sensory endings in the skin.
3. **Message to the Spinal Cord** – The axon of the sensory neuron enters the spinal cord and communicates with another neuron at a **synapse**. Neurotransmitters are released here, creating another graded potential.
4. **Upward Journey** – An action potential now travels up the sensory pathway to the **thalamus** in the brain. Another synapse passes the message along.
5. **Final Destination: Conscious Awareness** – The signal reaches the **cerebral cortex**, where you consciously recognize “Ahh... that water is hot (or cold)!”
6. **Decision Time** – After integrating information from other parts of the cortex, a **motor command** is issued from the **precentral gyrus** of the frontal lobe.
7. **Upper Motor Neuron Acts** – The upper motor neuron sends an action potential down to the spinal cord, targeting a lower motor neuron in the gray matter.
8. **Muscle Responds** – The axon of the **lower motor neuron** leaves the spinal cord and connects to a muscle at the **neuromuscular junction**. Neurotransmitter release triggers contraction, allowing you to pull your hand away (or keep it there if the water feels just right).

Big Picture

This little morning routine shows the **complete pathway of nervous system function**:

Sensory Input

Thermoreceptors detect the hot water.
Sensory input comes from the many sensory receptors that monitor changes occurring both inside and outside the body. The **total sum of the information gathered** by these receptors is called sensory input. The nervous system processes and interprets sensory input and decides what actions should be taken. The nervous system activates **effector organs such as muscles and glands** to cause a response called motor output.

Integration

Brain processes the message and decides on a response.
At a more integrative level, the primary function of the nervous system is to control and communicate information throughout the body. It does this by extracting information from the environment using sensory receptors. This sensory input is sent to the central nervous system, which determines an appropriate response.

Motor Response

Muscles contract to turn the dial.
Once the response is activated, the nervous system sends signals via motor output to muscles or glands to initiate the response.

In humans, the sophistication of the nervous system allows for language, abstract representation of concepts, transmission of culture, and many other features of society that would not otherwise exist.

Every action you take — from sipping coffee to sprinting across campus — uses the same basic loop.

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6.2: Organization of the Nervous System

The nervous system is a network of cells called neurons that coordinate actions and transmit signals between different parts of the body.

Master this section and you'll be able to

- Describe the basic structure and function of a neuron.
- Differentiate between the structural (CNS vs. PNS) and functional (somatic, autonomic, and visceral) divisions of the nervous system.

Neurons: Meet The Workers of the Nervous System

This is just a very brief introduction to the real "workers" of the nervous system: **neurons**. We will come back to them in more detail soon.

Neurons are specialized cells are the basic building blocks of communication. Each neuron:

- Sends electrical signals along long, thin extensions called **axons**.
- Passes messages at the ends of axons by releasing **neurotransmitters** (chemical messengers).
- Communicates across tiny junctions called **synapses**, forming connections with other neurons, muscles, or glands.

This design allows information to travel rapidly through the body, coordinating everything from simple reflexes to complex thoughts.

Now, if neurons are the workers, then the divisions of the nervous system are like the **departments they work in**. The nervous system (NS) can be divided in two main ways:

- **By anatomy (structure):** into the **central nervous system** (CNS) and the **peripheral nervous system** (PNS).
- **By physiology (function):** into the **somatic nervous system** (voluntary control) and the **autonomic nervous system** (involuntary control).

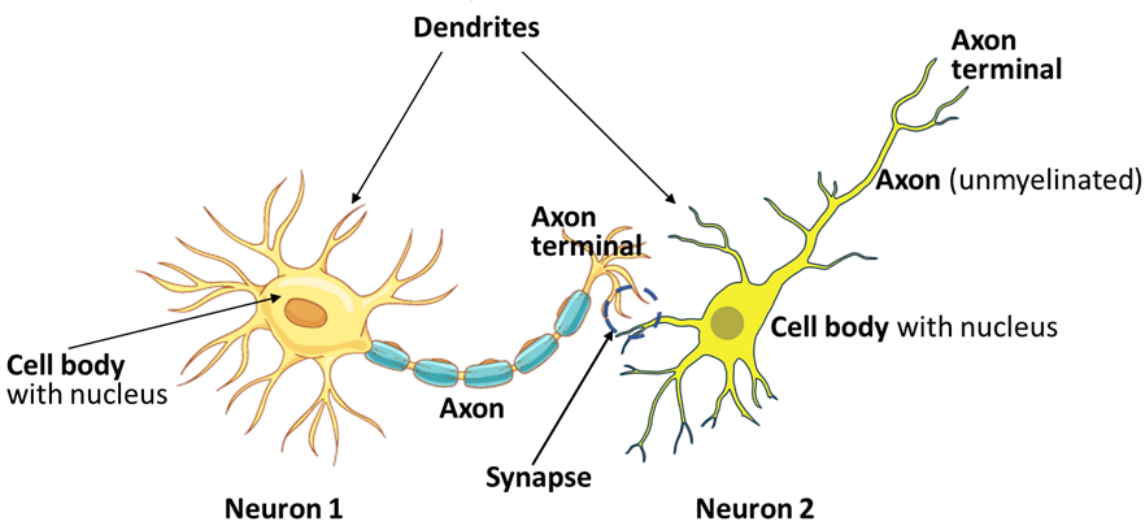


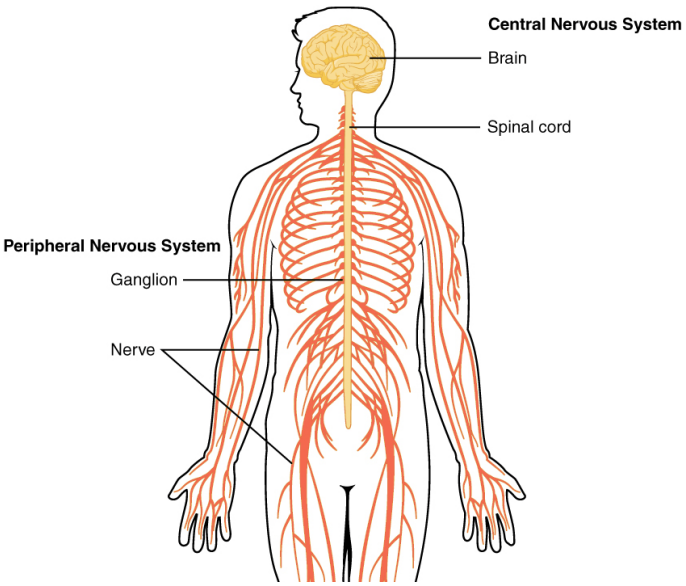
Figure 6.2.1: **Basic Neuron Anatomy.** Diagram showing two neurons connected with a synapse between the axon terminals of

neuron 1 and the dendrites of neuron 2.

Structural Organization of the Nervous System (NS)

Anatomically, the nervous system is divided into **CNS** and **PNS:**

1) Central Nervous System (CNS)



Think of the CNS as the **command center** of your body, safely housed inside protective headquarters:

- The **brain** sits inside the cranial cavity of the skull.
- The **spinal cord** runs through the vertebral canal of the vertebral column.

Together, the brain and spinal cord act as the **control hub** that interprets incoming information and sends out instructions to the rest of the body.

Organization Inside the CNS

Inside the CNS, neurons and their axons are organized in special ways:

- **Neuron cell bodies** group together to form **nuclei, cortexes, or horns**.
- **Bundles of axons** form **tracts** (also called **columns**).

These arrangements help keep the CNS efficient—like neatly organized wiring inside a control panel.

2) Peripheral Nervous System (PNS)

The PNS is like the *"network of messengers"* spreading out across the body. It includes **nerves** (bundles of axons) and **ganglia** (clusters of neuron cell bodies).

It is called “peripheral” because it extends beyond the brain and spinal cord into the rest of the body.

- Neuron cell bodies in the PNS form **ganglia** (singular: ganglion).
- Bundles of axons in the PNS are called **nerves**.

Nerves vs. Tracts: Same Wiring, Different Labels

Here is where it can get tricky. The same **bundle of axons** may be given two different names depending on its location:

- Outside the CNS as part of the **peripheral NS** → called a **nerve**
- **Inside the CNS** → bundles or axons are called a **tract**

Example: Axons leaving the retina are called the **optic nerve**. Once those same axons enter the brain, they are renamed the **optic tract**.

Functional Organization of the Nervous System

Two Ways to Think About Function

1. **Basic Functions**: sensation, integration, and response.
2. **Control of the Body: somatic** (voluntary control of skeletal muscles), **autonomic** (involuntary regulation of smooth muscle, cardiac muscle and glands), or **visceral ,** (sensory input from the internal organs, often processed through autonomic pathways).

1) Basic Functions of the Nervous System

Sensation

The nervous system begins its work by **gathering information through specialized sensory receptors** located throughout the body. These receptors are highly tuned structures that detect specific kinds of stimuli. The signals they pick up can come from **outside the body**, a process called *exteroception*. Examples include receptors in the eyes that detect light, in the skin that sense touch, temperature, and pressure, and in the ears that respond to sound and balance.

The system also monitors **internal conditions** through *interoceptors* and *proprioceptors*. Interoceptors track things like blood pressure, pH, oxygen levels, or the feeling of a full stomach, giving the brain constant updates about the body’s internal environment. Proprioceptors, located in muscles and joints, provide information about body position and movement, allowing for coordination and balance.

Once this information is detected, it is converted into **electrical signals (nerve impulses)** and transmitted along sensory neurons toward the central nervous system (CNS). From there, the brain and spinal cord interpret the incoming data, integrate it with past experiences and current needs, and decide how the body should respond.

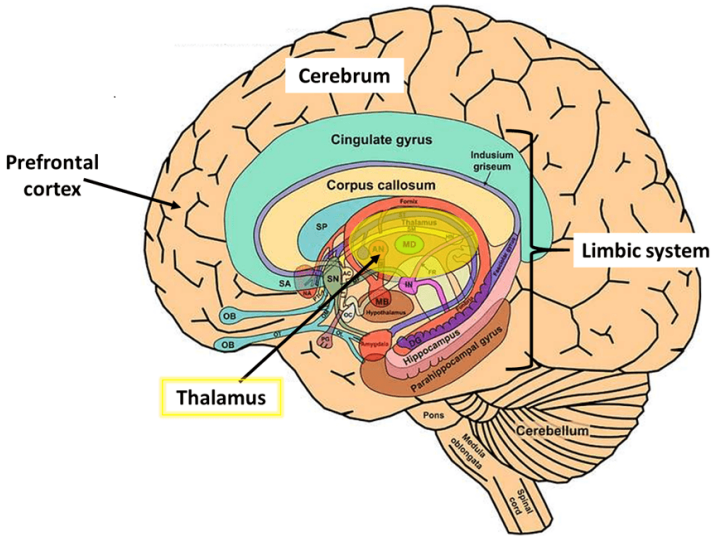
- **Special senses**: taste, smell, vision, hearing, balance. These rely on specialized organs.
- **General senses**: touch, pain, and temperature, found throughout the body.
- **Visceral senses**: unconscious sensations, such as the stretch of your bladder or the concentration of ions in your blood.

Sensory signals always move **toward the CNS**. This pathway is called **afferent** (think: *arrive*).

Integration

Once sensory signals reach the **central nervous system (CNS)**, the information takes different routes depending on how urgent and complex the situation is.

- **The spinal cord** acts as a rapid-response center for immediate, survival-related actions. It can process signals without needing to wait for the brain's input, producing what we call **reflexes**. For example, if you touch a hot surface, the spinal cord can instantly send a command to pull your hand back *before* the brain fully processes the pain. This "shortcut" reflex pathway protects the body by minimizing reaction time.



- **The brain**, on the other hand, handles more detailed and complex processing. Signals relayed upward from the spinal cord are sent to brain specialized regions:
    - The **thalamus** acts as a relay station, directing sensory input to the appropriate brain regions.
    - The **cerebral cortex** processes and interprets the details — such as identifying *what* the stimulus is and *what it means*.
    - The **limbic system** adds emotional weight, connecting incoming information with feelings of fear, pleasure, or comfort.
    - The **prefrontal cortex** takes this integrated information and evaluates it in the context of memory and current goals, supporting decision-making and planning.

In this way, the CNS operates like a highly efficient team: the spinal cord ensures that the body can react in fractions of a second to protect itself, while the brain provides more thoughtful, context-driven responses that shape behavior, choices, and long-term learning.

Example: You hear your phone ring. The **spinal cord** quickly orients your head toward the sound. The **brain** recognizes it as your phone, adds importance (maybe excitement or urgency), and helps you decide whether to answer. In summary: The spinal cord gives the fast, automatic response, while the brain makes sense of the situation and guides your choice.

Response

Finally, after gathering information and processing it, the **nervous system sends commands from the CNS back out to the body**. This stage relies on **motor neurons**, which carry instructions from the brain or spinal cord to muscles, glands, or organs.

- If the response is **movement**, motor neurons signal skeletal muscles to contract — like pulling your hand away from something hot, swinging a baseball bat, or simply smiling at a friend.
- If the response is more **automatic or internal**, signals may go to smooth muscles or glands, adjusting things you don't consciously control — such as slowing your heart rate, releasing digestive enzymes, or dilating your pupils in dim light.

This output stage ensures that the body doesn't just *sense and interpret* the world — it can also **act on that information**. In other words, the nervous system forms a complete loop: **receptors gather input, the CNS processes it, and motor pathways carry out the response.**

These signals travel **away from the CNS**. This pathway is called **efferent** (think: *exit*).

💡 Memory tip: **SAME** = Sensory Afferent, Motor Efferent.

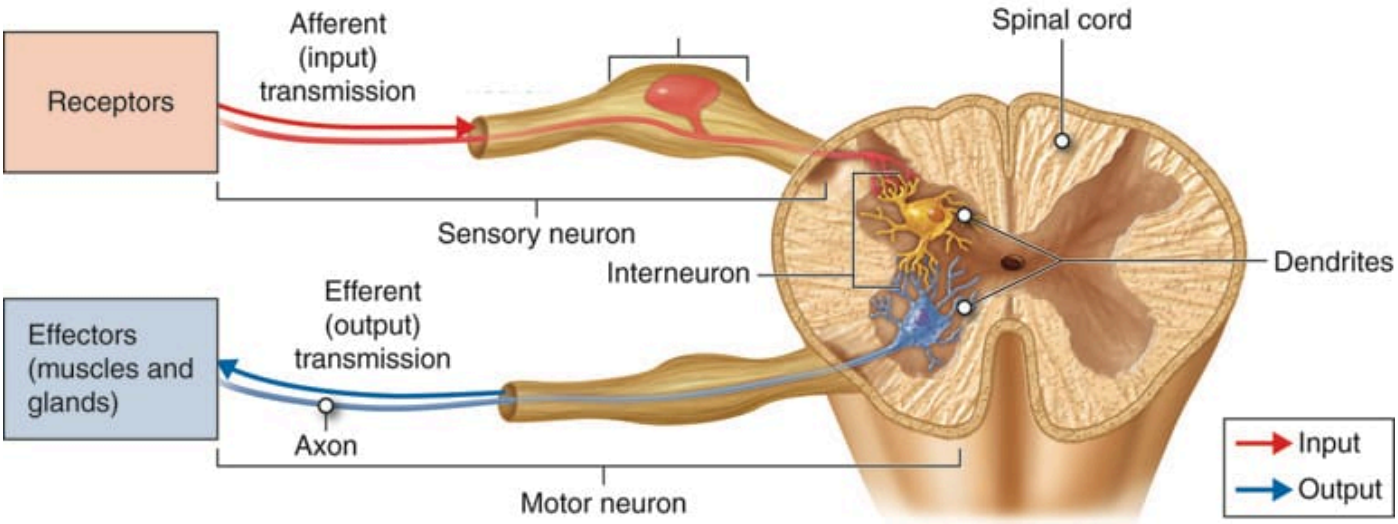


Figure 6.2.2: **Basic Functions of the Nervous System.** Sensory information travels along an afferent pathway toward the central nervous system while motor commands travel along an efferent pathway away from the central nervous system. Integration occurs at the interneurons within the spinal cord. *(Image credit: This work by Cenveo is licensed under CC BY 3.0).*

2) Controlling the Body: Somatic vs. Autonomic vs. Visceral

Think of your body like a car with **two ways to drive it**. The **somatic nervous system** is like *you at the wheel* — you control the steering, brakes, and gas. It handles your **voluntary actions** such as walking, talking, or swinging a bat, as well as quick reflexes like jumping when startled.

The **autonomic (visceral) nervous system** is like the car's **autopilot**. You don't consciously control it, but it keeps all the vital systems running smoothly in the background. It adjusts your heartbeat, breathing, digestion, and helps maintain balance inside your body. It even reacts to your emotions — for example, that "butterflies in your stomach" feeling when you're nervous.

Somatic Nervous System (SNS)

- Handles **conscious sensations** and **voluntary motor control**.
- Controls skeletal muscles.
- Includes **reflexes** (like jumping when startled).
- Includes **learned automatic behaviors** (like walking, chewing, or riding a bike).

Autonomic Nervous System (ANS)

- Handles **involuntary control** of **smooth muscle**, **cardiac muscle**, and **glands**.
- Regulates internal organ functions to maintain **homeostasis** (for example, sweating when hot).
- Can also respond to emotions (for example, sweating when nervous).

Visceral Nervous System (VNS)

- Refers to the **sensory input** that comes **from the internal organs** (the viscera), such as stretch, pressure, or pain.
- Signals travel to the CNS and are often processed through autonomic pathways to trigger the appropriate involuntary responses.

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6.3: Nervous Tissue - The Wiring of the Body

Nervous tissue is a specialized, excitable tissue made of neurons and neuroglia that rapidly communicates information through electrical and chemical signals.

Master this section and you'll be able to

- Identify the classes of cells that make up nervous tissue.
- Describe the structure and function of neurons.
- Compare the major types of neuroglial cells in the central and peripheral nervous systems, explaining their supportive functions and contributions to neural communication.

Nervous tissue is one of four major classes of tissues. It is highly specialized because it is **excitable**, meaning it can respond quickly to changes and send or receive **electrochemical signals** that provide the body with information. This tissue is made up of two main types of cells: **neurons** and **neuroglia.**

- **Neurons** are the signal carriers. They send information as tiny electrical impulses called **action potentials**, which then trigger the release of chemical messengers, so called **neurotransmitters**.
- **Neuroglia** are the support team. They **protect**, **nourish**, and **assist** neurons, helping regulate how signals are sent and processed. A typical neuron consists of a cell body, many dendrites, and an axon.

Together, these two cell types form the communication network that allows your body to sense, think, and respond.

Neurons: The Conductors of Information

Neurons have a very distinctive shape that matches their job: carrying messages quickly across the body. Although they vary in exact shape, each neuron has three main parts:

- **Cell body (soma):** Holds most of the cytoplasm, the organelles, and the nucleus.
- **Dendrites:** Thin, branching extensions that receive incoming signals and are responsible for responding to stimuli.
- **Axon:** A long “tail” that carries signals away from the cell body. Many axons are wrapped in **myelin**, an insulating layer made by helper cells.

At the end of an axon is the **synapse**, a tiny gap where a neuron communicates with the next cell — whether another neuron, a muscle, or a gland — using chemical messengers called **neurotransmitters**.

When a neuron is stimulated strongly enough, it fires an **action potential** (an electrical impulse). This impulse races down the axon to the synapse, where neurotransmitters are released to pass the message on.

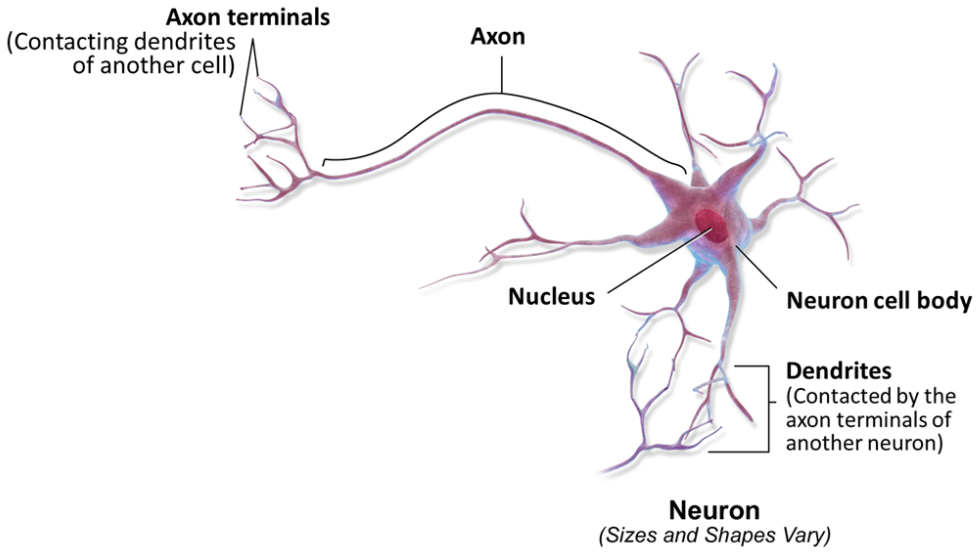


Figure 6.3.1: **Neuron Structure.** The large central region is the **cell body.** It contains the **nucleus**. Branching off the cell body are several short **dendrites**, which **receive signals** from other neurons. Extending from the cell body is a long **axon**, which carries signals away. At the far end, the axon splits into multiple **axon terminals**, which contact the dendrites of another cell to pass the signal along.

Neuroglia: The "Support Crew"

The second group of nervous system cells are the **neuroglia** (or **glial cells**). Traditionally described as "support" cells — the name *glia* even comes from the Greek for "glue" — they are now known to play far more complex roles in brain and nerve function.

Think of glial cells like a big team with many specialized players. We will not meet every single member of the team, and you only need to know the key players described below:

Glial Cells of the CNS

- **Astrocytes:** These star-shaped cells of the **CNS** have many radiating processes that allow them to cling to neurons and nearby capillaries. They support and brace neurons, anchoring them to their nutrient supply lines. Astrocytes also guide the migration of young neurons during development. In addition, they help maintain the chemical environment around neurons by regulating ion levels, recycling certain neurotransmitters, and contributing to the **blood–brain barrier** — a protective wall that separates the brain's delicate tissue from the bloodstream.

- **Microglia:** As the name implies, microglia are smaller than most of the other glial cells. They are the resident immune cells, acting as the "security guards" of the CNS. Like macrophages in the rest of the body, microglia patrol their territory, looking out for trouble. When they detect damaged or diseased cells — or invading pathogens — they step in, engulf the problem, and break it down.

- **Oligodendrocytes:** Also found in CNS tissue, their name literally means "cell with a few branches" (oligo = few, dendro = branches, cyte = cell). From its cell body, a few processes extend outward like little arms. Each of these arms can wrap around part of an axon of a neuron nearby, creating an insulating covering called **myelin**. A single oligodendrocyte can insulate multiple axon segments — sometimes on the same axon, sometimes on different ones.

  (What myelin specifically does for neurons is coming up soon — spoiler: it makes signals travel a whole lot faster.)

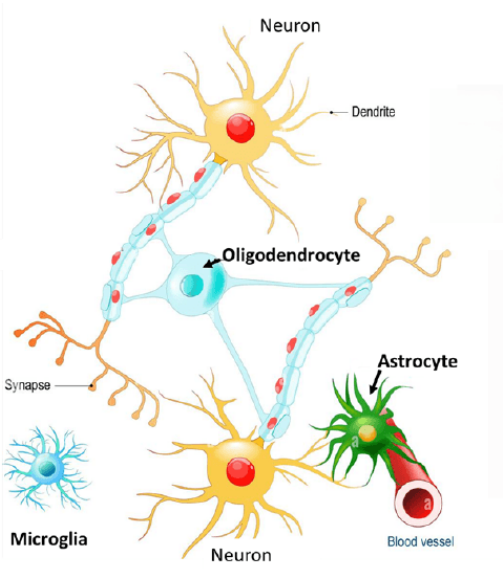


Figure 6.3.2: **Neurons and major glial cell types in the CNS.** The diagram shows two neurons whose axons are being wrapped in myelin by an oligodendrocyte. An astrocyte is attached to a nearby blood vessel, connecting and helping support the neuron by regulating the environment, while a microglial cell stands ready to respond to any threats or damage.

Glial Cells of the PNS

- **Schwann cell:** The glial cell in the periphery, which provides myelin insulation for axons outside the brain and spinal cord. Unlike oligodendrocytes, which can send out several processes to wrap around parts of many axons, each Schwann cell focuses on just **one axon segment**. Many Schwann cells are needed to cover a single axon, and each one completely wraps itself around the section it covers. In other words, an oligodendrocyte multitasks, while a Schwann cell commits fully to insulating a single section of a single axon.

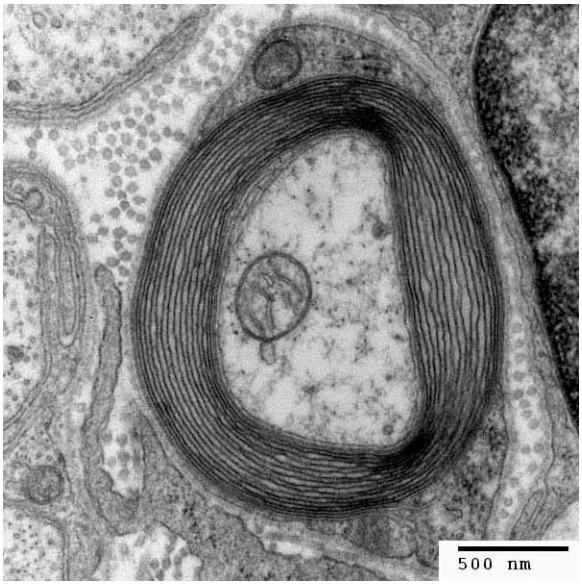


Figure 6.3.3: **Axon Cross Section showing Schwann Cells and the Myelin Sheath**: Transmission electron micrograph of a myelinated axon. The myelin layer (concentric) surrounds the axon of a neuron, showing Schwann cells.

Key Terms

- **Nervous tissue:** One of four major classes of tissues.The principal constituent of the CNS and PNS, comprised of neurons

and neuroglia cells.

- **Myelin**: A substance produced by cells of the neuroglia that increases the speed of impulses along the axon of the neuronal fiber.
- **Neurons:** Highly specialized nerve cells that generate and conduct nerve impulses.
- **Neuroglia:** Supporting cells that provide physical support, remove debris, and provide electrical insulation.

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6.4: Structural and Functional Diversity of Neurons

A number of neuron types have evolved to participate in different organismal functions.

Master this section and you'll be able to

- Identify and describe the major structural components of a neuron and explain how each contributes to information flow.
- Differentiate between structural and functional classifications of neurons and provide examples of each.

Neurons: The Fast-Track Messengers of the Body

As you already learned, neurons are electrically excitable cells and serve as the basic structural and functional unit of the nervous system. They act like the “wiring” that allows signals to move rapidly through the body.

Structural Classification of Neurons

The human nervous system is made up of **trillions of neurons**, and they don’t all look the same. Some are short, some are long, some branch like trees, and others are very simple. To make sense of this variety, scientists classify neurons in different ways — by their job (function), the chemical messengers they use, or even who discovered them. But one of the most basic and useful ways is by their **shape**.

Shape classification usually depends on the **number of processes (branches)** that extend from the **cell body**:

- The **axon** is the sending branch (it carries messages *away* from the cell body).
- The **dendrites** are the receiving branches (they bring signals *into* the neuron).

So, when we talk about the “shape” of a neuron, what we are really describing is its **polarity** — how many dendrites and axons it has and how they stick out from the soma (cell body).

1. Unipolar Neurons (*Pseudo-unipolar* in Humans)

- They look like they only have **one single process** coming off the cell body. But that process quickly splits into **two branches**:
    - One end has dendrites and goes ot to the **sensory receptors** that receive sensory input — like touch, pain, and temperature from the skin.
    - The other end forms synapses inside the CNS where the information is processed.
- The cell body itself does not sit inside the CNS, but rather in a little cluster of neuron cell bodies — called a **ganglion** — in the peripheral nervous system.
- They are **sensory neurons**, meaning they carry information from the body *to* the CNS.

2. Bipolar Neurons

- Have **two processes**, one axon and one dendrite, sticking out in *opposite* sides of the cell body. That’s it — a very simple and symmetrical structure.

- These are **rare** and designed to relay very specific types of sensory information. You can find them in the **retina** of your eye (vision), and in the **olfactory epithelium** of your nose (smell).

3. Multipolar Neurons

- Have **many dendrites** and **one axon**. They are the classic "tree-shaped" neurons you usually see in diagrams.
- They are by far the **most common type** of neuron in the human nervous system. They make up the majority of **motor neurons** (sending commands to muscles) and **interneurons** (processing and passing information between neurons inside the CNS).
- Because they have lots of dendrites, they can receive inputs from many different places at the same time. This is great for integrating information.

There are also **anaxonic neurons**, which are small neurons. Even though they have many processes coming out of the cell body, all processes look and behave similarly. They may not have an axon at all, or the axon cannot be distinguished from the dendrites. Because of this, they are classified as a separate type, not as multipolar. Anaxonic neurons usually participate in local circuit integration, especially in regions like the retina and olfactory bulb."

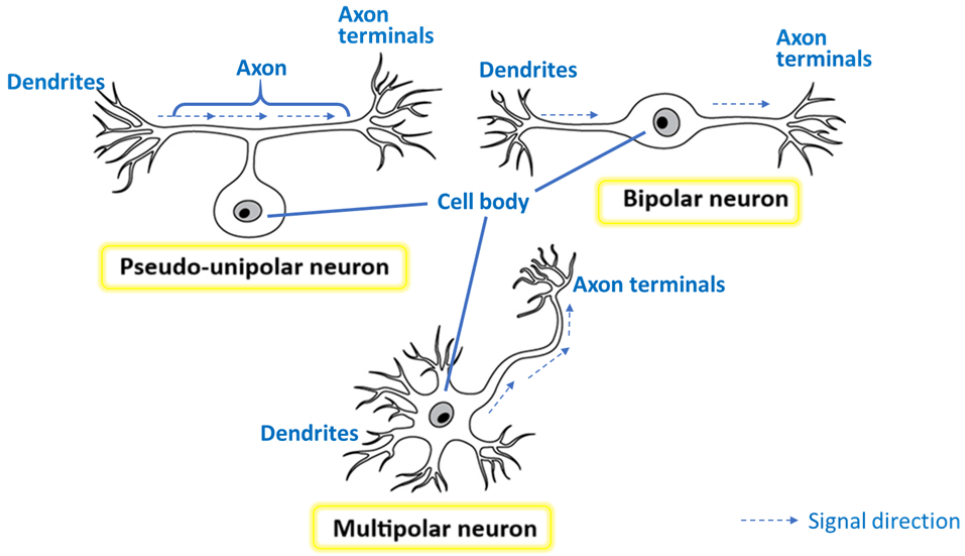


Figure 6.4.2: **Neuron Classification by Shape.** Neurons can be classified by the number of processes extending from the cell body. A **pseudo-unipolar neuron** has a single process that branches into two extensions and is typically found in sensory pathways. A **bipolar neuron** has one dendrite and one axon and is common in sensory organs such as the retina. A **multipolar neuron** has multiple dendrites and one axon, making it the most common type in the central nervous system, including motor neurons.

👉 Tip: When trying to remember these categories, think about the "number of roads" leading away from the cell body:

- **Uni = 1 process** (but it quickly splits into two).
- **Bi = 2 processes**.
- **Multi = many processes**.

Functional Classification of Neurons

Neurons are often grouped by the direction the action potential (*i.e.* information) travels relative to the CNS. Think of the neurons as the messengers that either bring news in, send orders out, or relay messages within.

The three classes are:

1. Afferent (Sensory) Neurons

- **Direction:** Afferent neurons carry information *into* the CNS from sensory receptors in tissues and organs.
- **Function:** These neurons alert the CNS about any changes in the **internal and external environment**, such as touch, temperature, pain, light, sound, and other stimuli.
- **Example:** If a person touches a hot object, afferent neurons transmit the signal to the brain or spinal cord for processing.
- **Correlation to Structure:** Most afferent neurons are structurally pseudounipolar.

2. Efferent (Motor) Neurons

- **Direction:** Transmit commands *out of* the CNS to **effectors** in the body — primarily **muscles and glands**, allowing us to move and react.
- **Function:** These neurons implement responses ordered by the CNS, such as making a muscle contract or a gland secrete.
- **Example:** When a person retracts their hand from something hot, it's the efferent neurons telling the appropriate muscles to move.
- **Correlation to Structure:** Most efferent neurons are structurally multipolar.

3. Interneurons (Association Neurons)

- **Direction:** Connect neurons to each other entirely within the CNS; they do not leave the brain or spinal cord.
- **Function:** These neurons act as the "**go-betweens**", connecting neurons to each other within specific regions of the CNS. They are the integrators — processing information, coordinating activity between afferent and efferent neurons, and playing a key role in reflexes, learning, and decision-making.
- **Location and correlation to structure:** They are the most numerous type and are found only in the CNS. Interneurons are usually multipolar as well, but there is structural diversity.

Although individual neurons have specialized tasks, together they form the vast communication network that makes thought, sensation, movement, and homeostasis possible.

👉 *Mnemonic Tip:* ***Afferent** = **Arrive** at the CNS // **Efferent** = **Exit** the CNS.*

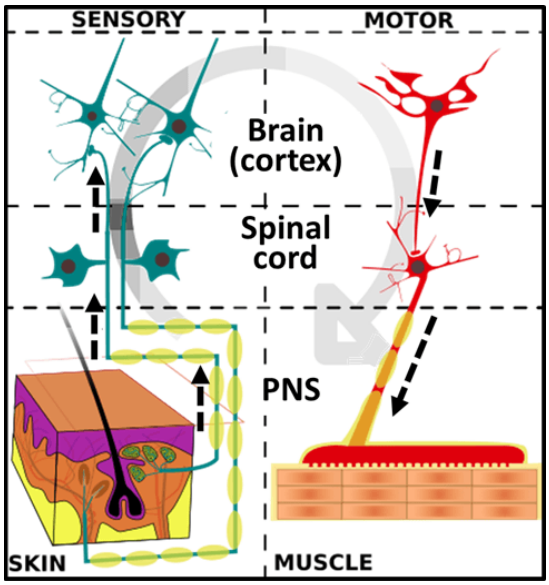


Figure 6.4.3: **Neuron Classification by Function.** Diagram illustrates how the nervous system coordinates sensory and motor neurons. Sensory receptors in the skin detect a stimulus and send signals via afferent neuron in the PNS) to the **spinal cord** and **brain (cortex)** for processing. The brain sends a command through efferent motor neurons to the muscles. The effector muscle then contracts, producing a response.

Other Naming Systems

In addition to structural and functional classification systems, neurons can also be named in other ways:

- **Location:** Where they are found. For example **hippocampal neurons** – located in the **hippocampus**, a brain region important for memory and learning.
- **Discoverer's name:** A famous example are the **Purkinje cells** (multipolar neurons in the cerebellum). They were named after Jan Evangelista Purkinje, a 19th century anatomist. These cells are famous for their elaborate, tree-like dendritic networks.
- **Neurochemistry:** Neurons can be classified based on the **neurotransmitter** (chemical messenger) they release to send signals. Examples are
    - **cholinergic neurons** — releasing **acetylcholine.** Cholinergic neurons are important for muscle contraction and autonomic nervous system functions.
    - **Adrenergic neurons** — releasing **adrenaline** (aka norepinephrine). Adrenergic neurons are important for activating the "fight-or-flight" response, increasing heart rate, blood pressure, and alertness during stress or emergency situations.
    - **Dopaminergic neurons** — releasing **dopamine.** Dopaminergic neurons are involved in reward, motivation, and motor control.

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6.5: Signal Speed — How Myelin Turns Nerves into Racetracks

Myelin insulates axons so nerve signals can jump between nodes, dramatically increasing conduction speed.

Master this section and you'll will be able to

- **Describe** the structure and function of myelin, including its lipid-rich composition, and explain how it increases the speed of nerve impulse conduction.
- **Differentiate** between myelination in the CNS and in the PNS, noting how each glial cell type contributes to axon insulation.
- **Explain** the process of saltatory conduction and how nodes of Ranvier enable rapid and efficient transmission of action potentials.
- **Compare** the regenerative capacity of axons in the PNS versus the CNS.

What is Myelin?

Think of the axons of your neurons as long electrical wires. If you have ever seen an extension cord, you know it works best when it is wrapped in thick plastic insulation so the electricity does not leak out. Myelin is the body's version of that insulation tape!

Here is the fun twist: unlike most cell membranes, which are like delicate soap bubbles made of phospholipid bilayers, myelin is **supercharged with cholesterol and other lipids**. This makes it tough, stable, and perfect for wrapping around axons in layer after layer — like rolling on electrical tape.

The result? Myelin keeps signals racing down neurons at lightning speed without short-circuiting.

Saltatory Conduction

Not all neurons are equally fast. Some send signals quickly, while others are slower. Speed matters — from an evolutionary point of view, when a lion is chasing you, you want those fast neurons firing so you can think fast and outsmart the predator!

The secret to speed lies in the **myelin sheath**, the covering made by special glial cells:

- **Oligodendrocytes in the central nervous system (CNS).**

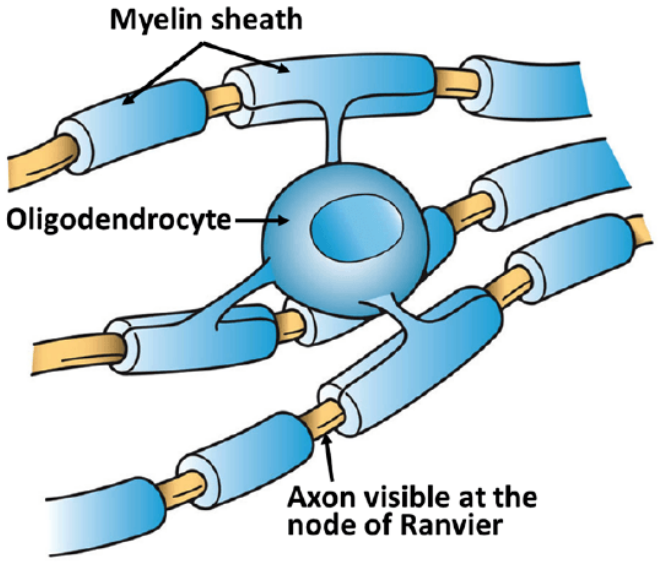


Figure 6.5.1: **Myelination by an Oligodendrocyte in the CNS.** An oligodendrocyte extends multiple processes that wrap around different axons to form myelin sheaths. A single **oligodendrocyte** can extend its processes to wrap around **30–50 different axons** (depending on axon diameter and location). Each process forms one segment of myelin on one axon.

- **Schwann cells in the peripheral nervous system (PNS)**

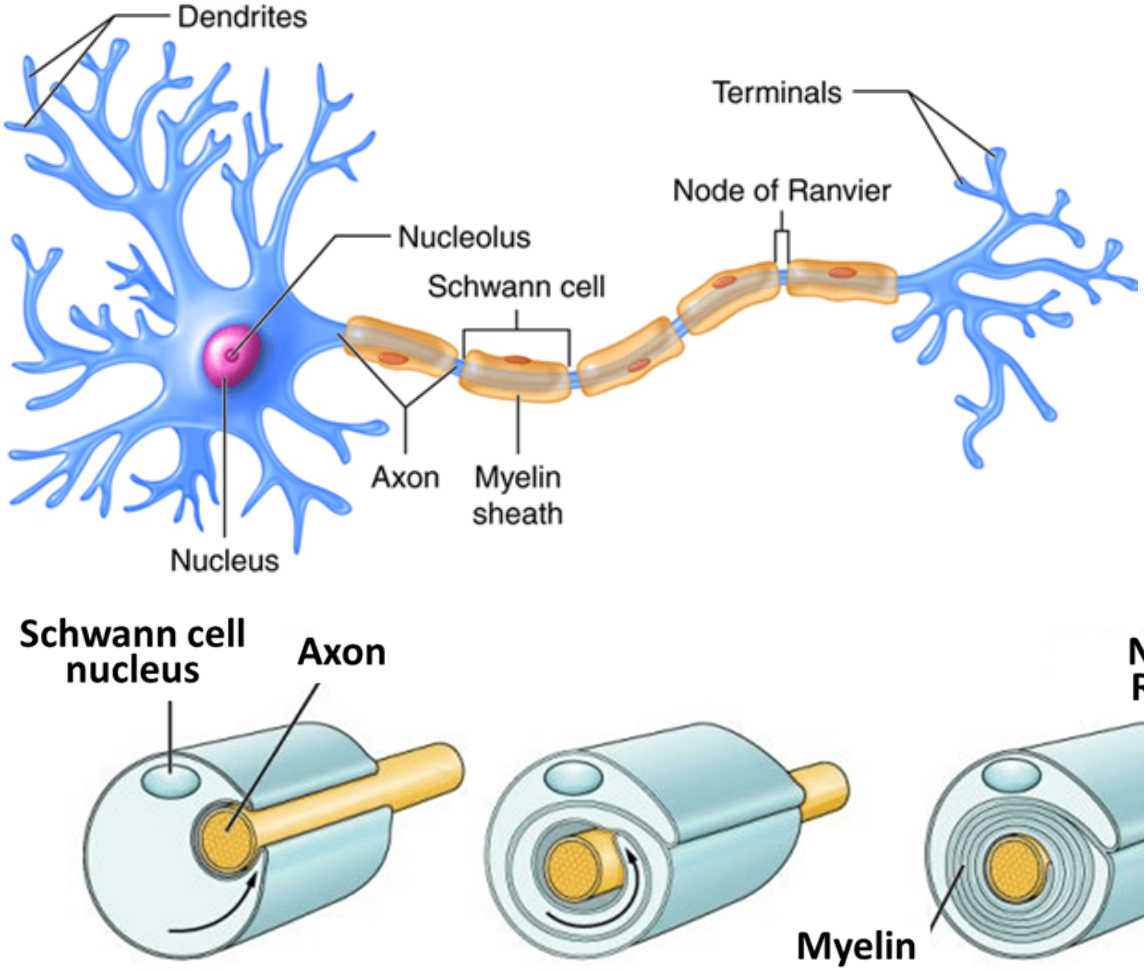


Figure 6.5.2: **Myelination by Schwann Cells.** In the PNS the whole Schwann cell spirals its membrane around a small segment of the axon to form the myelin sheath. Dozens — or even hundreds of Schwann cells — line up end-to-end along the axon's length. In fact, a very long axon, like the **sciatic nerve axon** (running from the spinal cord down to the foot), can be insulated by **thousands of Schwann cells**!

When the glial cells wrap their membrane around an axon many times, they squeezes out most of the cytoplasm until only thin layers of membrane remain stacked together. The result is a thick, multilayered covering called the **myelin sheath**, which acts like insulation on an electrical wire.

Myelin is a fatty, white substance made of about 70–80% lipids by dry weight, with **cholesterol especially abundant**. These lipids are organized in a unique multilamellar structure derived from the glial cell membranes.

A simple way to picture this: imagine a hot dog wrapped in pastry dough — the classic "pig in a blanket." The axon is the hot dog, and the layers of glial membrane are the pastry wrap. This wrapping allows neurons to send signals rapidly and reliably.

The myelin sheath is not continuous. Small gaps, called **nodes of Ranvier**, separate the myelin segments. These nodes are crucial because they allow ions to move in and out of the axon. That movement enables the electrical signal to **"jump"** from node to node in a process called **saltatory conduction**.

The word "saltatory" comes from the Latin *saltare*, meaning "to jump or leap." Strictly speaking, the signal does not really jump — it is regenerated at each node instead of along the entire axon surface. This shortcut allows the action potential to reach the axon terminal much faster.

In summary: in a myelinated axon, the electrical signal (action potential) does not crawl smoothly along the whole length. Instead, it leaps from one gap in the myelin to the next, making conduction much faster than in unmyelinated axons.



Figure 6.5.3: **Comparison of Signal Conduction in Unmyelinated and Myelinated Axons.** In an unmyelinated axon (left), the action potential moves continuously along the entire surface of the axon, resulting in slower conduction. In a myelinated axon (right), the action potential is regenerated only at the nodes of Ranvier, creating saltatory conduction. This process dramatically speeds up signal transmission.

Regeneration of Axons

Traumatic injuries can damage nerves in different ways depending on whether the injury occurs in the PNS or the CNS.

In the PNS, such as with a deep cut (laceration), the part of the axon beyond the injury site (distal segment) degenerates. The Schwann cells that had wrapped the injured axon respond by multiplying and forming new myelin tubes. These tubes act like "growth guides," providing both physical pathways and chemical signals to help the regenerating axons find their way back to

their original targets. In many cases, this repair is successful, and the nerve regains function. However, if the injury also damages the surrounding tissue, scar tissue can form. Axons cannot easily cross this barrier, and unless surgery removes the scar, regrowth will fail.

In the CNS, the situation is quite different. When axons are injured, the oligodendrocytes that normally provide myelin either die (apoptosis) or shut down. This contributes to scar formation. At the same time, nearby astrocytes release molecules that actively block axonal growth. As a result, damaged axons in the CNS cannot reconnect to their original targets. This is why spinal cord and brain injuries typically lead to permanent loss of function.

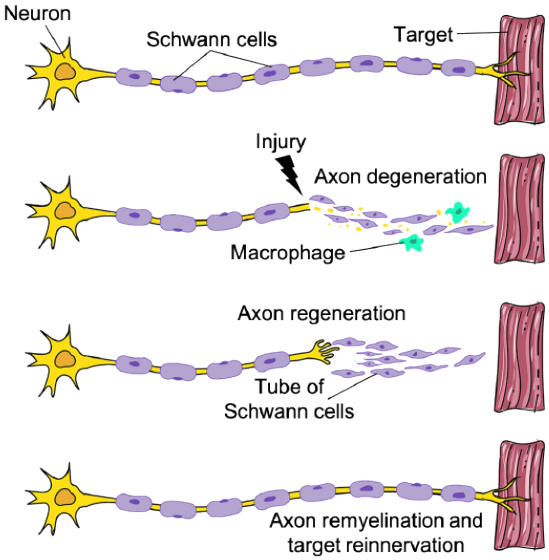
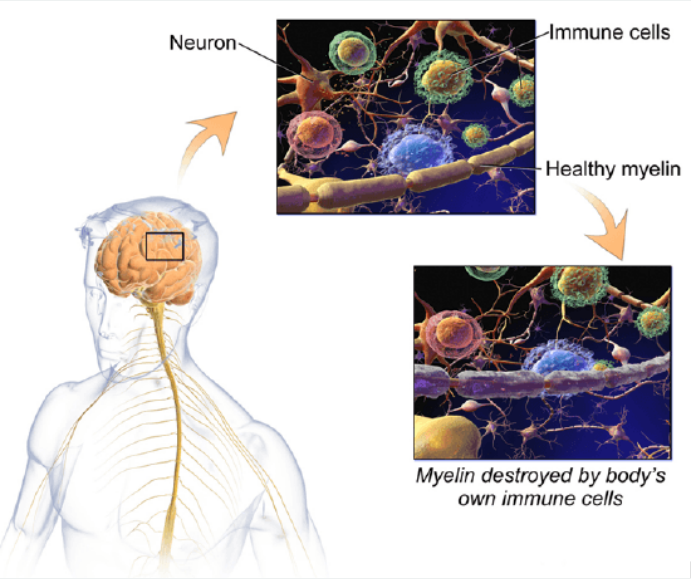


Figure 6.5.4: **Axon Regeneration in the PNS.** A neuron of the PNS innervates its target with its myelinated axon covered by Schwann cells. Following an injury, the part of the axon distal to the injury degenerates, leaving an axonal stump. The Schwann cells proliferate and produce new Schwann cells that form a tube to guide the axon back to its original target. Macrophages help clean up the debris from the axonal degeneration. The axonal stump grows following the tube of Schwann cells, which wrap it with myelin. The axon reaches the original target and the axon regeneration is complete. *(Image credit: "Axon Regeneration in the PNS" by Chiara Mazzasette is a derivative from the original work of Daniel Donnelly and is licensed by CC BY 4.0.)*

DISORDERS OF THE...



Nervous Tissue: Demyelinating Diseases

Demyelinating diseases occur when the myelin sheath around axons is damaged. Causes vary (genetic, infectious, or autoimmune), but the effect is the same: slower or blocked nerve signals.

In the U.S., **multiple sclerosis (MS)** is the most common demyelinating disease. It is an autoimmune disease of the **CNS** and usually develops between the ages of 20 and 50, with women two to four times more likely than men to be affected. The risk is highest in White people and nearly as high in Black people, with peak prevalence in women of childbearing age. The disease is much less common in Hispanic and Asian populations.

in MS the immune system attacks and destroys myelin, leaving hardened scars (*sclerosis*) in the brain and spinal cord.



CASE STUDY: Exploring the Interrelation Between the Nervous and Muscular Systems

Part 1 — Rise and Shine

Kathy, a 20-year-old woman, awakens one morning to a tingling, numb sensation covering both of her feet. Tis has happened to her a number of times throughout the year. In the past, when experiencing this sensation, within a couple of days to a week the numbness would subside, and so she is not too concerned. About a week later, she notices that the numbness and tingling not only persists, but has also spread up to her knees. Again, she ignores the abnormal sensation. By the end of a month's time, the numbness spreads to the midline of her body. At this point,
she becomes alarmed.

Kathy sees the nurse at her college who tells her that she should see a doctor. Kathy calls her doctor's office to schedule an appointment, but the soonest slot is in two weeks. She makes the appointment and goes about her daily routine.

The next morning, Kathy wakes, but when she attempts to get out of bed, she comes crashing to the floor. Because she is still groggy from sleep, she doesn't really understand what has just happened. As she tries to stand up, the muscles of her left leg engage, but as she also attempts pushing up with her right leg, she again falls to the floor. She sits in bewilderment as she tries to make sense of what has just happened and realizes that she has seriously scraped her knee in her fall. She does not feel the pain from her wound.

Kathy thinks about how odd this year has been. She remembers another medical issue she had earlier in the year when she had lost hearing in her right ear and wonders if there is a connection to her current condition. At that time, Kathy underwent extensive testing, but the ear, nose, and throat specialist remained baffled. He thought that a severe inner ear infection could have destroyed her ability to hear on that side, but there was no conclusive evidence to support this. In an attempt to recover any hearing he could, the doctor prescribed very high dosages of steroids; he told Kathy that she probably wouldn't see a change, but there were rare occurrences where steroids helped. To both Kathy and her doctor's surprise, after about a week of steroids, she completely regained hearing in her right ear. It was a "miracle."

Kathy wonders whether she can count on a new miracle to heal her current medical issues.

Questions

1. What components of the nervous system are involved in physical sensation? How does sensory impulse move throughout the body?

2. What components of the nervous system are involved in skeletal muscle movement? How does motor impulse move throughout the body? What is a "motor unit"?

3. What movements are involved in the action of standing up? What muscles need to contract to perform these actions?

4. What are the different levels of organization of a muscle down to myofilaments? What is a “sarcomere” and how are its proteins organized?

5. Starting from the release of acetylcholine by the motor neuron, what are the steps in muscle contraction? How is contraction ended?

6. Are Kathy’s medical problems related to her sensory neurons, motor neurons, or both? What in Kathy’s medical history supports your answer?

Part II – Diagnosis and Treatment

Kathy realizes that she cannot wait until her appointment to receive medical care; she quickly goes to the emergency room. After a mountain of questions about Kathy’s symptoms and medical history, the doctors decide to admit her for further testing. She is transferred to the neurology unit and the doctors request she undergo a series of laboratory tests, including an MRI and a spinal tap. In the meantime, the doctors prescribe high dosages of steroids to help alleviate the symptoms.

Upon reviewing Kathy’s medical history and the results of the various laboratory tests, the neurologists diagnose her with Multiple Sclerosis (MS). They explain to Kathy that MS is an autoimmune disease and that her own immune system has been attacking the myelin sheath that surrounds the nerves of her CNS. She remains in the hospital for a week until sensation is fully recovered in her lower body and strength is restored in her legs. She is discharged from the hospital and schedules a follow up appointment with the neurologist.

When she returns to the neurologist, they discuss Kathy’s different options for treatment. Because there is no cure for the disease, options in medication vary greatly. She decides to try daily injections of Copaxone, a medication that is similar in structure to a protein found in myelin.

Kathy continues to see the neurologist on a regular basis and gives herself an injection every evening. Over the course of seven months of therapy, she only experiences one occurrence of numbness, which subsides after a couple of days. She tries to stay positive and tries to minimize the disease’s impact on her life.

Questions

7. What is myelin and how does it affect the transmission of nerve impulses? Identify the cells responsible for the formation of myelin.

8. What are the “scleroses” in Multiple Sclerosis and where do they occur? How does this influence nerve transmission?

9. How do an MRI and spinal tap help confirm the diagnosis of Multiple Sclerosis?

10. Why did steroids help alleviate Kathy’s symptoms?

11. How does Copaxone work as treatment for Multiple Sclerosis? How do other types of medications differ?

12. Why did Kathy experience the altered sensation in her lower body? Was there something wrong with her skin?Why couldn’t she stand? Was there something wrong with the muscles of her right leg?

13. Did Kathy’s hearing loss have anything to do with the Multiple Sclerosis? Why/Why not?

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6.6: Structure of a Neuron

Motor neurons are the classic model of neuron anatomy, built to send fast signals that move your muscles.

Master this section and you'll be able to

- Identify and describe the major structural components of a neuron and explain how each contributes to information flow.
- Explain how myelination and nodes of Ranvier enhance the speed and reliability of nerve signal transmission.

The Classic Example: The Motor Neuron

Why do we almost always use motor neurons as an example? When you see a neuron diagram in this class (or in just about any textbook), chances are it is showing a motor neuron. That is because motor neurons have all the “classic parts” in one easy-to-see package: a big cell body, lots of branching dendrites, and one long axon that carries signals out to muscles.

Motor neurons also make the idea more relatable — they are the ones that actually let you move. Every time you walk, type, or even blink, motor neurons are hard at work. Since they are multipolar (remember: many dendrites, one axon), they also represent the most common neuron type in your nervous system.

In other words, motor neurons are the perfect “poster child” for learning basic neuron anatomy.

Let's look at the key parts of a motor neuron:

Cell Body (Soma)

The cell body is the central hub of the neuron. It contains the **nucleus**, which stores genetic material, and other organelles such as mitochondria (energy producers), ribosomes (protein factories), and endoplasmic reticulum (protein and lipid processing). Because of these structures, the cell body is sometimes called the **biosynthetic center** of the neuron. It is here that essential proteins, enzymes, and in many cases neurotransmitters are produced — materials that will later be transported out along the axon to support communication.

Dendrites

Branching out from the cell body are **dendrites**, which look like the spreading arms of a tree. These short, tapering extensions act as the **receptive regions** of the neuron. Their primary job is to **collect information** from other neurons or sensory receptors and channel it toward the cell body. Dendrites are covered with small projections called dendritic spines, which increase their surface area and allow for thousands of connections with other neurons. This makes dendrites the main entryway for incoming messages.

Axon:

Extending from a cone-shaped region of the cell body called the **axon hillock**, the axon is a long, thin projection that serves as the neuron’s **conducting region**. Unlike dendrites, which bring information in, the axon carries information **away** from the cell body. Electrical signals known as **nerve impulses** or **action potentials** are generated at the axon hillock and then travel down the axon, sometimes over great distances. At its far end, the axon branches into **axon terminals**, where the signal is passed to another cell at a specialized junction called a **synapse**.

Myelin Sheath

The **myelin sheath** is a protective layer of Schwann cell cell membrane wrapped around the axons of motor neurons. The myelin acts like the insulation on electrical wires, preventing electrical signals from leaking out and making signal

transmission much faster and more efficient. Because of myelin, impulses can race along axons at speeds up to 100 times faster than if there were no myelin. In motor units (where a motor neuron connects to muscle fibers), the myelinated axon ensures that commands from the nervous system reach muscles quickly, allowing for rapid and precise movements like reflexes or athletic actions.

When myelin is damaged, signals slow down, get blocked, or are lost altogether. This can cause symptoms such as muscle weakness, numbness, vision problems, and coordination difficulties. Several diseases can damage myelin. Two well-known examples are:

- **Multiple sclerosis (MS):** The most common demyelinating disease. In MS, the immune system attacks myelin in the brain and spinal cord, leading to problems with movement, sensation, and coordination.
- **Guillain-Barré Syndrome (GBS):** In this condition, often triggered by an infection, the immune system attacks myelin in the peripheral nerves. This can cause sudden muscle weakness and, in severe cases, paralysis.

Nodes of Ranvier

Along myelinated axons are tiny gaps called nodes of Ranvier. These gaps are critical for keeping signals fast and reliable. At each node, the electrical impulse is "recharged," ensuring the message stays strong all the way down the axon. Instead of traveling the whole axon in a slow crawl, the electrical signal "jumps" from node to node in a process called **saltatory conduction.** This jumping boosts signal speed and saves energy, making quick reflexes possible — like pulling your hand away from a hot stove before you even think about it.

Together, all these parts allow the neuron to operate as a highly efficient **one-way communication line.** Dendrites bring information in, the cell body processes it, and the axon sends the message on to the next destination.

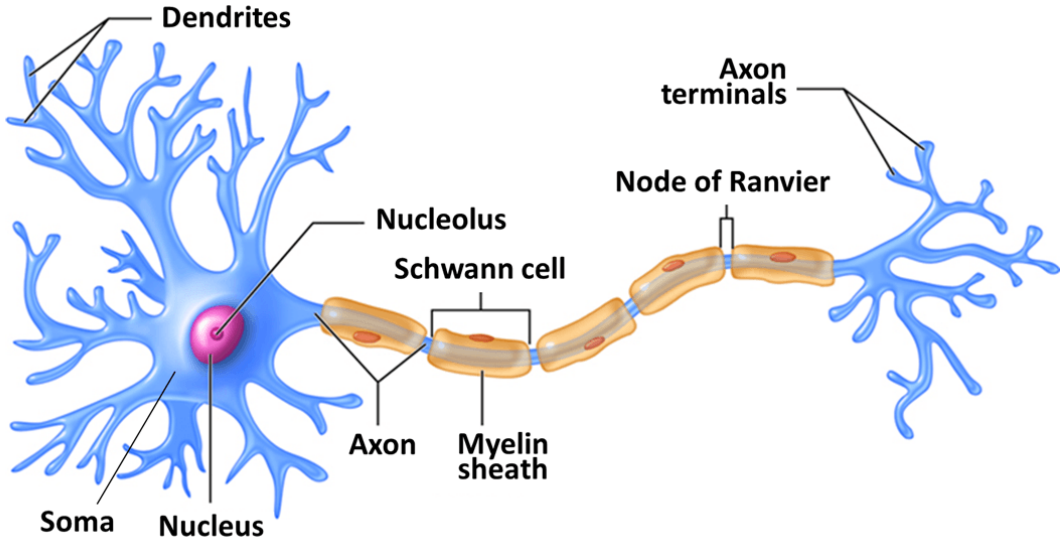


Figure 6.6.1: **Structure of a Motor Neuron.** The diagram illustrates the main structural components of a motor neuron. The **soma (cell body)** contains the **nucleus** and **nucleolus**, which house the cell's genetic material. Branching **dendrites** extend from the soma (cell body), receiving incoming signals. A single **axon** carries impulses away from the soma, insulated by segments of **myelin sheath** formed by **Schwann cells**. Gaps between myelin segments, called **nodes of Ranvier**, enable rapid signal conduction. The axon ends in **axon terminals**, which transmit signals to muscle fibers at synapses, allowing movement.

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6.7: Gray vs. White Matter- Headquarters and Highways in the CNS

The central nervous system consists of a central cavity surrounded by gray matter made of neuronal cell bodies and white matter made of myelinated axons.

Master this section and you'll be able to

- Differentiate between gray matter and white matter in terms of structure, location in the CNS, and primary functions.
- Explain how nuclei and tracts contribute to processing and communication within the CNS, using a couple of examples.

Headquarters: Gray Matter Hubs

Gray matter is a major component of the central nervous system (CNS). It is **composed primarily of neuronal cell bodies, dendrites, unmyelinated axons, glial cells, and capillaries**. Gray matter is critically involved in **processing** and **integration**, and is found in the cerebral cortex, cerebellar cortex, brainstem nuclei, and throughout the spinal cord. Nuclei are are localized collections of neuronal cell bodies deep inside the brain, such as the basal nuclei in the

Functions associated with gray matter include muscle control, sensory perception (such as vision and hearing), memory formation, emotions, speech, decision-making, and self-regulation.

In the brain, all capillaries are continuously perfused with blood, ensuring a constant supply of oxygen and nutrients. Remarkably, it has been estimated that nearly every neuron in the brain is served by its own capillary. Capillary density, however, is not uniform throughout the brain. It varies depending on the local energy demands of different regions. Areas with higher metabolic activity, such as gray matter, contain a greater density of capillaries compared to white matter, which is less metabolically demanding.

In the CNS, a localized collection of neuronal cell bodies is called a **nucleus.** For example, the **basal nuclei** (singular: *nucleus*; plural: *nuclei*; also called the **basal ganglia**) are clusters of gray matter located deep within the brain, beneath the cerebral cortex and surrounding the thalamus. They lie at the base of the forebrain and are arranged as mirror-image structures on both sides of the brain. Because of this central position, the basal nuclei can receive signals from the cerebral cortex and send information back to other areas such as the thalamus and brainstem. Their main role is to help control movement, making sure our actions are smooth, coordinated, and purposeful.

Highways: White Matter

A second major component of the CNS is white matter. It is composed mainly of **bundles of myelinated axons,** with very few neuronal bodies. White matter connects the various grey matter regions of the nervous system to each other and carries nerve impulses between neurons.

Within the CNS, these bundles of axons are called **tracts** (or **columns**) — whereas in the PNS they are called **nerves**. Importantly, the same group of axons may be referred to differently depending on its location. A classic example is the fibers projecting from the retina: they are the **optic nerve** as they leave the eye, but once inside the cranial cavity they are called the **optic tract**.

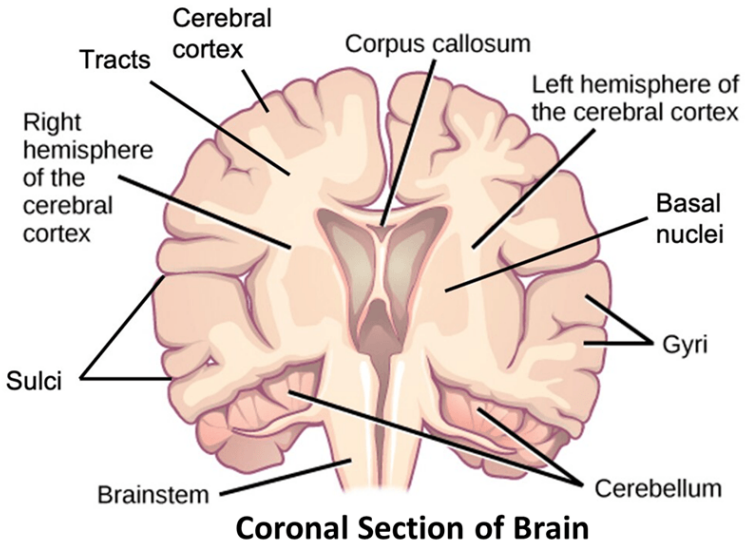
Here are another two clear examples of **tracts in the brain:**

1. **Corpus Callosum:** The largest white matter tract in the brain. It connects the left and right cerebral hemispheres, allowing them to communicate. Without it, the two sides of the brain would function almost independently.

2. **Corticospinal Tract:** A major motor pathway that starts in the cerebral cortex and travels down to the spinal cord. It carries signals that control voluntary movements, especially fine movements of the hands and fingers.

In summary: Think of the CNS tracts as highways that connect different “cities” of gray matter. The cities (cortex and nuclei)

handle the processing, while the highways (tracts) let information travel quickly between them.



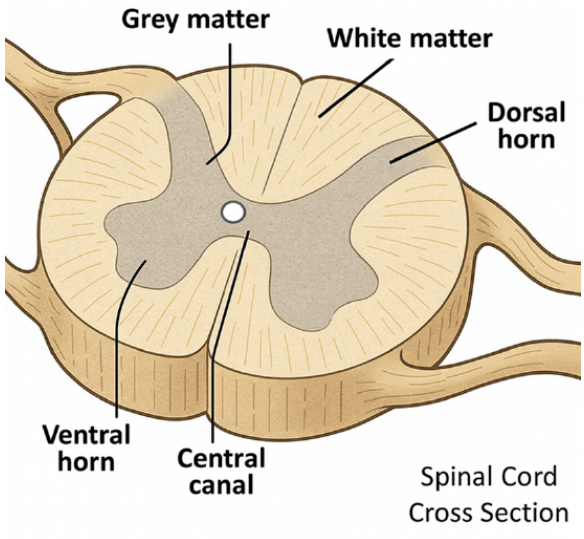


Figure 6.7.1: **Grey and White Matter of the Brain and Spinal Cord.** In the brain on the left, the coronal section shows the layers of the cerebrum. The superficial **gray matter** is the **cerebral cortex**, while the deep gray matter is organized in **basal nuclei**. The superficial and deep regions are connected by **myelinated axons (white matter) called tracts.** The corpus callosum is one of these tracts and connect the left and right hemispheres. (Image credit: "Brain Coronal Section" by Chiara Mazzasette is licensed under CC BY 4.0 / A derivative from the original work)
In the spinal cord on the right, the darker **grey matter** is in the center and is shaped like a butterfly. The lighter **white matter** surrounds it and contains bundles of myelinated axons that carry information up and down the spinal cord. The **dorsal horns** receive incoming sensory information, while the **ventral horns** send out motor commands. In the middle lies the **central canal**, a small space filled with cerebrospinal fluid.

Comparison of Gray Matter and White Matter in the CNS

Feature	Gray Matter	White Matter
Main Components	Neuronal cell bodies, dendrites, unmyelinated axons, glial cells, capillaries	Myelinated axons (nerve fibers), some unmyelinated axons, glial cells (esp. oligodendrocytes)
Appearance	Grayish-pink (due to cell bodies and blood supply)	Whitish (due to lipid-rich myelin)

Feature	Gray Matter	White Matter
Location in Brain	Outer layer (cerebral cortex, cerebellar cortex) and deep nuclei	Beneath the cortex, forming tracts that connect different brain regions
Location in Spinal Cord	Forms the central “H” or butterfly-shaped region	Surrounds the gray matter, forming ascending and descending tracts
Primary Functions	Processing and integration of information; control of movement, sensory perception, memory, emotions, decision-making	Rapid communication between gray matter regions; coordination of signals between brain and spinal cord

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6.8: Nerve and Ganglion Structure

The PNS is composed of the groups of neuron cell bodies (ganglia) and bundles of axons (nerves) that are outside of the brain and spinal cord.

Master this section and you'll be able to

- Distinguish between cranial nerves and spinal nerves.
- Explain the structural and functional differences between ganglia in the PNS and gray matter in the CNS.
- Describe the connective tissue layers that organize a peripheral nerve and compare them to connective tissue wrappings of skeletal muscle.

The peripheral nervous system (PNS) is everything of the nervous tissue that is not in the brain or spinal cord. In the peripheral nervous system, we use different words than in the central nervous system to describe groups of neurons and their fibers. Instead of “gray matter,” the PNS has **ganglia** — small clusters of neuron cell bodies that act like relay stations, collecting and sending information. A single cluster is called a **ganglion**, while more than one are called **ganglia**.

Instead of “white matter,” the PNS has **nerves** — bundles of axons that carry signals back and forth between the body and the CNS. Just like electrical cables wrapped together, nerves contain many axons traveling side by side, transmitting messages to and from the brain and spinal cord.

Some peripheral structures are incorporated into the other organs of the body. In describing the anatomy of the PNS, it is necessary to describe the common structures, the nerves and the ganglia, as they are found in various parts of the body. Many of the neural structures that are incorporated into other organs are features of the digestive system; these structures are known as the **enteric nervous system** and are a special subset of the PNS. The enteric nervous system controls many aspects of digestion — such as moving food through the intestines and regulating secretions — and it can even function independently of the brain and spinal cord, which is why it is sometimes called the “second brain” of the body.

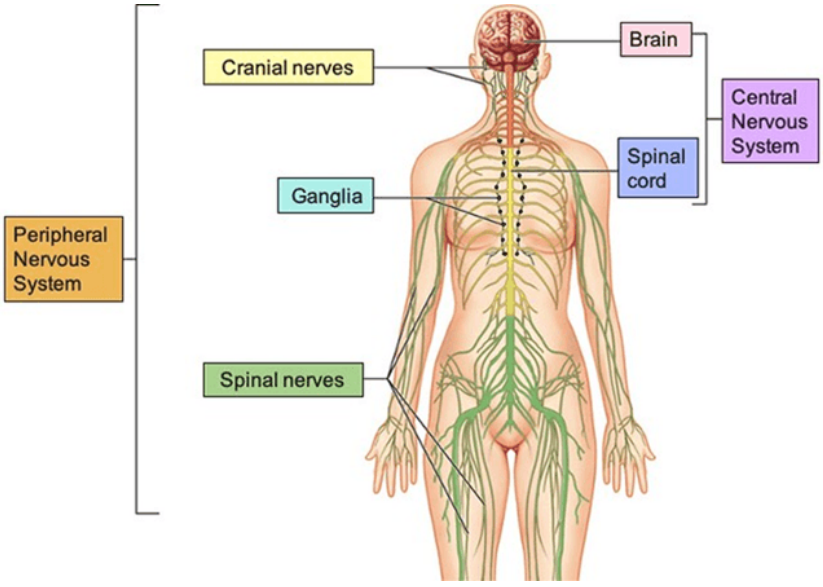


Figure 6.8.1: **The structures of the PNS are ganglia and nerves.** Nerves can be divided into cranial if they originate from the brain and spinal if they originate from the spinal cord. Spinal nerves originate laterally from the spinal cord. Ganglia are enlarged regions of the nerves that house neuron cell bodies and glial cells within the PNS. (Image credit: "Structural divisions of the nervous system" by Chiara Mazzasette is licensed under CC BY 4.0 / A derivative from the original work)

Nerve Structure

Bundles of axons in the peripheral nervous system are called **nerves**. These are different from their central counterpart, which are called **tracts**. Unlike tracts, nerves are considered **organs** because they are made of more than just nervous tissue. They also contain **connective tissue layers** that give them structure and **blood vessels** that supply nutrients.

The outer surface of a nerve is wrapped in a tough layer of dense irregular connective tissue called the **epineurium**. Inside the nerve, axons are grouped into bundles called **fascicles**, each surrounded by another dense irregular connective tissue layer called the **perineurium**. Finally, every individual axon (or nerve fiber) is cushioned by a thin layer of areolar connective tissue called the **endoneurium.** These three layers are very similar to the connective tissue wrappings you learned about in muscles.

Nerves are named based on where they connect to the central nervous system (CNS). Those that attach to the brain are called **cranial nerves**, while those that attach to the spinal cord are called **spinal nerves**.

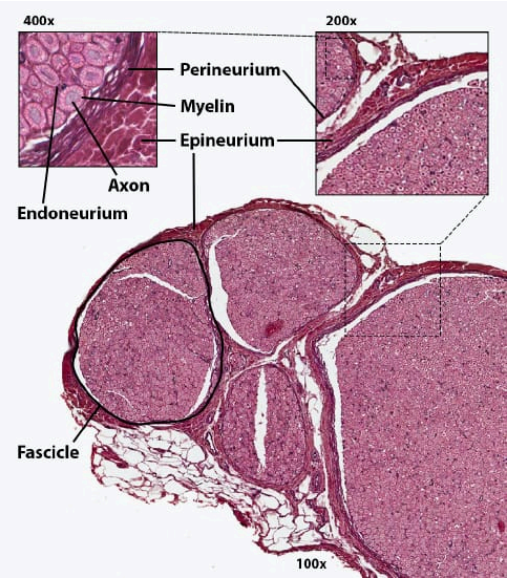


Figure 6.8.2: **Nerve Structure.** The structure of a nerve is organized by the layers of connective tissue on the surface, around each fascicle, and surrounding the individual nerve fibers. *(Image credit: "Nerve Structure" by Jennifer Lange; micrographs provided by Virginia Commonwealth University under CC BY-NC-SA 4.0)*

Cranial Nerves

The nerves attached to the brain are called **cranial nerves**. Most control the sensory and motor functions of the head and neck, but one also extends to organs in the thoracic and abdominal cavities as part of the parasympathetic nervous system. There are **twelve cranial nerves**, labeled **CN I through CN XII** using Roman numerals in order from front (rostral) to back (caudal) when looking at the underside of the brain (Figure 12.3.1).

Cranial nerves can be **sensory**, **motor**, or **mixed** (both). Sensory nerves carry information into the brain from sensory ganglia outside the cranium. Motor nerves send signals from nuclei in the brainstem to skeletal muscles of the head and neck or to autonomic ganglia. Of the twelve, **three are purely sensory**, **five are purely motor**, and **four are mixed nerves**.

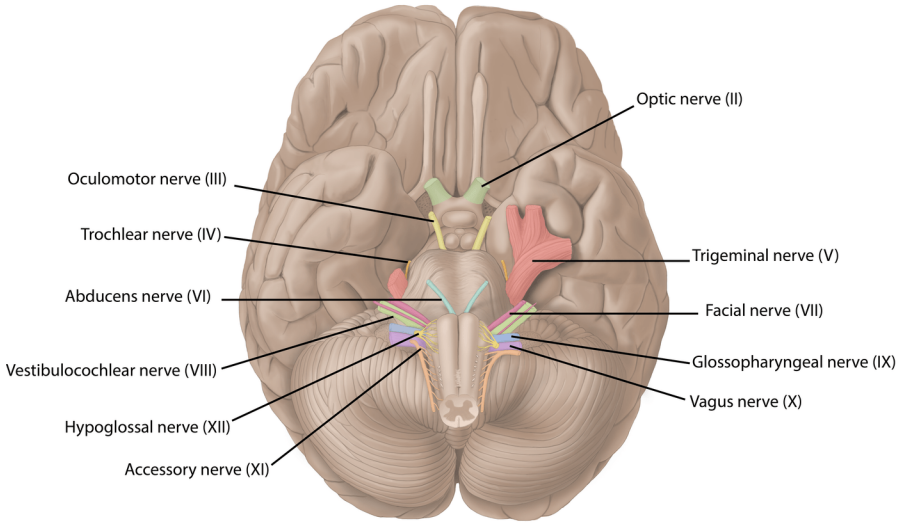
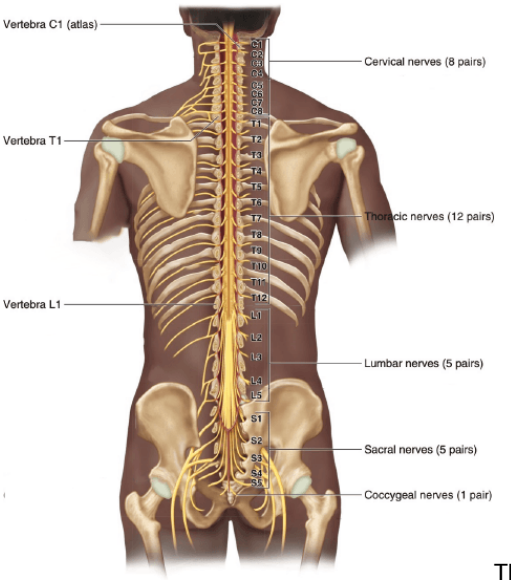


Figure 6.8.3: **Cranial Nerves.** The anatomical arrangement of the roots of the cranial nerves observed from an inferior view of the brain. Cranial nerves are numbered with Roman numbers from I to XII based on their exit from the brain, from rostral to caudal (CN I is not seen). *(Image credit: "Cranial Nerves" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*

Spinal Nerves



The nerves connected to the spinal cord are the spinal nerves. The arrangement of these nerves is much more regular than that of the cranial nerves. All of the spinal nerves are combined sensory and motor axons that separate into two nerve roots. The sensory axons enter the spinal cord as the dorsal nerve root. The motor fibers, both somatic and autonomic, emerge as the ventral nerve root.

There are 31 spinal nerves, named for the level of the spinal cord at which each one emerges (Figure 12.4.1). There are

- eight pairs of cervical nerves designated C_1 to C_8,
- twelve pairs of thoracic nerves designated T_1 to T_{12},
- five pairs of lumbar nerves designated L_1 to L_5,
- five pairs of sacral nerves designated S_1 to S_5, and
- one pair of coccygeal nerves designated Co_1.

The nerves are numbered from the superior to inferior positions, and each emerges from the vertebral column through the intervertebral foramen at its level. The first nerve, C1, emerges between the first cervical vertebra and the occipital bone. The

second nerve, C2, emerges between the first and second cervical vertebrae. The same occurs for C3 to C7, but C8 emerges between the seventh cervical vertebra and the first thoracic vertebra. For the thoracic and lumbar nerves, each one emerges between the vertebra that has the same designation and the next vertebra in the column. The sacral nerves emerge from the sacral foramina along the length of that unique vertebra.

Ganglia

Ganglia are enlarged regions along nerves within the PNS that contain the cell bodies of neurons as well as supporting glial cells. Ganglia are generally divided into two main types: **sensory ganglia** and **autonomic ganglia**, depending on their primary function.

One type of sensory ganglion is the **cranial nerve ganglion**. While the roots of cranial nerves are found inside the cranium, their ganglia are located just outside the skull. For example, the **trigeminal ganglion** lies on the surface of the temporal bone, even though its nerve connects to the mid-pons region of the brainstem. The neurons within cranial nerve ganglia are typically **unipolar** in shape and are supported by surrounding **satellite cells** — small glial cells that protect neuron cell bodies within ganglia and help regulate their chemical environment, much like astrocytes do in the CNS.

The **dorsal root ganglia**, are a series of sensory ganglia found along the spinal nerves. Each spinal nerve has its own ganglion, which houses the cell bodies of sensory neurons that carry information from the body (below the head) into the spinal cord. Like cranial nerve ganglia, the neurons in spinal ganglia are unipolar and are surrounded by satellite cells.

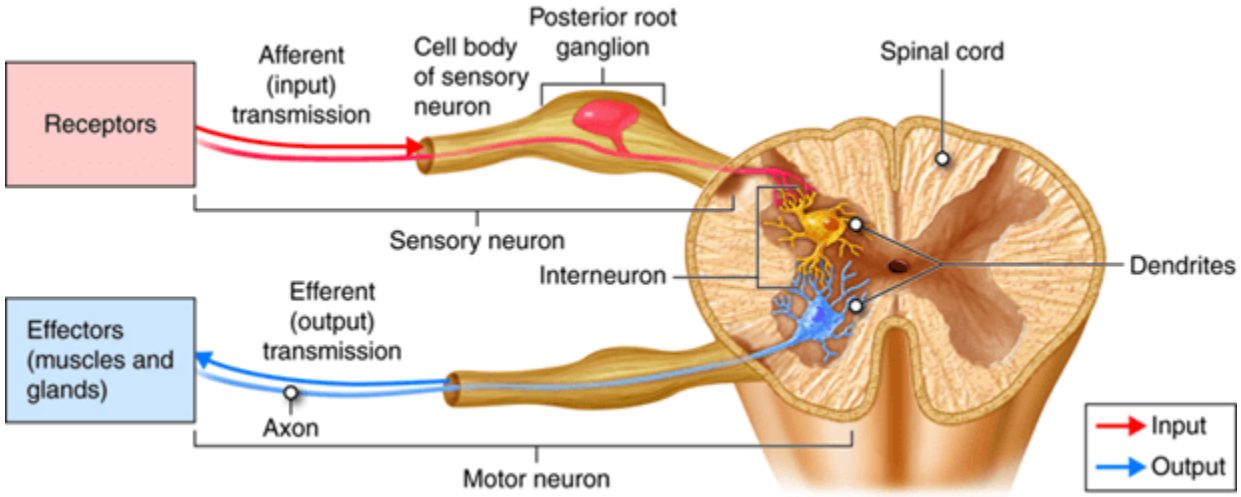


Figure 6.8.4: **Dorsal (posterior) Root Ganglion.** Sensory information travels along an afferent pathway toward the central nervous system while motor commands travel along an efferent pathway away from the central nervous system. Integration occurs at the interneurons within the spinal cord. *(Image credit: This work by Cenveo is licensed under CC BY 3.0).*

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6.9: Inside the Brain — Your Control Tower

The brain coordinates everything from basic survival functions to complex processes like movement, sensation, memory, and learning through the specialized roles of its major regions.

Master this section and you'll be able to

- Identify the four major regions of the brain.
- Analyze how the folding of the cerebral cortex increases processing capacity and why this is important for brain function.
- Locate major cortical landmarks (gyri, sulci, fissures) and explain their role in dividing functional brain regions.
- Describe the functional areas (and lobes) of the cerebral cortex and their locations.

The **central nervous system (CNS)** has two main organs: the **brain** and the **spinal cord**.

The brain is divided into **four major regions**:

- **Cerebrum** – The largest part of the brain, responsible for thinking, memory, senses, and voluntary movement.
- **Diencephalon** – The relay and control center, containing the thalamus and hypothalamus, which direct sensory input and regulate homeostasis.
- **Brainstem** – The life-support hub that controls breathing, heart rate, and connects the brain to the spinal cord.
- **Cerebellum** – The coordinator of balance, posture, and fine-tuned movements.

The Cerebrum

The **cerebrum** is the large, outer “gray mantle” of the brain and makes up

]\most of its mass. It is responsible for many of the “higher” neurological abilities that make us human.

The main functions of the cerebrum are:

- Initiating and coordinating movement
- Processing sensory information (both general and special senses)
- Managing higher-level tasks like judgment, reasoning, problem solving, memory, learning, emotion, and consciousness

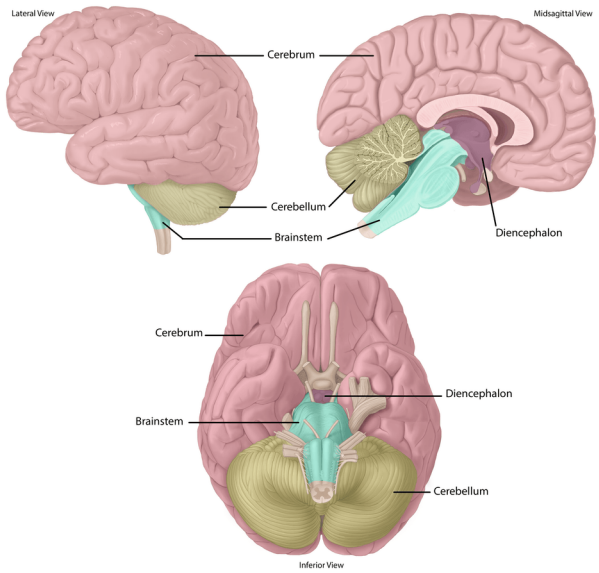


Figure 6.9.1: **Major Brain Regions.** On the external, lateral surface only three of the four major regions are visible: the cerebrum, the brainstem, and the cerebellum. The diencephalon is deep within the brain and can only be seen in inferior and midsagittal views. *(Image credit: "Major Brain Regions" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0)*

Wrinkles with a Purpose: The Cerebral Cortex

The cerebrum is wrapped in a continuous layer of gray matter called the **cerebral cortex**. This thin, wrinkled sheet of tissue is where the brain's higher functions happen—things like reasoning, memory, and decision-making.

- A **gyrus** (plural = gyri) is one of the raised ridges.
- A **sulcus** (plural = sulci) is the groove between gyri.

Think of it like the brain's way of cramming more "mental storage space" into a limited skull. If you could peel off the cortex and flatten it out, it would cover about **one square meter** — roughly the size of a large pizza box! Folding lets more gray matter fit into the cranial cavity.

During embryonic development, as the forebrain (telencephalon) expands, the cortex folds in a predictable pattern. That is why, despite small differences, everyone's brain has a broadly similar "map" of wrinkles.

Landmarks of the Cortex

The brain's surface can be mapped using large gyri and sulci:

- **Central sulcus** – divides motor regions in front from sensory regions behind.
  - **Precentral gyrus** (in front) = primary motor cortex.
  - **Postcentral gyrus** (behind) = primary somatosensory cortex.
- **Lateral fissure (sulcus)** – separates the temporal lobe from the frontal and parietal lobes.
- **Parieto-occipital sulcus** – separates the parietal lobe from the occipital lobe.
- **Longitudinal fissure** – a deep groove that splits the cerebrum into left and right **hemispheres**.

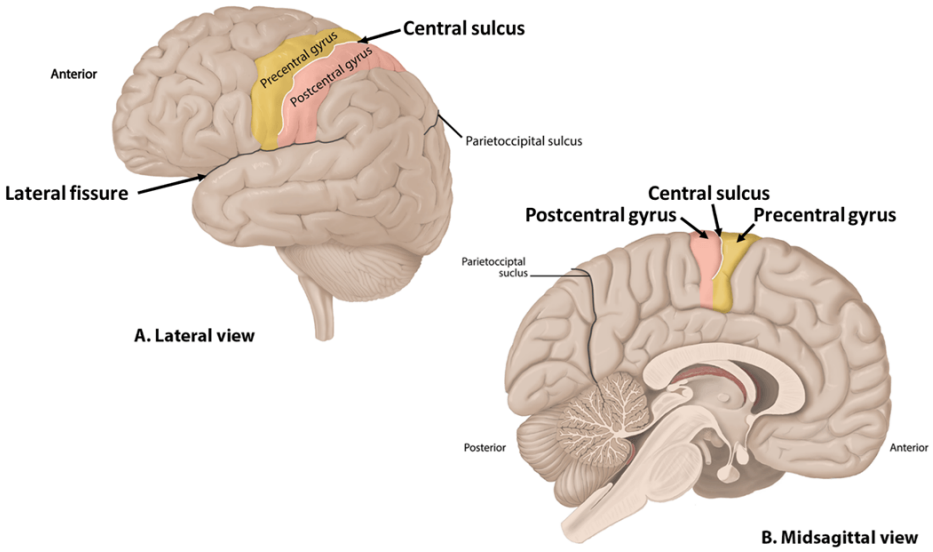


Figure 6.9.2: **Cerebrum: Major Gyri and Sulci, Lateral & Midsagittal Views.** The cerebrum presents ridges called gyri and

grooves called sulci. The main sulci are the central sulcus, lateral fissure (sulcus) and parieto-occipital sulcus. The gyrus anterior to the central sulcus is called precentral gyrus, while the posterior one is the postcentral gyrus. *(Image credit: "Gyrus and Sulcus - Lateral and Midsagittal Views" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0)*

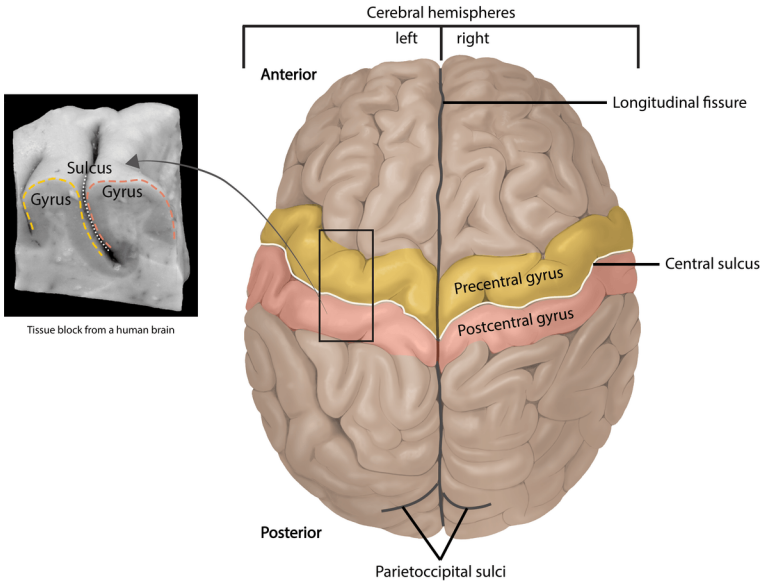


Figure 6.9.3: **Superior View of the Brain.** The cerebrum is medially divided by the longitudinal fissure into left and right hemispheres. The central sulcus is visible cutting the cerebrum in a coronal section. The gyrus anterior to the central sulcus is called precentral gyrus, while the posterior one is the postcentral gyrus. The enlargement shows a human brain tissue block containing the central sulcus and the two adjacent gyri. *(Image credit: "Gyrus and Sulcus - Superior View" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0; inset image: "Pre- and Post-central gyrus" by Geyer S, Weiss M, Reimann K, Lohmann G and Turner R, via Wikimedia Commons, as modified by Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*

Lobes of the Cerebral Cortex

The cortex can be separated into major regions called lobes. The lateral sulcus separates the **temporal lobe** from the other regions. Superior to the lateral sulcus are the **parietal lobe** and **frontal lobe**, which are separated from each other by the central sulcus. The posterior region of the cortex is the **occipital lobe**, which has no obvious anatomical border between it and the parietal or temporal lobes on the lateral surface of the brain.

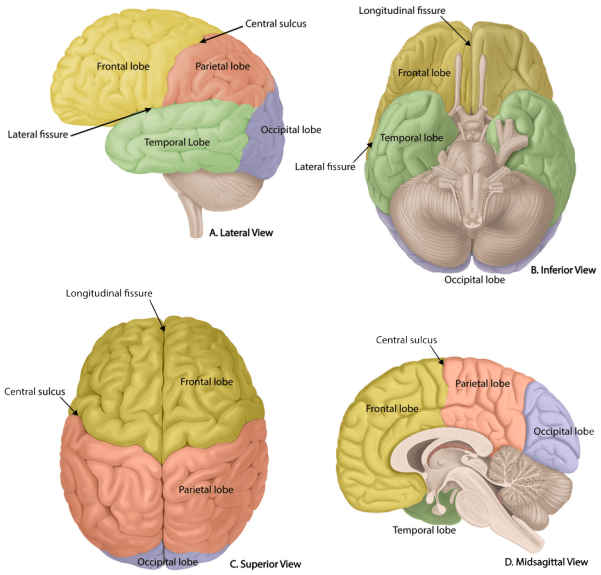


Figure 6.9.4: **Lobes of the Cerebral Cortex.** The cerebral cortex is divided into four lobes by the major sulci. The central sulcus separates the frontal and parietal lobes. The parieto-occipital sulcus separates the parietal and occipital lobes. The lateral sulcus separated the temporal and parietal lobes. The fifth lobe is the insula which is deep to the frontal and temporal lobes (not shown here). Each lobe corresponds to specific functions of the cerebral cortex. *(Image credit: "Lobes of the Cerebral Cortex" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*

The different lobes of the brain contain areas that process our sensations and control movement.

- **Parietal lobe**: The postcentral gyrus holds the **primary somatosensory cortex**. This is where sensations such as touch, pressure, tickle, pain, itch, and vibration are processed, along with body position (**proprioception**) and movement (**kinesthesia**). Nearby, the **somatosensory association area** helps make sense of these inputs.
- **Occipital lobe**: At the very back is the **primary visual cortex**, which begins processing vision. Surrounding areas, called **visual association areas**, help interpret what we see.
- **Temporal lobe**: The **primary auditory cortex** first processes sound, and the **auditory association area** refines it. Deeper in this lobe is the **primary olfactory cortex**, which processes smell.
- **Insula**: Contains the **primary gustatory cortex**, where taste is processed.
- **Frontal lobe**: The precentral gyrus holds the **primary motor cortex**, which sends commands (via upper motor neurons) to move skeletal muscles. Just in front of it are the **motor association areas** (premotor and supplementary motor cortices), which help plan and coordinate complex movements and also contribute to speech and memory.

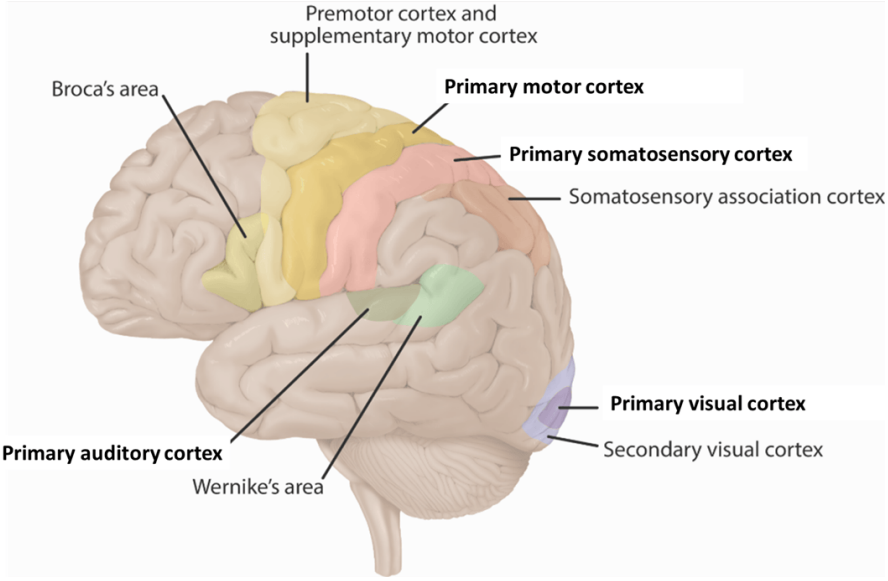


Figure 6.9.5: **Functional Cortical Areas.** The functions of the cerebral cortex are localized within their respective lobes. Although the exact boundaries can vary from person to person, their general area and their relative positions remain the same. *(Image credit: "Functional Areas of the Cerebral Cortex" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*

Memory and Learning

Memory is not stored in just one place in the brain. Different regions handle different parts of the process.

- **Hippocampus (temporal lobe):**
  Acts like a "memory hub." It helps form new declarative memories (facts, events, experiences) and plays a key role in recalling spatial information and context. The hippocampus holds information briefly as short-term memory, then sends it on to the cortex for long-term storage and meaning. It is also central to **memory consolidation** — turning new experiences into lasting memories.

- **Amygdala (temporal lobe):**
  Works closely with the hippocampus. It is especially important for emotional memories, particularly fear. The amygdala can either enhance or dampen how strongly memories are stored.

- **Cerebellum:**
  Handles implicit (procedural) memories — skills and habits we learn by practice, such as playing an instrument, riding a bike, or typing. It also supports motor learning and classical conditioning. The cerebellum allows us to perform tasks "on autopilot," like walking through a dark room or driving a familiar route.

- **Prefrontal cortex:**
  The "workspace" of the brain. It is where **working memory** operates, letting us temporarily hold and use information. This supports reasoning, decision-making, and problem-solving — for example, remembering a code just long enough to type it in, or considering complex choices like treatment options.

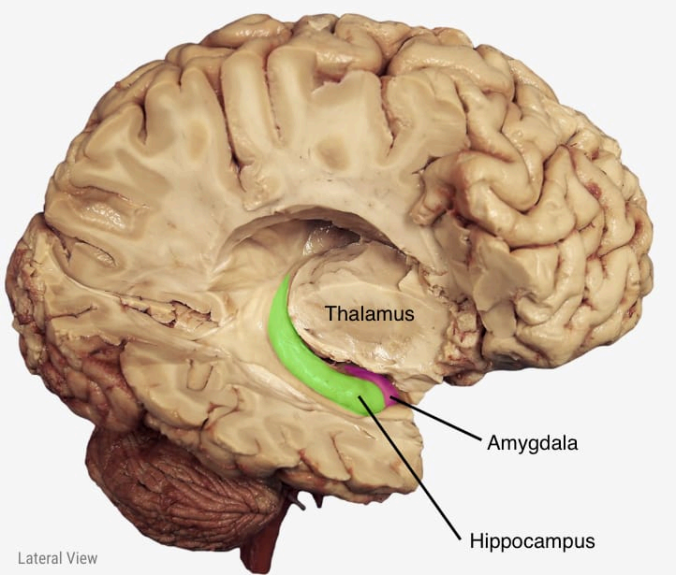


Figure 6.9.6: **Hippocampus and Amygdala.** Both the hippocampus and the amygdala are located within the medial aspect of the temporal lobe. The hippocampus serves as the floor of the inferior portion of the lateral ventricle. *(Image credit: "Hippocampus and Amygdala" by Functional Neuroanatomy at the University of British Columbia is licensed under CC BY-NC-SA 4.0; labels added by Jennifer Lange.)*

Explore 3D Brain Models

Explore human brain specimens in 3D! Each of the following specimens will have slight differences in the pattern of gyri and sulci, as such variation is normal between individuals.

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Whole brain with gross anatomy annotations by TavorLab on Sketchfab

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6.10: Cortical Homunculus

The cortical homunculus consists of two main types: the sensory (somatosensory) homunculus and the motor homunculus.

Master this section and you'll be able to

- Explain how the brain's cortex is organized into sensory and motor regions and describe the significance of the cortical homunculus as a representation of body part control and sensation.
- Compare and contrast the motor and sensory homunculi.

The **brain's cortex** is the thin, outer layer of the brain made of gray matter. Because gray matter is composed mainly of neuron cell bodies, the cortex is packed with them and is responsible for many higher functions, such as thinking, memory, language, decision-making, and processing sensory information. The folds and grooves increase its surface area, allowing more neurons to fit and making it highly efficient.

A **cortical homunculus** can be described as a "**map of the whole human body in the cortex**." It shows how different body parts are represented in the **primary motor cortex** (responsible for movement) and the **primary somatosensory cortex** (responsible for receiving and processing sensory information such as touch, pressure, pain, and temperature).

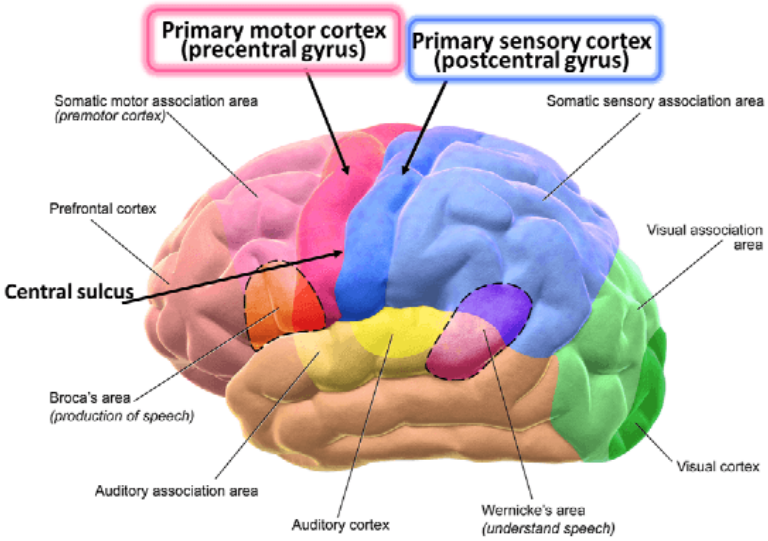


Figure 6.10.1: **Motor and Sensory Regions of the Cerebral Cortex.** Lateral view of the human brain highlighting the primary motor cortex (precentral gyrus, red) and the primary sensory cortex (postcentral gyrus, blue), located on either side of the central sulcus.

How Your Brain Sees Your Body

The **homunculus** (Latin for "little man") is the brain's body map. It is not drawn to scale like a normal body. Instead, it shows each body part in proportion to how much **brain tissue** is devoted to controlling its movement or processing its sensations. Basically, it is the neurological map showing how much brainpower is devoted to sensing (or moving) each body part. It is the **body as the brain sees it**, not as the mirror sees it

- Hands, lips, and the face appear **huge** on the homunculus because they require very fine motor skills and have many sensory receptors.
- Other regions, like the back or thighs, appear **tiny** because they have fewer nerve connections to the brain.

The result is a distorted, cartoon-like figure — a little creepy, almost comical, but highly informative.

Motor vs. Sensory Homunculus

There are **two types of homunculus maps**:

- **Motor homunculus**: Found in the **precentral gyrus** of the frontal lobe (primary motor cortex). It shows which parts of the brain send signals to muscles for voluntary movement.
- **Sensory homunculus**: Found in the **postcentral gyrus** of the parietal lobe (primary somatosensory cortex). It shows where sensory information from the body is received and processed.

Both maps are arranged in an **upside-down fashion**: the feet and legs are represented near the top of the cortex, while the face and hands are closer to the lateral sulcus (near the temples).

The distorted proportions are the key. The more sensitive or precise the body part, the more “real estate” it gets in the cortex. This is why the homunculus ends up looking like a bizarre figure with:

- **Huge lips and tongue** → taste and speech need lots of precision.
- **Oversized hands** → fine motor skills for grasping and tool use.
- **Small trunk and legs** → fewer sensory and motor nerves.

The idea of the cortical homunculus was developed by Wilder Penfield, a groundbreaking researcher and highly original surgeon, who treated patients with severe epilepsy by destroying nerve cells in the brain where the seizures originated. To guide these surgeries, he created maps of the sensory and motor cortices by stimulating different regions of the cortex before and during operations. Remarkably, these maps are still used today, largely unchanged.

Penfield's work became widely known through his landmark book with Herbert Jasper, *Epilepsy and the Functional Anatomy of the Human Brain* (1954), which contained the refined and now-classic versions of the motor and sensory homunculi.

Organization of the Sensory Map

As far as motor and sensory control goes, each brain hemisphere receives information from the opposite side of the body. For example, your **right primary somatosensory cortex** processes sensations from your **left arm and leg**, while your **right visual cortex** receives input from the **left visual field**.

The brain organizes sensory information in **topographic maps**. This means that neighboring spots on your sensory organs connect to neighboring spots in your cortex.

The **somatotopic map of touch** is often illustrated as the **somatosensory homunculus** — a funny, distorted “little human” drawn across the cortex. The body parts are out of proportion: giant lips and hands, tiny torso. Why? Because the amount of cortex given to each body part depends on how many sensory nerves it has.

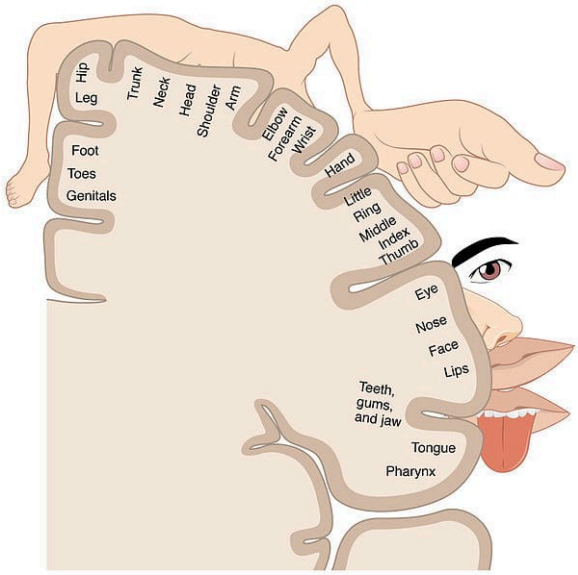


Figure 6.10.2: **(Somato-)Sensory Homunculus**: The cortical homunculus is a distorted human figure drawn across the primary somatosensory cortex. Body parts are sized according to the amount of sensory cortex devoted to them. Highly sensitive areas — such as the lips, tongue, and fingertips — appear much larger than areas like the back or legs. It reflects the brain's "map" of sensation, not the body's actual proportions.

Organization of the Motor Map

The motor homunculus is located in the **primary motor cortex** (the precentral gyrus, just in front of the central sulcus). This "map" shows from where the brain sends motor commands to muscles.

Think of it as the **"control panel for movement."** Bigger body parts on the map mean more fine motor control.

Motor vs. Sensory Maps

The sensory homunculus is about **incoming signals** (feeling).
The motor homunculus is about **outgoing commands** (moving).

Both are distorted, since the brain gives more space to areas that require precision. But they are not identical, because **sensation and movement are not always prioritized the same way.**

Key Similarities

- Both exaggerate the **hands, face, lips, and tongue**, since these areas are crucial for either fine movement or sensation.

Key Differences

- **Hands:** Huge in both, but even bigger in the motor map for precise tasks like typing, drawing, or playing guitar.
- **Lips and Tongue:** Giant in both, but especially large in the sensory map, since they are packed with touch receptors.
- **Trunk/Back:** Small in both, but slightly bigger in the motor map (posture control matters, even if your back is not super sensitive).

- **Feet/Legs:** Similar in size, but the motor map highlights the toes (balance, walking), while the sensory map highlights the soles (lots of touch receptors).

Bottom Line

- **Sensory map = brain real estate for feeling.**
- **Motor map = brain real estate for moving.**

And yes—the proportions differ, reflecting the different demands of **sensation** versus **control**.

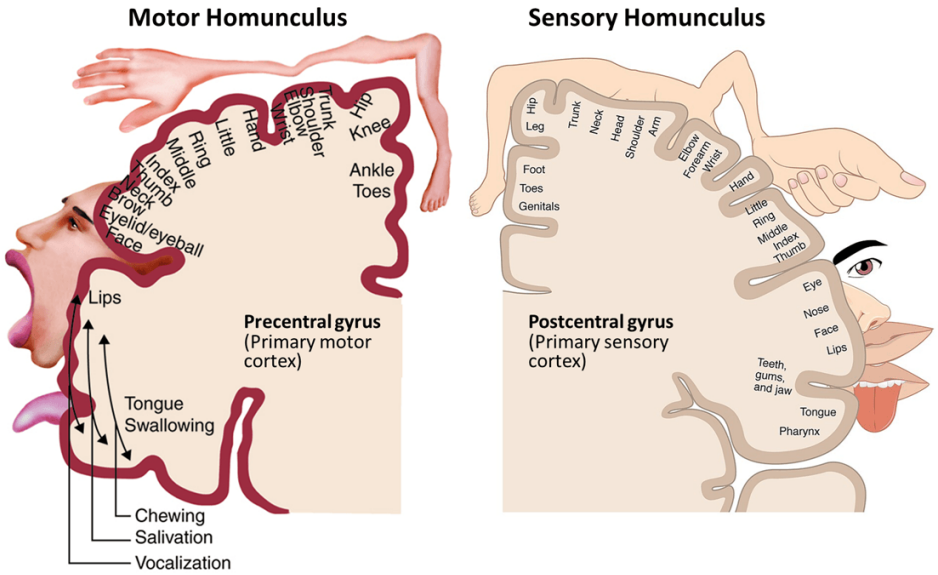


Figure 6.10.3: **Comparison of Motor and Sensory Homunculi.** The distorted "little man" diagrams represent how the body is mapped in the brain's cortex. On the left, the motor homunculus shows the precentral gyrus (primary motor cortex), where outgoing motor commands originate. On the right, the sensory homunculus shows the postcentral gyrus (primary somatosensory cortex), where incoming sensations such as touch, pressure, and pain are processed. Notice how the hands, lips, and tongue appear exaggerated in both maps, reflecting the high degree of fine motor control and sensory input in these regions.

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6.9B: More Brain Highlights — Diencephalon and Brainstem

The diencephalon, brainstem, and cerebellum work together to relay and process information, regulate vital body functions, and coordinate movement, balance, and motor learning.

Master this section and you'll be able to

- Identify the basic components of the diencephalon and describe their functions.
- Identify the basic structures of the brainstem and describe their functions.
- Describe the basic structure and function of the cerebellum.

Diencephalon

The **diencephalon** sits deep inside the brain, beneath the cerebrum, and makes up the walls of the third ventricle. Its name means “through brain” because almost all signals going to and from the cerebrum must pass through it. The one exception is the sense of smell, which connects directly to the cerebrum. The diencephalon includes three major regions: the **epithalamus**, **thalamus**, and **hypothalamus**.

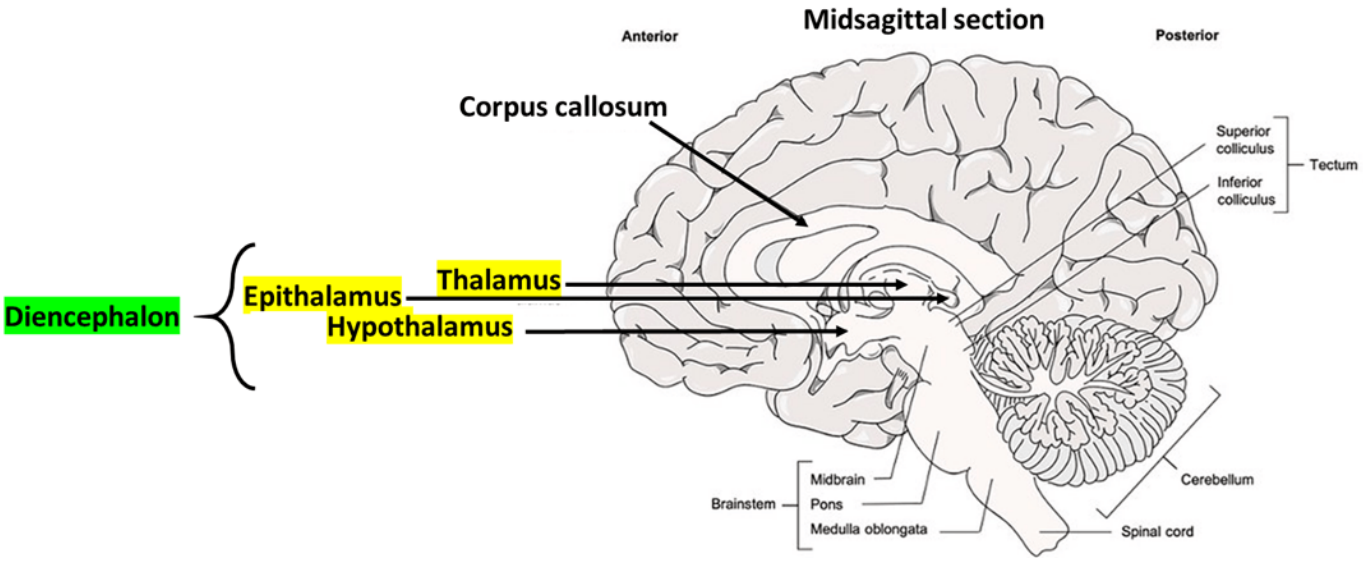


Figure $6.9B.1$: **Diencephalon**. Midsagittal section of the diencephalon and its major subdivisions in relation to surrounding brain structures. The diencephalon consists of the thalamus, hypothalamus, and epithalamus. These regions form the walls of the third ventricle and serve as critical relay and regulatory centers.

Epithalamus

The **epithalamus** forms the back roof of the third ventricle and contains the **pineal gland**, which produces melatonin to regulate sleep-wake cycles (the circadian rhythm). Other nuclei in this region also connect with the limbic system and influence emotional responses to odors.

Thalamus

The **thalamus** is a pair of oval structures packed with many nuclei. It acts as the brain’s “**relay station"**, the switchboard of information. All sensory information (except for smell) passes through thalamic nuclei before reaching the cerebral cortex.

But the thalamus does more than relay — it also helps decide what sensory input is important, such as which sights or sounds

to pay attention to. It also communicates with the cerebellum and brainstem to help coordinate motor commands from the cerebrum. Thalamic nuclei have strong reciprocal connections with the cerebral cortex, forming thalamo-cortico-thalamic circuits that are believed to be involved with consciousness. The thalamus plays a major role in regulating arousal, awareness level, and activity. Damage to the thalamus can lead to permanent coma.

Hypothalamus

The **hypothalamus**, located just below the thalamus, is a key regulator of **homeostasis**. It controls the autonomic nervous system and influences the endocrine system through its connection with the pituitary gland. By releasing special neurohormones (hypothalamic releasing and inhibiting hormones), it regulates the secretion of pituitary hormones.

The hypothalamus is essential for maintaining body temperature, hunger, thirst, fatigue, sleep, and circadian rhythms. It also contributes to memory and emotion as part of the limbic system. At its posterior end, the **mammillary bodies** play a critical role in episodic memory, or the recall of everyday events.

Overall, the hypothalamus coordinates a wide range of vital functions, many of which relate directly or indirectly to the regulation of visceral activities through the autonomic nervous system and other brain regions.

Brainstem

The brainstem is the lowest part of the brain, where it directly connects with the spinal cord. Although small in size, it is one of the most vital regions because nearly all communication between the brain and the body passes through it.

Beyond serving as a **"highway" for signals** — both sensory (touch, pain, temperature) and motor commands — the brainstem also functions as a **control center**. It regulates breathing, heart rate, and blood pressure, and it plays a central role in consciousness, alertness, and the sleep–wake cycle. The brainstem also gives rise to cranial nerves III through XII, which control most of the motor and sensory functions of the head and neck.

Structurally, the brainstem consists of three regions: the **midbrain**, **pons**, and **medulla oblongata**. Together, these form a tapering structure that links the brain to the spinal cord. Attached to the back of the brainstem, though considered a separate region, is the **cerebellum**.

The cranial nerves connect through the brainstem, carrying sensory input and motor output for the head and neck, including most of the special senses (vision, hearing, taste, and balance). In addition, the brainstem serves as the passageway for major ascending (sensory) and descending (motor) pathways between the spinal cord and the cerebrum.

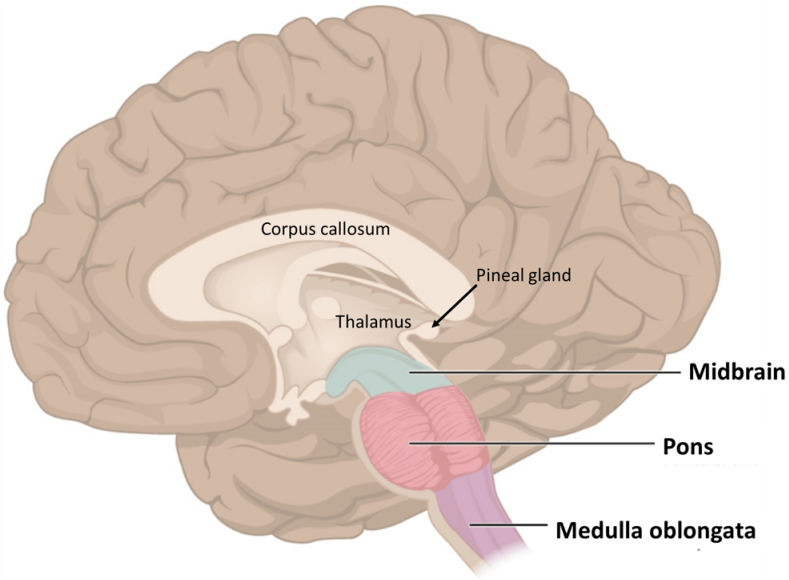
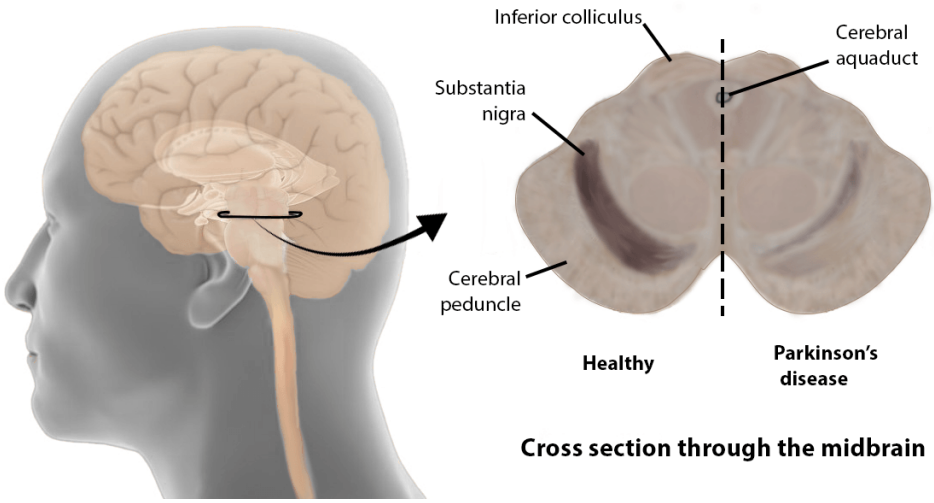


Figure 6.9B.2: **Brainstem.** The three main components — **midbrain**, **pon**s, and **medulla** — are highlighted.

Midbrain



The midbrain is the uppermost part of the brainstem. It is a relatively small section of the brain located between the **thalamus** (above) and the **pons** (below). It acts as a communication highway, passing signals between the brain, spinal cord, and other brainstem regions.

It contains structures that help process what is seen and heard, control eye movements, and regulate reflexes like pupil responses.

The midbrain also has **nuclei**, including the **substantia nigra** (Latin for "black substance," due to its dark appearance in the brain), which is key for movement control because it creates **dopamine**. Dopamine acts as the brain's "messenger" for movement: it helps fine-tune signals so that people can start, stop, and control their movements fluidly.

Figure 6.9B.3: **Midbrain in Health and Parkinson's Disease.**
The image shows the location of the midbrain in a sagittal view of the brain (left) and a transverse section through the midbrain (right). In the healthy brain (left half of the transverse section), the substantia nigra appears as a darkly pigmented band. In Parkinson's disease (right half of the section), this pigmentation is lost due to degeneration of dopaminergic neurons. *Image credit: "Midbrain Cross Section" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

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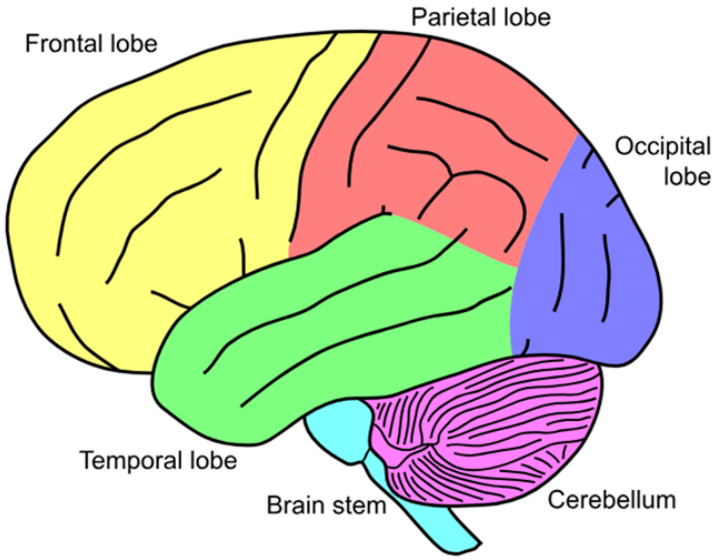
Midbrain: Parkinson's Disease

Parkinson's disease is a disorder of the basal nuclei, specifically of the substantia nigra, that demonstrates the effects of the direct and indirect pathways. Parkinson's disease is the result of neurons in the substantia nigra pars compacta dying. These neurons release dopamine into the striatum. Without that modulatory influence, the basal nuclei are stuck in the indirect pathway, without the direct pathway being activated. The direct pathway is responsible for increasing cortical movement commands. The increased activity of the indirect pathway results in the hypokinetic disorder of Parkinson's disease.

Parkinson's disease is neurodegenerative, meaning that neurons die that cannot be replaced, so there is no cure for the disorder. Treatments for Parkinson's disease are aimed at increasing dopamine levels in the striatum. Currently, the most common way of doing that is by providing the amino acid L-DOPA, which is a precursor to the neurotransmitter dopamine and can cross the blood-brain barrier. With levels of the precursor elevated, the remaining cells of the

substantia nigra pars compacta can make more neurotransmitter and have a greater effect. Unfortunately, the patient will become less responsive to L-DOPA treatment as time progresses, and it can cause increased dopamine levels elsewhere in the brain, which are associated with psychosis or schizophrenia.

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



Cerebellum

The **cerebellum**, as the name suggests, is the "little brain". Similar to the brain, the cerebellum contains an outer layer of gray matter, an inner layer of white matter and deep **cerebellar nuclei**. The white matter of the cerebellum is called **arbor vitae** ("tree of life") for its appearance that reminds that of branches of a tree.

The cerebellum is the part of the brain that helps with **movement**, **balance**, and **coordination**. It has a middle region, called the **vermis**, which connects the two sides of the cerebellum. The vermis is important for balance and movements of the body's center, like walking.

When the motor cortex in the frontal lobe sends a command to the spinal cord (such as to start walking), a copy of that command is also sent to the cerebellum. The cerebellum then compares that plan with sensory feedback from muscles, joints, and balance organs. If conditions change, such as walking on uneven ground or against strong wind, the cerebellum sends corrective signals to adjust the movement.

The cerebellum is also important for procedural memory, or "muscle memory." This is the type of learning involved in skills like riding a bike or playing an instrument.

Alcohol or drugs such as ketamine have a strong effect on the **cerebellum**, the brain's movement coordination center. The cerebellum depends on accurate communication between sensory input (balance, proprioception, vision) and motor output

(muscle commands). Alcohol interferes with how neurons in the cerebellum receive and send signals. This disruption makes it harder for the cerebellum to compare sensory feedback with planned movements. As a result, movements become unsteady, speech can be slurred, and balance is lost. These problems are called **ataxia** — a lack of voluntary coordination of muscle movements.

That is why someone who has been drinking may stagger when walking, sway while standing, or fail a field sobriety test like "walking in a straight line."

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- 12.4: Brain- Diencephalon, Brainstem, Cerebellum and Limbic System by Whitney Menefee, Julie Jenks, Chiara Mazzasette, and Kim-Leiloni Nguyen is licensed CC BY 4.0.

6.11: Neurophysiology

When a neuron is stimulated, an electrical impulse is generated and conducted along the length of its axon. This process, called action potential, underlies many nervous system functions.

Master this section and you'll be able to

- Define voltage and current and explain how they relate to charge movement across the cell membrane.
- Describe how ion gradients and diffusion contribute to the resting membrane potential.
- Differentiate between ion channels and ion pumps, giving examples of leak, gated, and sodium–potassium pumps.
- Explain how membrane potential changes during depolarization, hyperpolarization, and action potentials.
- Distinguish between graded potentials and action potentials, including their size, distance, and role in signaling.

Principles of Electricity

Voltage: Stored Electrical Energy

Voltage is a measure of **potential energy created by separating charges.** It is measured in **volts** or **millivolts**. The bigger the difference in charge between two points, the higher the voltage. In neurons, voltage tells us how much work would be needed to move a charge across the cell membrane. Voltage can represent energy waiting to be used (like a charged battery) or energy that is being released or lost.

Current: The Flow of Charge

Current is the **actual movement of electrical charge** from one point to another. How much charge flows depends on two things:

- **Voltage** (the driving force)
- **Resistance** (the hindrance to flow)

In the nervous system, resistance is influenced by things like the myelin sheath, which acts as an insulator to reduce charge leakage.

Electricity in the Body

In neurons, electrical currents are created by the movement of **ions** (charged particles) across the plasma membrane. Because there is a small difference in the number of positive and negative ions inside versus outside the cell, a **potential difference** (voltage) exists across the membrane.

Role of Diffusion

Ions naturally spread out through **diffusion**, moving from areas of high concentration to low concentration. This movement changes the electrical potential across the membrane and influences how current flows. In neurons, this process is the foundation of nerve signals.

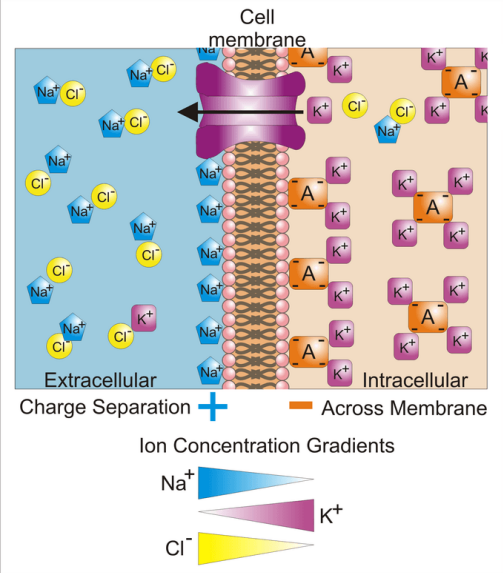
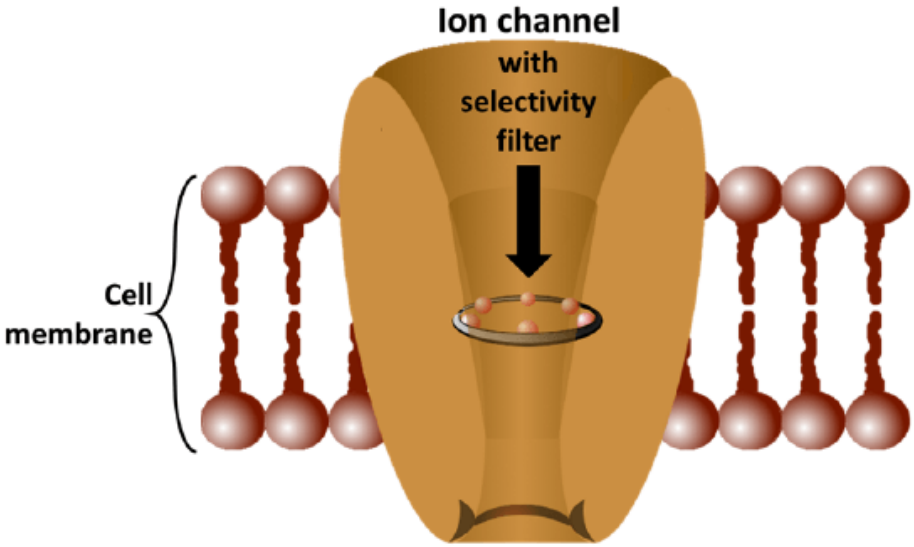


Figure 6.11.1: **Different Ion Concentrations Across the Cell Membrane.** Differences in ion concentrations across a cell's membrane create an electrical voltage known as the membrane potential. Several ions contribute to this gradient. Potassium (K^+) is more concentrated inside the cell than outside, while sodium (Na^+) and chloride (Cl^-) are more concentrated outside the cell than inside. These gradients store potential energy, which drives the generation and maintenance of the membrane potential.

Ion Channels



Ion channels are special proteins in the cell membrane that let ions move into or out of the cell. They are highly selective, usually allowing only one type of ion to pass. Because the channel pores are very narrow, ions move through them one at a time — like people passing through a turnstile gate.

Some ion channels, called **leak channels**, are always open, allowing ions to move steadily across the membrane.

Most ion channels, called **gated channels,** shift between **open** or **closed** states in response to different signals.

- In their **closed state**, the pore may contract so the ion cannot fit through, or another part of the protein may act like a "stopper" blocking the passage.
- In their **open state**, the pore is clear, and ions can move through freely.

When a channel opens, ions flow through the pore according to their **concentration gradient** and **electrochemical driving**

force. The **rate of flow** depends on two factors:

1. The channel's maximum conductance (how well it lets ions through).
2. The electrochemical driving force for that particular ion.

Three Main Types of Gated Ion Channels

1. **Ligand-gated (chemically gated) channels:** These channels open when a specific chemical signal (a **ligand)**, binds to them. Many of these channels serve as **neurotransmitter receptors** at postsynaptic sites, where they open in response to neurotransmitters released from the presynaptic axon terminal. Depending on the channel, ligands may bind on the **outside** of the membrane (extracellular) or on the **inside** (intracellular).

2. **Voltage-gated channels:** These channels open or close in response to changes in the voltage across the membrane (the **membrane potential**). Each type is selective for a particular ion and responds to a specific voltage range. Many are also **time-dependent**, meaning they do not open instantly when the voltage changes but after a short delay. These channels are crucial for generating and propagating **action potentials**, the electrical signals that travel along neurons.

3. **Mechanically gated channels:** These channels open or close in response to **physical (mechanical) forces** which deforms the cell membrane, such as due to pressure. **Stretching, vibration, or touch** can also be used as a signal. When the membrane is pushed or pulled, the channel's protein structure changes shape, allowing ions to pass through.
   In the skin, mechanically gated channels let us sense **touch and pressure**. In the ear, they play a key role in **hearing**, where vibrations from sound waves bend tiny hair cells and open the channels.

Ion Pumps

Ion pumps **are not ion channels**, but are critical membrane proteins that carry out **primary active transport** by using cellular energy (ATP) to **"pump" the ions against their concentration gradient.** Such ion pumps take in ions from one side of the membrane (decreasing its concentration there) and release them on the other side (increasing its concentration there).

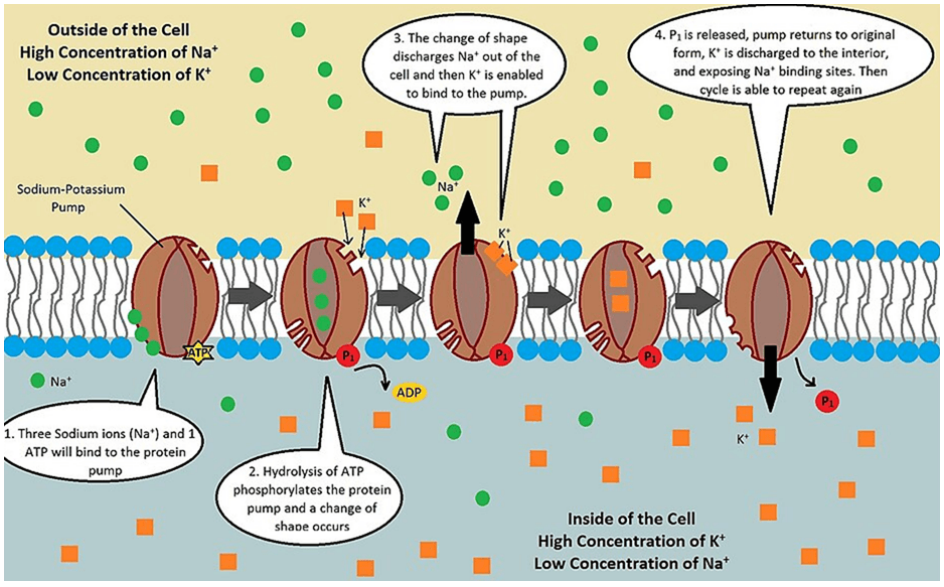


Figure 6.11.2: **The Sodium–Potassium Pump.** This pump uses energy from ATP to move ions across the cell membrane. For every cycle, it pushes 3 sodium ions (Na^+) out of the cell and brings 2 potassium ions (K^+) in. This creates and maintains the concentration differences needed for nerve signals, muscle contractions, and many other cell functions.

Membrane Potentials as Signals

What Is Membrane Potential?

The **membrane potential** is the difference in electrical charge between the inside and outside of a cell. Most animal cells have a **negative charge inside** compared to the outside.

The plasma membrane, made of a lipid bilayer with proteins, acts like both an **insulator** and a **selective gate**, controlling which ions can move in or out.

In the paragraphs above you have learned **how ions can move.** Let's review briefly:

- **Active transport (pumps):** Some proteins (like the sodium-potassium pump) use energy to push ions across the membrane against their concentration gradient, thereby creating concentration gradients.
- **Passive transport (channels):** Ion channels let ions flow back down those gradients without using energy, a process called **facilitated diffusion**.

Membrane potentials work like **batteries**, providing energy to run many cell processes. They are the key for sending electrical signals in neurons and muscle cells (the two excitable cells in the human body.) Signals are created when ion channels open or close, changing the membrane potential at one spot and spreading the current along the membrane.

Resting Potential and Changes

At rest, most neurons have a **resting membrane potential of about –70 millivolts.** This means the cell membrane is polarized, with the inside of the cell more negative than the outside.

👉 If the inside becomes **less negative** (e.g., –70 mV → –60 mV), this is called **depolarization**.

👉 If it becomes **more negative** (e.g., –70 mV → –80 mV), this is called **hyperpolarization**.

A **graded potential** is a small, temporary change in a cell's membrane potential that varies in size (it can be bigger or smaller depending on how many ion channels open). Unlike an action potential, it does not travel long distances — it stays local and fades as it spreads.

In electrically active tissue, the potential difference between any two points can be measured by inserting an electrode at each point and connecting both electrodes to to a specialized voltmeter.

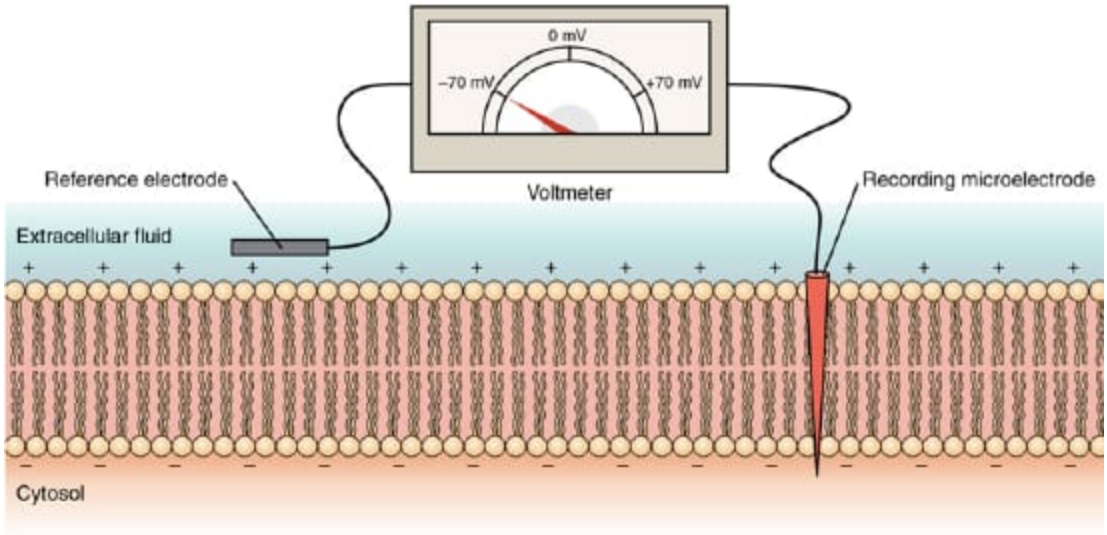


Figure 6.11.3: **Measuring the Voltage Across a Cell Membrane.** A recording microelectrode is placed inside the cell and a reference electrode is placed in the extracellular fluid. The voltmeter shows a resting membrane potential of about –70 mV, with the inside of the cell negative relative to the outside.

Action Potential (AP)

If a depolarization is strong enough, it triggers an **action potential (AP)**: a rapid, large, temporary change in membrane potential from -70mV to +30mV. , sometimes flipping the inside to positive. This lasts only a few milliseconds and is driven by special **voltage-gated ion channels**. APs are how neurons and muscles send fast signals.

An AP is a brief reversal of membrane potential where the membrane potential changes from -70mV to about +40mV. An AP occurs when the membrane potential at the **axon hillock reaches threshold**, triggering a rapid reversal of the membrane potential (depolarization) that travels down the axon.

The action potential has three phases. First is depolarization, followed by repolarization and a short period of hyperpolarization. These three events happen over just a few milliseconds:

1. **Depolarization:** also called the rising phase, it is caused when positively charged sodium ions (Na^+) suddenly rush through **open voltage-gated sodium channels** into a neuron. As additional sodium rushes in, the membrane potential actually reverses its polarity to a positive value for a moment (+40 millivolts).

2. **Repolarization:** also called the falling phase, it is caused by the slow closing of sodium channels and the **opening of voltage-gated potassium channels.** As the sodium ion entry declines, the **voltage-gated potassium channels open and potassium ions rush out of the cell.** This expulsion acts to restore the localized negative membrane potential of the cell.

3. **Hyperpolarization** is a short phase where some potassium channels remain open and sodium channels have closed and reset. The excessive potassium efflux before the potassium channels close leads to a hyperpolarization as seen in a slight dip to about -74 mV following the AP spike.

The propagation of APs is independent of stimulus strength but dependent on refractory periods. The period from the opening of the sodium channels untl; kil the sodium channels begin to reset is called the absolute refractory period. During this period, the neuron cannot respond to another stimulus, no matter how strong.

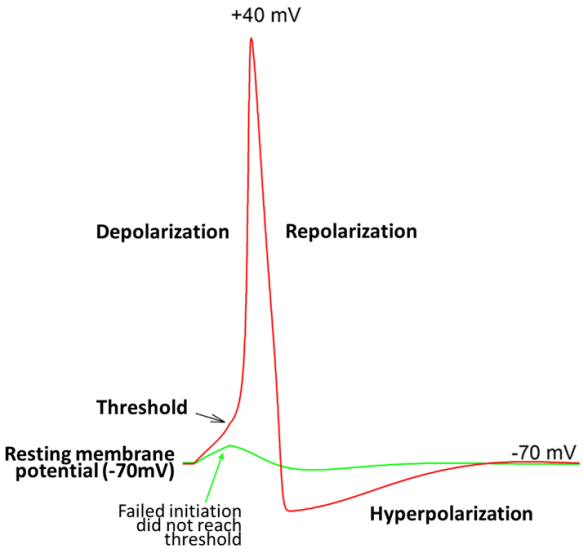


Figure 6.11.4: **Action potential stages.** The red trace shows the changes in membrane voltage during an action potential. At rest, the neuron sits at –70 mV. If a stimulus brings the membrane to threshold, sodium ions rush in and cause **depolarization**, peaking around +40 mV. Potassium ions then exit the cell, driving **repolarization**. The potential briefly dips below resting (**hyperpolarization**) before returning to the resting membrane potential. The green trace shows a subthreshold stimulus that fails to initiate an action potential.

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6.12: Synapses

A synapse is a structural junction that mediates information transfer from one neuron to the next or from one neuron to an effector cell as in muscle or gland.

Master this section and you'll be able to

- Describe the role of a synapse in nervous tissue.
- Compare and contrast electrical and chemical synapses in terms of their structure and function.
- Outline the pathophysiology of two common CNS diseases.

Neurons communicate with other neurons, muscles, or glands by forming synapses with their target cells. The neuron that generates and conducts the action potential down its axon is called the **presynaptic neuron**. The target cell receiving the signal is called the **postsynaptic cell**. The presynaptic cell is always a neuron (since only neurons have axons and can form synapses), but the postsynaptic cell may be another neuron or a different type of cell such as skeletal, cardiac, or smooth muscle, or even a gland.

In Figure 6.13.1, a presynaptic neuron forms synapses with two postsynaptic neurons. The signal, or nerve impulse, travels from the presynaptic neuron to the postsynaptic cell by crossing the narrow gap between them, called the **synaptic cleft**. This transmission occurs in two ways:

1. **electrical synapses,** and
2. **chemical synapses** (more common and more versatile).

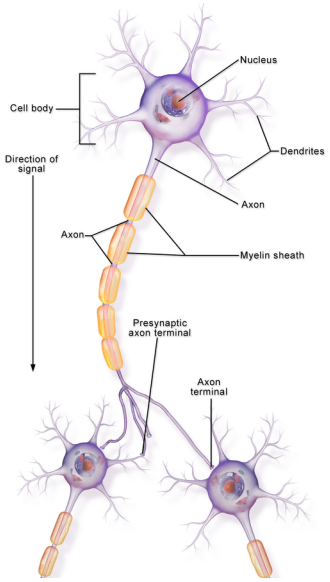


Figure 6.12.1: **Presynaptic and postsynaptic neurons.** A presynaptic neuron on top forms synapses with two postsynaptic neurons at the bottom. The parts of the presynaptic neuron are labeled as cell body, nucleus, dendrites and axon covered in a myelin sheath. The direction of signal shows that the electrical signal (action potential) travels from the axon of the presynaptic neuron to the axon terminals of the presynaptic neuron that are in contact with the dendrites and cell body of the postsynaptic neurons. *(Image credit: "Neuron Part 1" by BruceBlaus is licensed under CC BY-SA 4.0.)*

Chemical Synapses

There are two varieties of synapses: electrical and chemical synapse. Most synapses in the nervous system are **chemical**

synapses, where information is passed from one cell to another using chemical messengers, molecules called **neurotransmitters**.

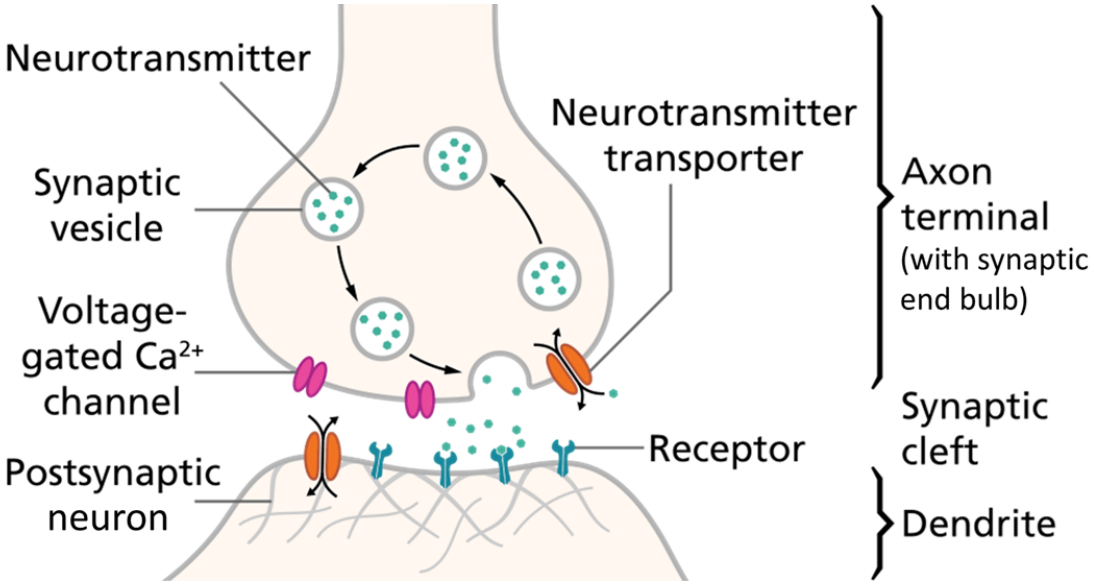
In a chemical synapse, the plasma membrane of the **presynaptic neuron** (the sender) lies very close to the plasma membrane of the **postsynaptic cell** (the receiver), but the two do not touch. Instead, they are separated by a tiny gap called the **synaptic cleft**. The close alignment of the two cells is maintained by specialized synaptic adhesion molecules.

When an **action potential** arrives at the axon terminal of the presynaptic neuron, it triggers the opening of **voltage-gated calcium channels**. Calcium ions rush in and stimulate synaptic vesicles to fuse with the presynaptic membrane, releasing neurotransmitters into the synaptic cleft.

These neurotransmitters then diffuse across the cleft and bind to specific **receptors** on the postsynaptic membrane. Each neurotransmitter has its own set of receptors — for example, **acetylcholine**, **noradrenaline** (also known as norepinephrine), **serotonin**, and **glutamate** all have distinct receptor types. Because of this receptor diversity, chemical synapses can be classified by the neurotransmitter they use, for example: **Cholinergic synapses** (use acetylcholine) and **adrenergic synapses** (use noradrenaline).

Depending on which neurotransmitter is released and which receptor is activated, the postsynaptic cell may:

- Generate a new **electrical response** (excitatory or inhibitory).
- Activate a **second messenger pathway**, leading to more complex and longer-lasting effects.



Despite their diversity, all chemical synapses share these core components — *compare to Figure* 6.12.2 *on the right:*

- **Synaptic end bulb** of the presynaptic neuron
- **Neurotransmitters** packaged in vesicles
- **Synaptic cleft**
- **Receptors** for neurotransmitters
- **Postsynaptic membrane** of the postsynaptic cell

Figure 6.12.2: **Chemical Synapse.** The axon of the presynaptic neuron terminates at the axon terminal in a synaptic end bulb where the action potential arrives. The arrival of action potential causes the synaptic vesicles containing neurotransmitters to fuse with the membrane and release the neurotransmitters. The neurotransmitters diffuse across the synaptic cleft to bind to its receptor, in this case ligand-gated channels. Neurotransmitters will eventually be cleared from the synapse, in some cases reabsorbed into the presynaptic axon terminal.

Neurotransmission at a Chemical Synapse

Communication between neurons at a chemical synapse happens in a series of quick, coordinated steps:

1. **Arrival of the Action Potential** at the presynaptic axon terminal depolarizes the membrane. --> This depolarization opens voltage-gated **calcium (Ca^{2+}) channels.**
2. **Calcium ions entering the axon terminal** trigger a signaling cascade helping the vesicles containing the neurotransmitter to fuse with the presynaptic membrane.
3. **Neurotransmitter Release** into the synaptic cleft by **exocytosis**. --> The neurotransmitter diffuses across the synaptic cleft.
4. **Neurotransmitter binds to ligand-gated ion channels** (receptors). --> This binding causes the ion channels to open, changing the postsynaptic membrane potential. Depending on the neurotransmitter, the effect may be **depolarization** (excitation) or **hyperpolarization** (inhibition).
5. **Signal Termination.** Neurotransmitters only affect the postsynaptic cell while they are bound to receptors. Their action lasts just a few milliseconds before being stopped by one of three mechanisms:
    - **Reuptake** into the presynaptic neuron or nearby astrocytes.
    - **Enzymatic breakdown** in the cleft (for example, acetylcholinesterase degrades acetylcholine).
    - **Diffusion** away from the synaptic cleft.

Electrical Synapses

Unlike chemical synapses, **electrical synapses** create a direct physical connection between the presynaptic and postsynaptic cells. This connection is formed by **gap junctions**, which are protein channels made of connexins. These channels allow **ions and small molecules** to flow freely between the two cells.

Because the membranes are directly coupled, the **electrical charge of an action potential** in one cell can pass immediately into the next. As a result, if one cell fires, the joined cell will also generate an action potential (Figure \PageIndex3{6{.}12{.}\eatSpaces{3} \endSpaces}\PageIndex3). This transmission is extremely **fast** and more reliable than chemical synapses, since there is no delay for neurotransmitter release and binding.

Electrical synapses, however, lack the ability to **amplify or modify signals** the way chemical synapses can. They simply pass the signal along at the same strength. Although they represent a minority of synapses in the nervous system, electrical synapses are important in specific places where **speed and coordination** are critical. For example, they occur between **cardiac muscle cells in the heart**, where synchronized activity is essential.

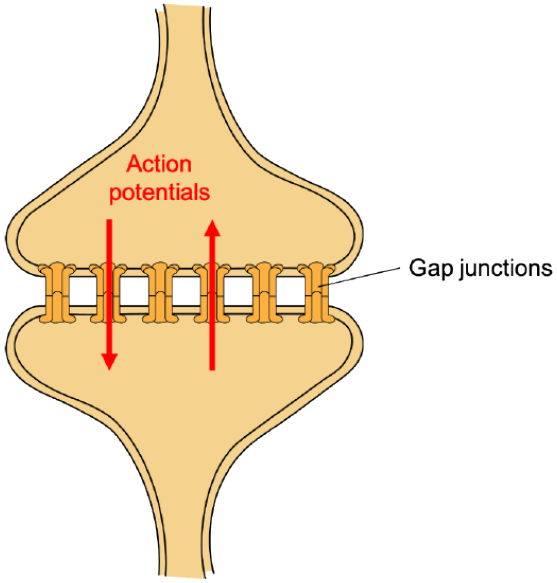


Figure 6.12.3: **Electrical Synapse.** Two synaptic end bulbs form an electrical synapse where gap junctions allow the passage of action potentials from one cytoplasm to the other, and vice versa. *(Image credit: "Electrical Synapse" by Chiara Mazzasette is a derivative from the original work of Daniel Donnelly and is licensed by CC BY 4.0*

DISORDERS OF THE...

Nervous System: Proteopathies in Neurodegenerative Disease

For proteins to work properly, they must fold into precise three-dimensional shapes. This folding depends on the physical and chemical properties of their amino acids. When folding goes wrong — because of aging, genetic mutations, or cellular stress — **misfolded proteins** can build up, lose their normal function, and even gain toxic effects.

In many neurodegenerative diseases, the problem is not just the loss of protein function, but the **toxic accumulation and aggregation** of these misfolded proteins. Their clumping interferes with normal communication between neurons and slowly damages brain cells.

Two well-known examples are **Alzheimer's disease** and **Parkinson's disease**. Both belong to a broader group of disorders called **proteopathies (or proteinopathies)**. In these diseases, specific proteins misfold, lose their normal role, and form aggregates — or clumps — in the brain. Over time, these protein deposits are toxic to neurons and disrupt their cellular health.

Although both Alzheimer's and Parkinson's cause a gradual breakdown of brain function, they affect **different regions of the brain** and therefore produce **distinct sets of symptoms.**

Alzheimer's Disease

Alzheimer's disease is the **most common cause of dementia**, a general term for memory loss and cognitive decline. It mainly affects the **cerebral cortex**, especially areas involved in **memory, reasoning, and personality**.

- In Alzheimer's, abnormal clumps of protein called **beta-amyloid plaques** (dense deposits of a protein fragment) aggregate between neurons in the brain, especially in the **cerebral cortex.** Instead of being cleared by **microglia** (the brain's maintenance cells), these protein fragments accumulate, driving inflammation and neuron loss. Alzheimer's is also characterized by **neurofibrillary tangles** of another protein, **tau**, which further disrupts neuronal function.
- These changes damage and eventually kill neurons, leading to **brain shrinkage** (atrophy) in advanced stages.
- Early symptoms include mild forgetfulness and difficulty finding words. Over time, the disease leads to **severe memory loss**, **confusion**, p**ersonality changes**, and **loss of basic functions** like swallowing.

In short, Alzheimer's progressively destroys **neuronal connections** in the cortex, which explains the decline in thinking, memory, and behavior.

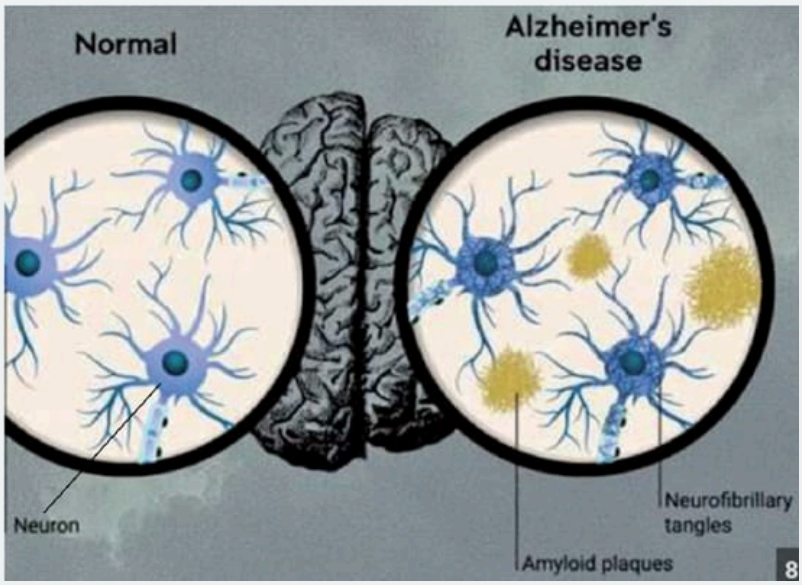


Figure 6.12.4: **Brain Changes in Alzheimer's Disease.** The normal brain on the left shows normal neurons with intact cell bodies and dendrites. On the right is an excerpt of a brain with Alzheimer's disease. The neurons are surrounded by amyloid plaques (yellow clumps) and contain neurofibrillary tangles (twisted fibers inside neurons).

Parkinson's Disease

Parkinson's disease is also a progressive disorder of the nervous system, but it mainly affects movement. It develops when brain cells that normally make **dopamine** begin to die. Dopamine is a chemical messenger (neuromodulator) that helps coordinate smooth and controlled movements. Without enough dopamine, the brain's motor circuits cannot work properly. The symptoms usually become worse over time. While there is no cure, treatments such as medications, physical therapy, and sometimes surgery can help manage the symptoms and improve quality of life.

- A key feature of Parkinson's is the abnormal build-up of a protein called **alpha-synuclein**, which clumps into **Lewy bodies** inside dopamine-producing neurons of the **substantia nigra** (a part of the midbrain). Over time, these neurons degenerate, reducing dopamine levels.
- With less dopamine available, the basal nuclei cannot properly control motor output.
- Symptoms include **tremors (shaking at rest), muscle rigidity, slowness of movement (bradykinesia), and problems with balance and posture**. In later stages, speech and cognitive function may also be affected.

In short, Parkinson's disrupts the **dopamine pathways** in motor areas of the brain, leading to difficulty initiating and controlling movement.

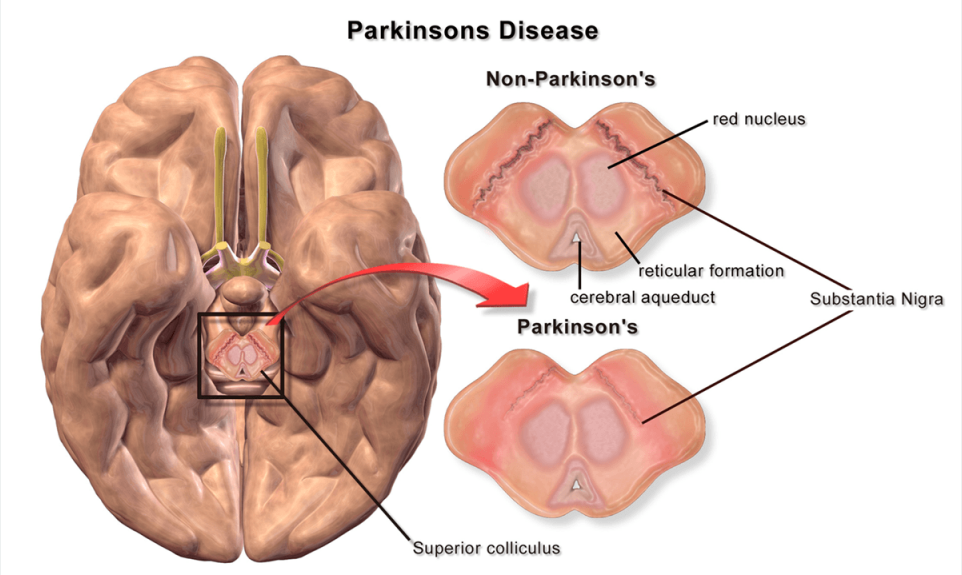


Figure 6.12.5: **Brain Changes in Parkinson's Disease.** Comparison of a healthy brainstem cross-section and one affected by Parkinson's disease. The substantia nigra, a midbrain structure critical for dopamine production, is darkly pigmented in a healthy brain but shows significant loss of pigmentation in Parkinson's disease. This degeneration of dopamine-producing neurons disrupts motor control pathways, leading to the characteristic movement symptoms of Parkinson's disease.

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6.13: Somatic and Autonomic Reflexes

A reflex is a rapid, automatic response to a stimulus that occurs without conscious thought to help protect the body or maintain homeostasis.

Master this section and you'll be able to

- Describe the components of a reflex arc and distinguish between monosynaptic and polysynaptic reflexes.
- Compare and contrast the efferent pathways of the somatic nervous system and the autonomic nervous system.
- Explain how somatic reflexes (e.g., patellar reflex) and autonomic reflexes (e.g., baroreflex) differ in their effectors, speed, and integration pathways.
- Apply knowledge of the baroreflex by explaining how the body adjusts heart rate and blood pressure in response to sudden postural changes (e.g., lying down to standing).

Comparison of Somatic and Autonomic Efferent Systems

The **somatic nervous system (SNS)** is the part of the peripheral nervous system that transmits sensory information from skin, muscles, and joints to the CNS and **controls voluntary movements** via skeletal muscles, allowing you to move consciously.

Somatic reflexes are **automatic, involuntary responses that involve skeletal muscles.** They are controlled by the somatic nervous system, but unlike voluntary movements, they do not require conscious thought. Instead, the response happens quickly and automatically through a reflex arc:

1. **Stimulus detected** – sensory receptors (like pain or stretch receptors) sense a change, such as heat, pressure, or a tap on the tendon.
2. **Signal sent** – sensory neurons carry the information from the receptor to the spinal cord.
3. **Processing** – the spinal cord (sometimes with help from interneurons) interprets the signal without needing the brain's input.
4. **Response command** – lower, somatic motor neurons carry signals from the spinal cord to the skeletal muscles.
5. **Action** – the muscle contracts, producing a quick, automatic movement (like pulling your hand away from something hot).

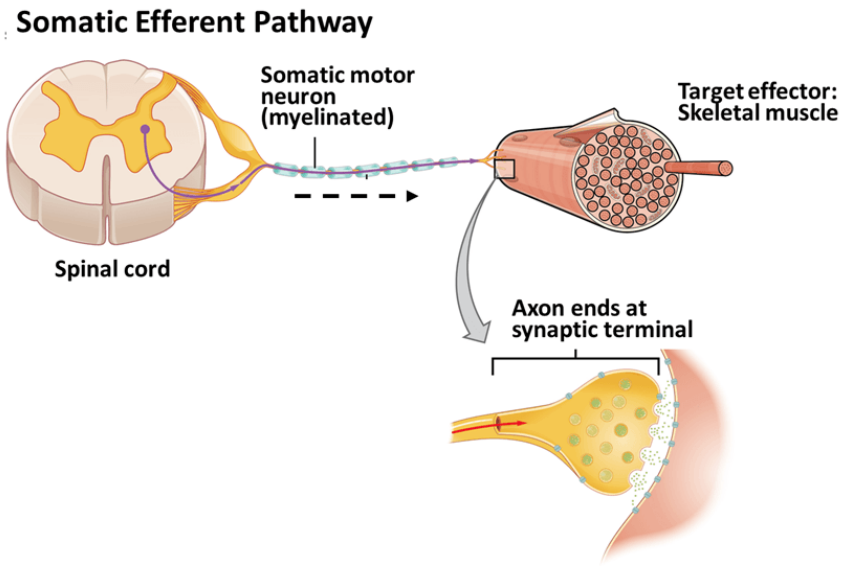


Figure 6.13.1: **Somatic Efferent Pathway.** A motor neuron carries signals from the spinal cord to skeletal muscle. Its axon is myelinated for fast conduction and ends at a synaptic terminal, where it releases neurotransmitters to activate the muscle.

The **autonomic nervous system (ANS)** is the part of the peripheral nervous system that controls the body's involuntary functions. It **regulates the activity of smooth muscle, cardiac muscle, and glands** — things like heart rate, blood pressure, breathing, digestion, and sweating — without you having to think about them.

The ANS maintains balance in the body through its **two divisions:**

- The **sympathetic division**, which prepares the body for action (the "fight-or-flight" response).
- The **parasympathetic division**, which promotes rest, recovery, and energy conservation (the "rest-and-digest" mode).

Most organs receive **dual innervation**, meaning they are controlled by both divisions. The two systems usually work in opposition to maintain homeostasis. For example, the sympathetic division speeds up the heart rate, while the parasympathetic division slows it down, creating a balance that keeps the body stable.

An **autonomic (visceral) reflex** is an **automatic, involuntary response that regulates the activity of smooth muscle, cardiac muscle, or glands.** For example, adjusting heart rate, controlling blood pressure, or making pupils constrict in bright light.

1. **Stimulus detected** – receptors (such as baroreceptors for blood pressure or chemoreceptors for blood gases) sense a change in the internal environment.
2. **Signal sent** – sensory (visceral afferent) neurons carry the information to the spinal cord or brainstem.
3. **Processing** – integration occurs in the spinal cord or brainstem, often involving interneurons.
4. **Response command** – motor signals travel through autonomic motor neurons (preganglionic → postganglionic neurons).
5. **Action** – smooth muscle, cardiac muscle, or glands adjust activity (for example, blood vessels constrict, heart rate slows, glands secrete).

A key difference between somatic and visceral reflexes lies in their **efferent (response) pathways**

- In a **somatic reflex** (for example, the withdrawal reflex), the output is simple: a lower motor neuron in the ventral horn of the spinal cord sends its axon directly to a skeletal muscle, causing it to contract.
- In a **visceral reflex**, the output is more complex and uses a two-neuron chain. A preganglionic neuron begins in the

lateral horn of the spinal cord or a cranial nucleus in the brainstem and projects to an autonomic ganglion. From there, a postganglionic neuron carries the signal to the target effector (such as smooth muscle, cardiac muscle, or a gland).

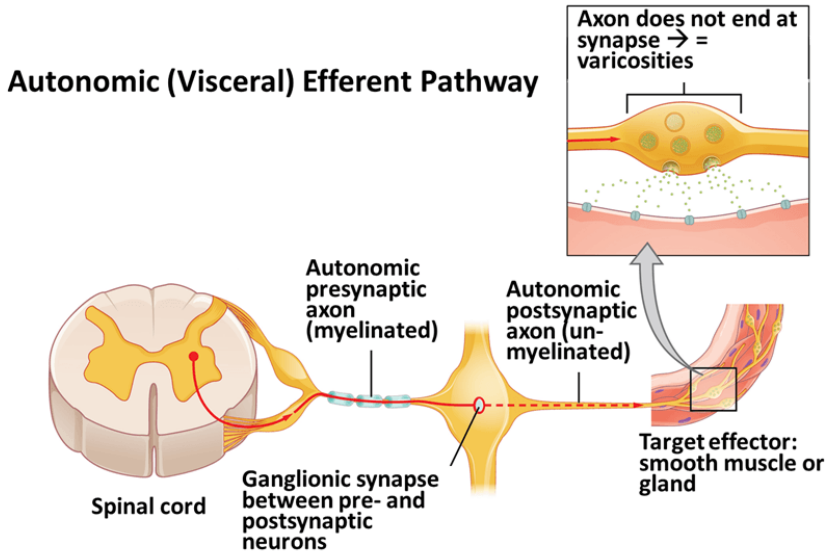


Figure 6.13.2: **Autonomic (Visceral) Efferent Pathway.** Signals from the spinal cord travel along a myelinated presynaptic axon to a ganglion, where they pass to an unmyelinated postsynaptic axon. This axon releases neurotransmitters from many swellings called varicosities to affect smooth muscle or glands, the target effectors.

Somatic vs. Autonomic Reflex Arcs

Feature	Somatic Reflex Arc	Autonomic Reflex Arc
Effector	Skeletal muscle	Smooth muscle, cardiac muscle, glands
Conscious control	None (automatic), but involves voluntary muscles	None (completely involuntary)
Pathway	Sensory receptor → sensory neuron → spinal cord (integration) → **motor neuron** → **skeletal muscle**	Sensory receptor → sensory neuron → spinal cord/brainstem (integration) → **preganglionic neuron** → **postganglionic neuron** → **effector**
Example	Knee-jerk reflex, withdrawal from hot surface	Pupillary light reflex, baroreceptor reflex (blood pressure control)
Speed	Very rapid (direct motor neuron to skeletal muscle)	Slower (two-neuron chain in motor pathway)

Examples of Somatic Reflexes

Patellar (Knee-Jerk) Reflex

The knee-jerk (patellar) reflex tests the femoral nerve. View the video showing an example of the patellar reflex test.

1. Allow the subject to sit comfortably with their legs hanging. Their feet should NOT touch the ground.
2. Strike the ligament portion of the patellar tendon just below the patella (kneecap) and observe the resulting contraction of the quadriceps muscles and extension of the lower leg.

View the video showing an example of the ankle-jerk reflex.

YouTube Video

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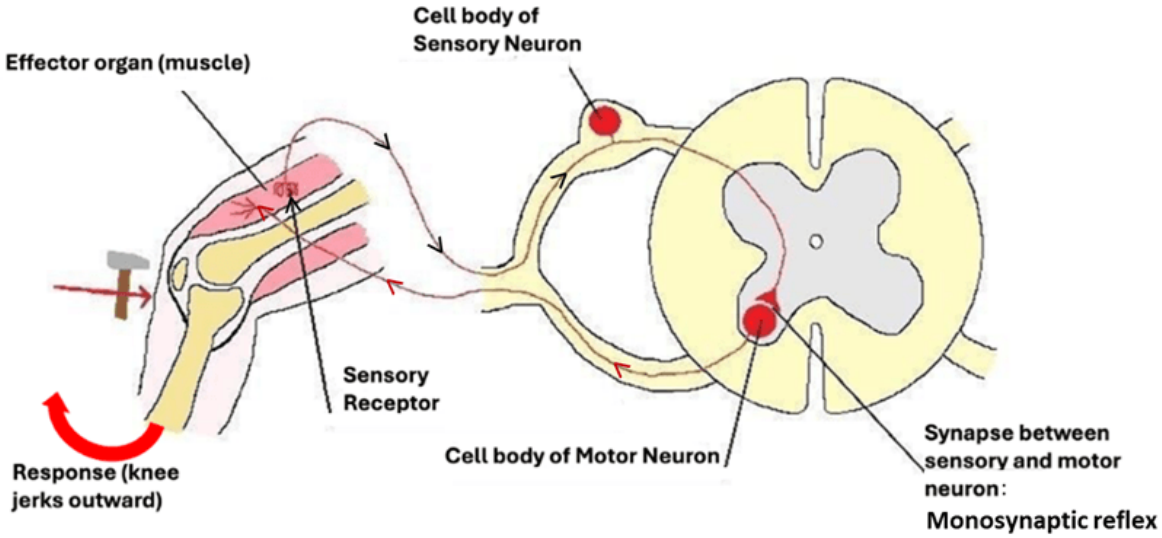


Figure 6.13.3: **Monosynaptic Reflex Arc (Knee-Jerk Reflex).** The patellar tendon tap stretches the quadriceps muscle, activating sensory receptors (muscle spindles). A sensory neuron carries the signal to the spinal cord, where it directly synapses with a motor neuron (monosynaptic reflex). The motor neuron sends an impulse back to the quadriceps muscle, causing contraction and the outward jerk of the lower leg.*(Image credit: "Русский" by* Вера Милова; Лида Милова, *licensed under CC0 1.0, via wikimedia commons) / Labels by Harmony Folse*

Achilles Tendon (Ankle-Jerk) Reflex

The ankle-jerk reflex tests nerves within the sacral plexus.

1. Have the subject sit comfortably on the table with his or her legs free over the edge.
2. With the shoe off, hold and push the subject's foot upward slightly then strike the Achilles (calcaneal) tendon at the level of the ankle and observe the resulting plantar flexion of the foot. **Plantar flexion** is seen as a downward movement of the foot, as occurs when a person points their toes.

View the video showing an example of the ankle-jerk reflex.

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Examples of Autonomic Reflexes

As mentioned above, **autonomic reflexes** are involuntary, unconscious responses mediated by the autonomic nervous system. They help regulate essential bodily functions, such as heart rate, digestion, blood pressure, respiratory rate, and pupil size. Unlike somatic (voluntary) reflexes, which control skeletal muscle, autonomic reflexes affect internal organs, smooth muscle, and glands.

A common example of an **autonomic reflex** is the **pupillary light reflex**. When bright light shines into your eyes, the pupils automatically constrict and get smaller to protect the retina from too much light. This happens without you thinking about it, because smooth muscles in the iris are controlled by the autonomic nervous system, not by voluntary control. We will study this reflex in more detail when we cover the eye and vision.

The Baroreflex: Your Built-In Blood Pressure Regulator

Another important autonomic reflex is the **baroreflex**, which helps keep your blood pressure in balance without you ever having to think about it. Special stretch receptors called **baroreceptors** sit in the walls of your **aorta** and **carotid arteries** (specifically in the **carotid sinuses**). When blood pressure rises, these receptors sense the stretch and send a signal to your brain.

- **Carotid baroreceptors** send their signal through the glossopharyngeal nerve (cranial nerve IX).
- **Aortic baroreceptors** send theirs through the vagus nerve (cranial nerve X).

The signals travel to the cardiovascular centers in the medulla of the brainstem. The brain then tweaks your autonomic nervous system: it eases up on sympathetic stimulation and boosts parasympathetic signals, slowing the heart rate and relaxing blood vessels. The end result is a gentle lowering of blood pressure back toward normal.

Here is a real-life example: Imagine a student who forgot about an exam and suddenly hears me announce: "Exam Time!" Their blood pressure spikes instantly. The baroreceptors sense the stretch, send emergency messages to the brain, and the medulla quickly calms things down by slowing the heart and relaxing the blood vessels (= vasodilation). Thanks to the baroreflex, the student's body is at least calmer — even if their brain is still panicking about the exam.

Baroreflex Arc (Simplified):

- **Stimulus:** Blood pressure rises → blood vessel walls stretch.
- **Receptors:** Baroreceptors (stretch receptors) in carotid sinus and aortic arch take notice.
- **Signal:** Glossopharyngeal nerve (IX) + vagus nerve (X) are the afferent pathway to the medulla.
- **Integration:** Medulla integrates info and sends autonomic output.
- **Response:** ↓ Sympathetic activity, ↑ Parasympathetic activity.
- **Effectors:** Heart rate slows, vessels dilate (relax) → blood pressure falls back to normal.

Baroreflex Demo: Try It Yourself



1. Lie down for a few minutes. Take your pulse at your wrist (use index and middle fingers just below the thumb. See image on the right).

2. Stand up quickly and take your pulse again — it should be faster.

Why?
Standing up makes blood pool in your legs, lowering blood pressure. Baroreceptors sense this drop and signal the brain to raise heart rate so your blood pressure goes back up and your blood keeps flowing to your brain.

Watch this video to review the Baroreflex:

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

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Key Terms

- **Reflex:** Involuntary, almost instantaneous movements in response to a specific stimulus.
- **Motor neuron**: A neuron located in the central nervous system that projects its axon outside the CNS and directly or indirectly control muscles.
- **Sensory neuron**: These are typically classified as the neurons responsible for converting various external stimuli that come from the environment into corresponding internal stimuli.
- **Reflex arc**: A neural pathway that controls an action reflex. In higher animals, most sensory neurons do not pass directly into the brain, but synapse in the spinal cord. This characteristic allows reflex actions to occur relatively quickly by activating spinal motor neurons without the delay of routing signals through the brain, although the brain will receive sensory input while the reflex action occurs. There are two types of reflex arcs: autonomic reflex arc (affecting inner organs) and somatic reflex arc (affecting muscles).
- **Monosynaptic reflex arc:** Contain only two neurons, a sensory and a motor neuron. Relatively rare. Examples of monosynaptic reflex arcs in humans include the patellar reflex and the Achilles reflex.
- **Polysynaptic reflex arc :** Most common. Neural pathway that contains multiple interneurons between the sensory and motor neurons.

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6.14: Meninges- Support and Protection of the Brain

The meninges are protective layers of connective tissue that wrap around the brain and spinal cord, cushioning, supporting, and helping shield the CNS from harm.

Master this section and you'll be able to

- Identify and describe the four major protective systems of the central nervous system and explain their role in safeguarding brain and spinal cord function.
- Differentiate the three meningeal layers in terms of location, structure, and function.
- Describe how problems like epidural and subdural hematomas or meningitis can happen.

Protection of the Central Nervous System

By now you know that the CNS is essential for controlling and coordinating nearly every function of the body. Because of its importance, the CNS is guarded by several layers of protection. Any compromise in these protective systems can result in serious problems. The four protective systems of the brain are:

1. **Skull** – The skull is the brain's first line of defense, acting like a hard helmet that protects it from injury.

2. **Blood–Brain Barrier (BBB)** – Unlike other organs, the brain cannot allow just anything from the blood to pass freely into its tissue. This selectivity is due to the **blood–brain barrier (BBB)**, which tightly regulates the movement of substances from the bloodstream into the CNS. The BBB works like a security checkpoint, letting nutrients in while blocking toxins and harmful pathogens, such as bacteria and viruses.

3. **Cerebrospinal Fluid (CSF)** – To further protect and support the brain, some blood is filtered into a clear fluid called **cerebrospinal fluid (CSF)**. CSF circulates through the **ventricles** of the brain and the **subarachnoid space**, cushioning the CNS, maintaining stable chemical conditions, and helping remove waste products. Venous sinuses then carry deoxygenated blood and excess CSF away from the brain. We will take a closer look at CSF in the next section.

4. **Meninges** – Beneath the skull, three layers of **connective tissue membranes**, called the **meninges**, surround the brain and spinal cord. The meninges support, stabilize, and partition the nervous tissue, helping anchor the CNS within the cranial and vertebral cavities.

In this section, we will take a closer look at the three meninges and how each helps protect the brain and spinal cord.

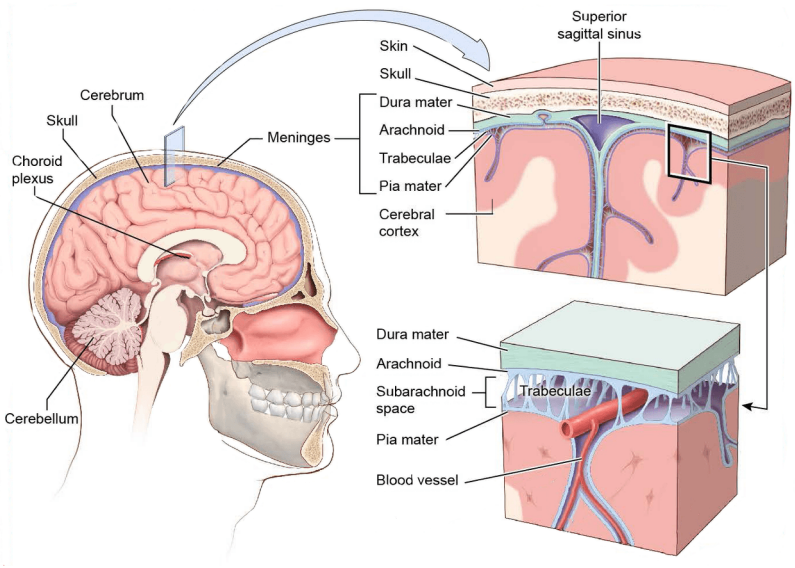


Figure 6.14.1: **Protective structures of the brain.** Superficially, the skin of the scalp and bones of the skull create the first layer of protection. Deep to these layers, the meninges (represented by the dura mater, arachnoid mater and pia mater) cover and partition the brain. Within the meninges, blood inside blood vessels and sinuses, and cerebrospinal fluid within the subarachnoid space and ventricles circulate to support the brain's function. *(Image credit: "Cranial Meninges" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0, modification of image by NIH Medical Arts.)*

Meninges

The outer surface of the CNS (both brain and spinal cord) is wrapped in protective coverings called the meninges. These membranes, made of connective tissue, provide support, stability, and separation. From outermost to innermost, the meninges are the **dura mater, arachnoid mater,** and **pia mater**.

- **Dura mater** – This tough, fibrous layer forms a strong protective sheath around the brain. It is anchored firmly to the inside of the skull and the vertebral canal.
- **Arachnoid mater** – A thin, delicate membrane that loosely envelopes the brain. Beneath it lies the **subarachnoid space**, filled with cerebrospinal fluid and spanned by fine fibers called **arachnoid trabeculae**. These fibers look like a spider's web, which is where the name "arachnoid" comes from.
- **Pia mater** – The innermost layer, a very thin, delicate membrane that clings closely to the brain's surface, following every fold (gyri) and groove (sulci).

Together, these three layers cushion and stabilize the CNS, much like wrapping delicate equipment in several layers of protective padding.

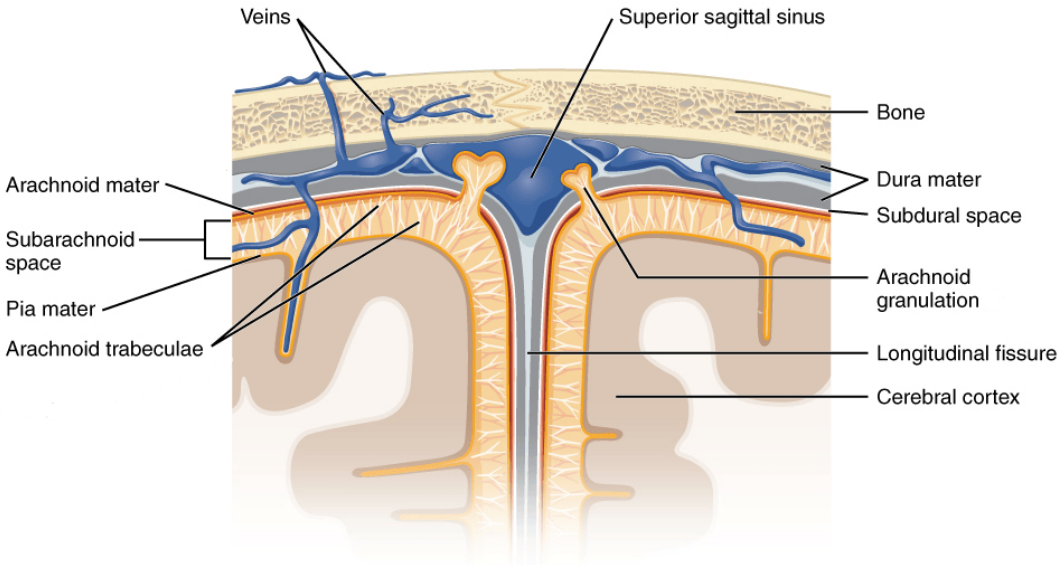


Figure 6.14.2: **Meningeal Layers of the Brain.** The layers of the meninges are shown under neath the bones of the skull. The dura mater is adjacent to the inner surface of the cranium. Within it, veins and the superior sagittal sinus lie. The pia mater is adjacent to the surface of the brain. The arachnoid and subarachnoid space are in-between. An arachnoid villus is shown emerging into the dural sinus to allow CSF to filter back into the blood for drainage. *(Image credit: "Meningeal Layers" by OpenStax is licensed under CC BY 4.0, modifications by Jennifer Lange.)*

Dura Mater

The dura mater is the outermost, toughest meningeal (connective tissue) layer around the brain and spinal cord. Its name is derived from Latin and literally means "**tough mother**".

In the brain, the dura has two layers:

- **Periosteal layer** — attaching directly to the skull , and
- **Meningeal layer** — beneath it.

Most of the time the two layers are fused, but in some areas they separate to form large spaces filled with venous blood called **dural sinuses**.

Around the brain, the space between the skull and dura (**epidural space**) is only a "potential" space, but trauma can cause bleeding here, creating an **epidural hematoma**.

The situation is quite different in the **spinal cord:**

- There, the dura mater has **only the meningeal layer.**
- The **spinal epidural space is a real space**, filled with fat and connective tissue that cushions the cord. This is the site where **epidural injections** are given.

Just beneath the dura mater is another potential space, the **subdural space**, which can also fill with blood after injury, forming a **subdural hematoma.**

The meningeal layer of the dura mater also folds inward to form **sheet-like partitions** that help support and separate parts of the brain An example is the

- **Falx cerebri** → separates the two cerebral hemispheres.
- **Falx cerebelli** → separates the two cerebellar hemispheres.
- **Tentorium cerebelli** → forms a "tent" separating cerebellum from cerebrum.

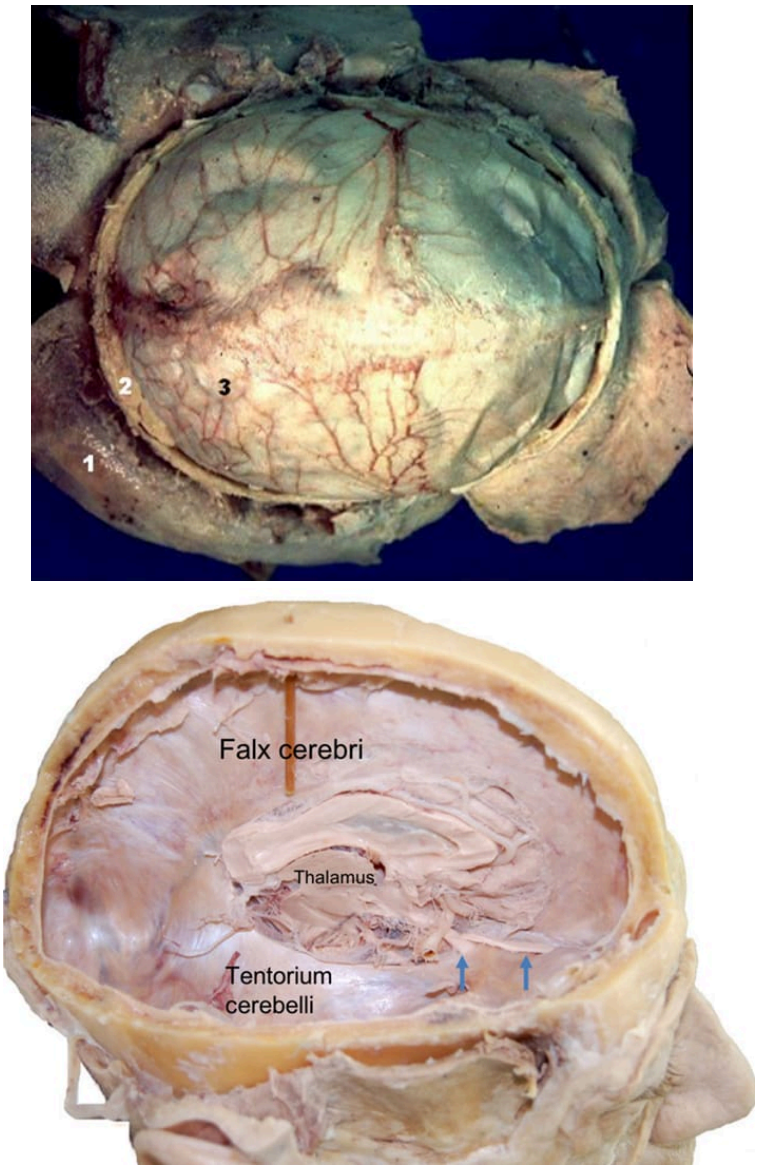
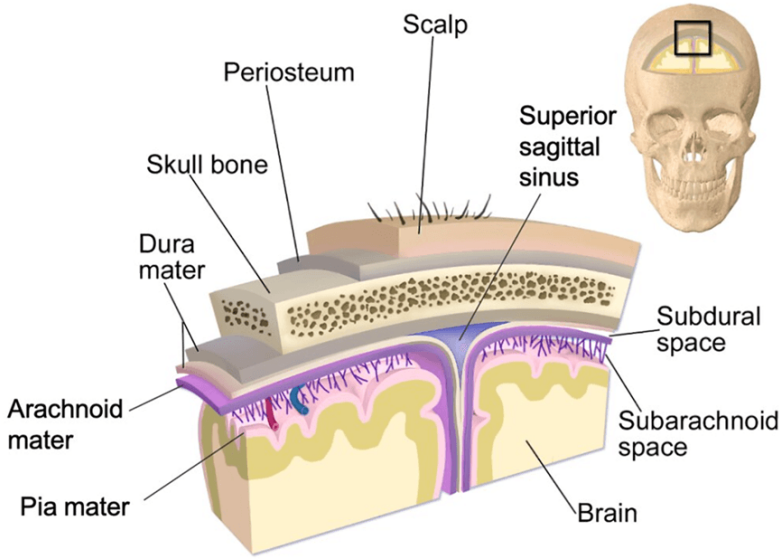


Figure 6.14.3: **Human Brain Showing the Dura Mater.** The dura mater is the outermost of the three meninges.

Image on the left: Following removal of the skull cap, the "tough mother" becomes visible. The numbers represent: 1) skin; 2) skull bone; 3) dura mater.

Image on the right: The **falx cerebri** goes through the midline separation of the brain while the **falx cerebelli** separates the two cerebellar hemispheres. The **tentorium cerebelli** separates the cerebellum from the superior part of the brain (cerebrum), forming a tent-like shape.

Arachnoid Mater



Deep to the subdural space lies the arachnoid mater, the middle meningeal layer (see image on the right). Its name comes from the spider-web appearance of the arachnoid trabeculae — thin strands that stretch across the **subarachnoid space** to the pia mater.

The subarachnoid space is a **real space**, filled with circulating cerebrospinal fluid (CSF).

The arachnoid mater also forms small projections called **arachnoid granulations**, which extend into the dural sinuses. Here, CSF is filtered back into the blood for drainage. (See figure 6.20.2)

Pia Mater

The **pia mater** is the innermost meningeal layer, a thin and delicate fibrous membrane. Its name comes from the Latin for "**tender mother**," reflecting its role as a gentle covering for the CNS.

The pia mater closely follows every fold and groove of the brain and spinal cord. It is anchored to the glial membrane that helps form the blood–brain barrier.

Blood vessels that supply the nervous tissue lie between the pia mater and the CNS itself.

In summary: Think of the meninges like layers of protective clothing. The **dura mater** is a tough leather jacket, the **arachnoid mater** is a soft padded sweater, and the **pia mater** is a thin silk undershirt that clings tightly to the brain and spinal cord.

DISORDERS OF THE...

Meninges: Meningitis

Meningitis is an inflammation of the meninges, the three layers of fibrous membrane that surround the CNS (Figure $6.14.4$). Meningitis can be caused by infection by bacteria or viruses. The particular pathogens are not special to meningitis; it is just an inflammation of that specific set of tissues from what might be a broader infection. Bacterial meningitis can be caused by Streptococcus, Staphylococcus, or the tuberculosis pathogen, among many others. Viral meningitis is usually the result of common enteroviruses (such as those that cause intestinal disorders), but may be the result of the herpes virus or West Nile virus. Bacterial meningitis tends to be more severe.

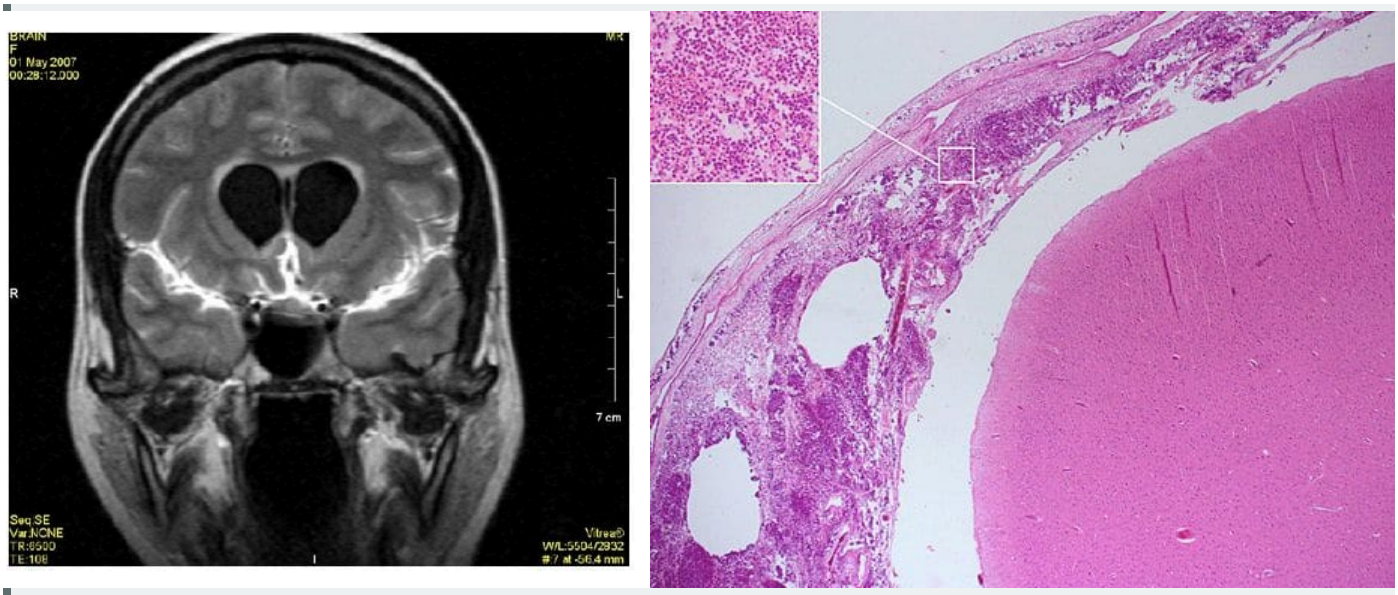


Figure 6.14.4: Meningitis. Inflammation from meningitis shows in an MRI as bright enhancements of meninges at the tentorium and in dilatation of the ventricles. White blood cells accumulate within the meningeal layers. *(Image credits: "FLAIR MRI of Meningitis" by Aneel Kumar Vaswani, Waseem Mehmood Nizamani, Muhammad Ali, Geeta Aneel, Bhesham Kumar Shahani, and Sajjad Hussain Uploaded by Mikael Häggström is licensed under CC BY 3.0, via Wikimedia Commons; "Meningitis Histopathology" by Marvin 101 is licensed under CC BY-SA 3.0, via Wikimedia Commons.)*

The symptoms associated with meningitis can be fever, chills, nausea, vomiting, light sensitivity, soreness of the neck, or severe headache. More important are the neurological symptoms, such as changes in mental state (confusion, memory deficits, and other dementia-type symptoms). A serious risk of meningitis can be damage to peripheral structures because of the nerves that pass through the meninges. Hearing loss is a common result of meningitis.

The primary test for meningitis is a lumbar puncture. A needle inserted into the lumbar region of the spinal column through the dura mater and arachnoid membrane into the subarachnoid space can be used to withdraw the fluid for chemical testing. Fatality occurs in 5 to 40 percent of children and 20 to 50 percent of adults with bacterial meningitis. Treatment of bacterial meningitis is through antibiotics, but viral meningitis cannot be treated with antibiotics because viruses do not respond to that type of drug. Fortunately, the viral forms are milder.

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6.15: Cerebrospinal Fluid and Its Circulation

Cerebrospinal fluid is a clear fluid that acts as a cushion for the brain and maintains overall central nervous system homeostasis.

Master this section and you'll be able to

- Describe the production, flow, and turnover of cerebrospinal fluid (CSF).
- Explain the function of CSF.
- Explain how CSF can be used as a diagnostic tool.

Location of Cerebrospinal Fluid (CSF)

Cerebrospinal fluid, or CSF, is a clear, watery fluid that surrounds and protects the brain and spinal cord. It is located inside

- the **subarachnoid space** occupying the **space between the arachnoid mater** (the middle layer of the meninges) **and the pia mater** (the meningeal layer closest to the brain), and
- **all intracerebral ventricles** (spaces inside the brain), and
- the **central canal of the spinal cord.**

CSF Production and Flow

Most CSF is made in special capillary networks, called the **choroid plexuses**, which lack a blood–brain barrier. Most CSF is made in the **lateral and third ventricles**, and about **100–150 ml** circulates through the CNS at any given time. Its movement is helped by the pulsing of nearby blood vessels, so the fluid is always in motion.

CSF is not identical to blood plasma. It has **less protein, glucose, urea, and certain ions** (like calcium, potassium, and bicarbonate) but **more sodium and chloride**. Its composition is very similar to the fluid that surrounds neurons (interstitial fluid), which highlights its role in maintaining the brain's delicate chemical environment and supporting proper neuron function.

The CSF follows a specific pathway through the brain:

Lateral ventricles → Through the interventricular foramen → Into the **third ventricle** → Down the cerebral aqueduct → Into the **fourth ventricle** → Out into the **subarachnoid space,** where it is called extra-axial CSF and flows around the brain and spinal cord.

Cerebrospinal fluid (CSF) is produced at a steady rate of about 500 milliliters per day. Since the subarachnoid space around the brain and spinal cord can only hold about 135–150 milliliters at any given time, the excess CSF must be drained. This happens through **arachnoid granulations,** which act like one-way valves, releasing CSF into the superior sagittal sinus (a large venous blood channel in the brain).

Because of this, CSF is completely replaced, or "turned over," about 3–4 times each day. This steady circulation helps wash away waste products and keeps the brain environment stable by diluting larger molecules that cannot easily cross the blood-brain barrier.

CSF is not identical to blood plasma, but it does contain a small amount of protein — only about 0.3% of what is found in plasma. This equals roughly 15–40 mg/dL, depending on where the sample is taken.

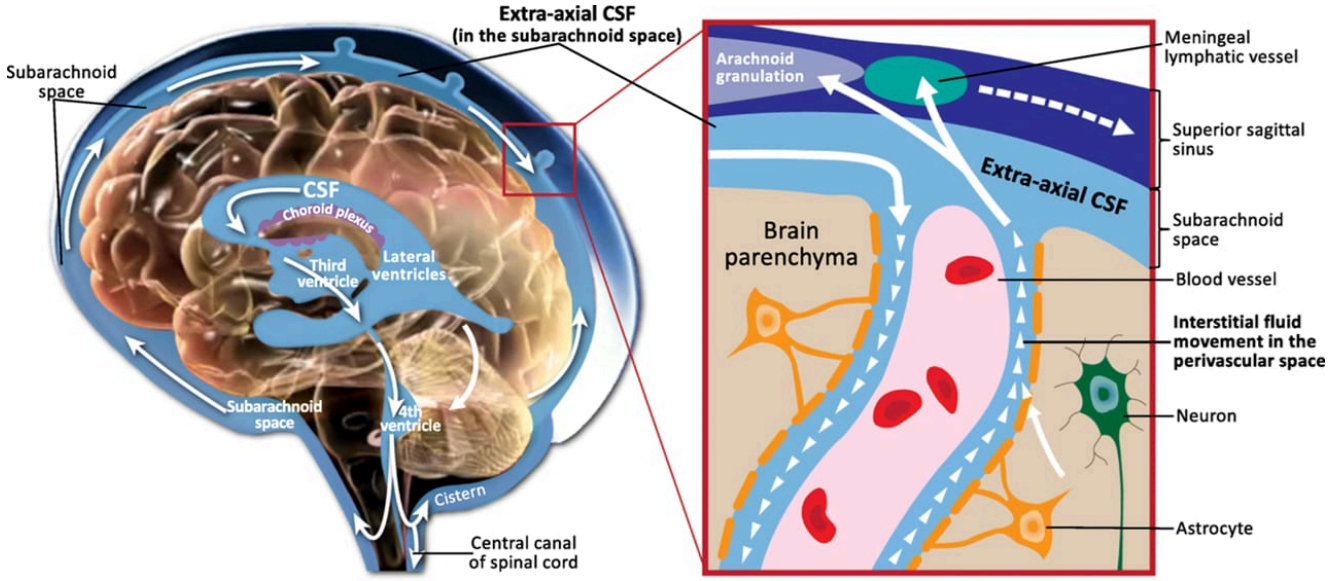


Figure 6.15.1: **Circulation and drainage of cerebrospinal fluid (CSF).** CSF is produced in the choroid plexus of the ventricles and flows through the ventricular system into the subarachnoid space, where it circulates around the brain, providing cushioning and nutrient exchange. CSF is absorbed into the venous blood through arachnoid granulations into the superior sagittal sinus and also interacts with meningeal lymphatic vessels. On the cellular level (right), CSF and interstitial fluid exchange occurs in the perivascular space surrounding blood vessels, involving neurons and astrocytes.

Key Functions of CSF

- **Cushions the brain** and spinal cord and acts as a shock absorber, preventing nervous tissue from directly slamming into bone when the body is jolted or hit.
- **Provides buoyancy** (so the brain "floats" and does not crush itself against the base of the skull). The actual mass of the human brain is about 1,500 grams; however, the net weight of the brain suspended in the CSF is equivalent to a mass of 25 grams. Hence, the entire brain density is cushioned, protecting it from crushing into the bony cranium.
- Helps **remove waste products from the CNS**: The CSF constantly circulates through the ventricles of the brain, around the spinal cord, and through the subarachnoid spaces. Along the way, it picks up waste products.
    - This "used" CSF is then absorbed into the bloodstream through the **arachnoid villi/granulations,** tiny structures that let CSF (and its waste) flow back into venous blood.. Once in the blood, the wastes can be processed and eliminated by the kidneys and liver.
    - Recent research suggests that the brain also has a specialized **glymphatic system**, which uses lymphatic channels to drain waste into nearby lymph nodes. This system is especially active during sleep, when it helps wash away **larger molecules** such as amyloid-beta and tau proteins. Clearing these proteins is important, since their buildup is linked to diseases like Alzheimer's.

  Why it matters: Since neurons are highly sensitive and do not regenerate easily, keeping their environment **free from toxins** is essential for brain health and function. CSF waste removal ensures that the brain maintains the right chemical balance to send and receive signals properly.

Watch this animation on the ventricles and the flow of CSF through the brain and the spinal cord:

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

CSF as a Diagnostic Tool

Cerebrospinal fluid (CSF) is not only important for protection of the brain and spinal cord — it is also an important diagnostic tool. Because CSF bathes the entire central nervous system, changes in its composition often reflect diseases or injuries affecting the brain and spinal cord.

Doctors typically obtain CSF through a **lumbar puncture (spinal tap)** and analyze it for abnormalities in **cells, proteins, glucose, and other biomarkers.** This analysis can help detect conditions such as meningitis and encephalitis (infections), multiple sclerosis (autoimmune disease), subarachnoid hemorrhage (bleeding in the brain), and neurodegenerative disorders like Alzheimer's disease.

CSF can provide clues about infection, inflammation, bleeding, or even cancer. Modern laboratory techniques are expanding its usefulness, allowing detection of disease-specific proteins, such as those linked to neurosyphilis, prion diseases, or early Alzheimer's.

By revealing the biochemical and cellular environment surrounding the central nervous system, CSF analysis plays a key role in early diagnosis, guiding treatment decisions, and predicting outcomes for patients.

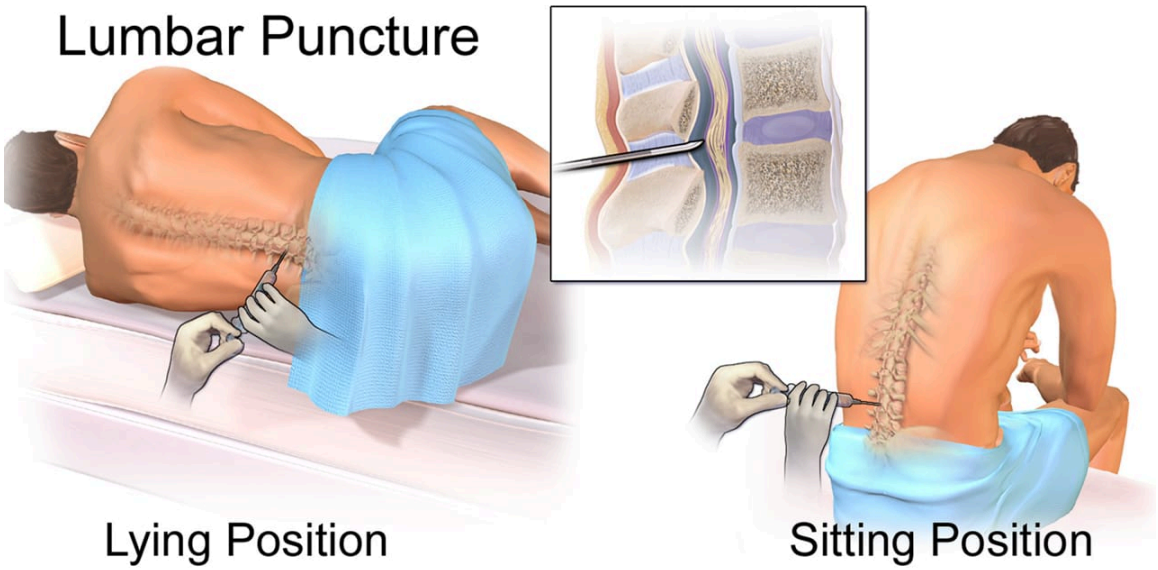


Figure 6.15.2: **Lumbar puncture (spinal tap).** A needle is inserted between the lumbar vertebrae into the subarachnoid space to collect cerebrospinal fluid (CSF) for diagnostic testing. The procedure can be performed with the patient either lying on their side or sitting while leaning forward to open the spaces between the vertebrae.

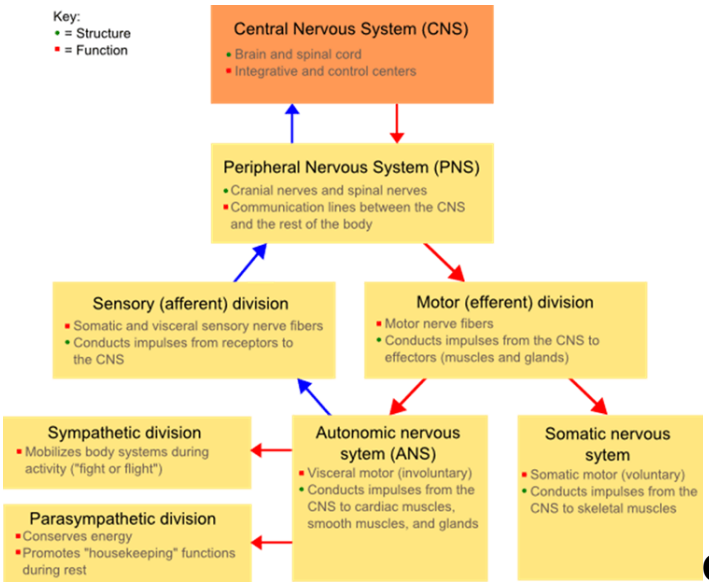
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6.16: The Autonomic Nervous Systems

The peripheral nervous system has a voluntary (somatic) branch and an involuntary (autonomic) branch. The autonomic branch is further divided into the sympathetic (SNS) and parasympathetic (PNS) nervous systems.

Master this section and you'll be able to

- Identify the differences between the somatic and autonomic nervous systems.
- Distinguish between the parasympathetic and sympathetic subsystems of the autonomic nervous system.



Comparing the Somatic and Autonomic Nervous Systems

The **peripheral nervous system (PNS)** is divided into the **somatic nervous system and the autonomic nervous system**.

The **somatic nervous system** is responsible for voluntary control of skeletal muscles and for carrying sensory information (such as touch, pain, temperature, and proprioception) from the skin, muscles, and joints to the central nervous system (CNS). The core of the somatic system consists of **sensory (afferent)** neurons bringing sensory input to the CNS and **motor (efferent)** neurons carrying voluntary motor commands to skeletal muscle fibers.

The **spinal nerves** are mixed nerves that carry both somatosensory information (from body to CNS) and motor commands (from CNS to skeletal muscles). There are **31 pairs of spinal nerves**, which connect most of the body to the CNS. They are vital for both movement and sensation.

The Autonomic Nervous System (ANS)

The **autonomic nervous system** works “below the level of consciousness,” regulating homeostasis and survival processes. It is a division of the peripheral nervous system that acts mostly as an involuntary control system for vital visceral functions — including heart rate, digestion, respiratory rate, salivation, perspiration, pupillary responses, urination (micturition), and sexual arousal.

Most ANS actions are involuntary, but **breathing** is a notable exception: voluntary control (somatic) can override the ANS, though autonomic regulation will resume if conscious control lapses (as during sleep or unconsciousness).

The ANS is **classically divided into the sympathetic and parasympathetic nervous systems (SNS and PSNS)**. The two have

often opposing effects — “**fight-or-flight**” vs “**rest-and-digest**” responses.

The **enteric nervous system** (ENS), which governs (largely independently) the gastrointestinal tract function, is sometimes classified as part of the ANS and sometimes as an independent network — both views are supported in current literature. In this course we will not specifically cover the ENS.

Some body functions, such as breathing and urination, involve both voluntary (somatic) and involuntary (autonomic) control. For example, you can **choose** to hold your breath underwater for a certain time, but your body will eventually **take over automatically** to make sure you keep breathing.

Sympathetic Nervous System (SNS)

The sympathetic nervous system is in charge of the “fight or flight” response. When the body senses danger or stress, the SNS activates many organs at once to prepare you to act — for example, it **speeds up the heart, opens the airways, and slows digestion**.

The SNS nerves branch out from the spinal cord in the chest and upper lower back region (**T1–L2**), which is why it is sometimes called the **thoracolumbar system**. These nerves connect to clusters of neuron cell bodies called **sympathetic chain ganglia**, which run alongside the spine.

A message from the spinal cord travels along a short **preganglionic fiber** to the ganglion, then continues along a longer **postganglionic fiber** to reach the target organ (like the heart, lungs, or digestive tract). This setup allows the SNS to spread its signals widely and quickly throughout the body.

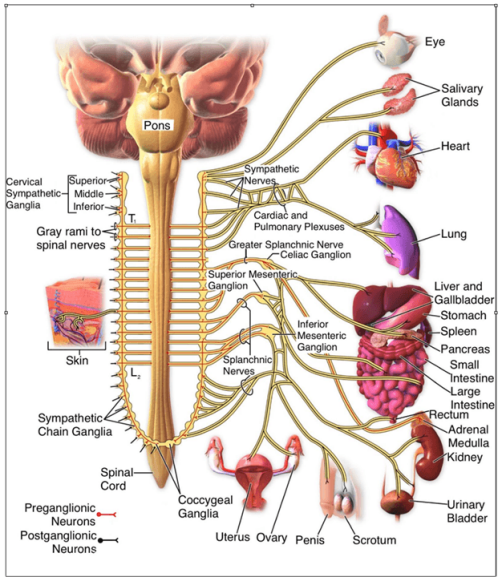


Figure 6.16.1: **Anatomical Organization of the Sympathetic Division of the Autonomic Nervous System.** [3] The sympathetic division arises from the thoracic and lumbar regions of the spinal cord, forming a chain of ganglia adjacent to the vertebral column called the sympathetic chain or paravertebral ganglia. Preganglionic neurons originating from the spinal cord synapse with postganglionic neurons in these ganglia. Postganglionic neurons then project to target organs, including smooth muscle, cardiac muscle, and glands, to regulate various physiological responses, such as the fight-or-flight response.

Parasympathetic Nervous System (PSNS)

The parasympathetic nervous system is in charge of “rest and digest.” It helps the body save energy and carry out everyday functions, like slowing the heart rate, stimulating digestion, and promoting relaxation.

Parasympathetic nerves branch out mainly from the **brainstem** and the **sacral region of the spinal cord** (so it is also called the **craniosacral system**). These nerves connect to ganglia that are usually located very close to — or even inside — the organs they control.

Because of this setup, **preganglionic fibers** in the PSNS are usually long, while **postganglionic fibers** are very short. This allows the parasympathetic system to send more specific, targeted signals, often to just one organ at a time, instead of activating the whole body.

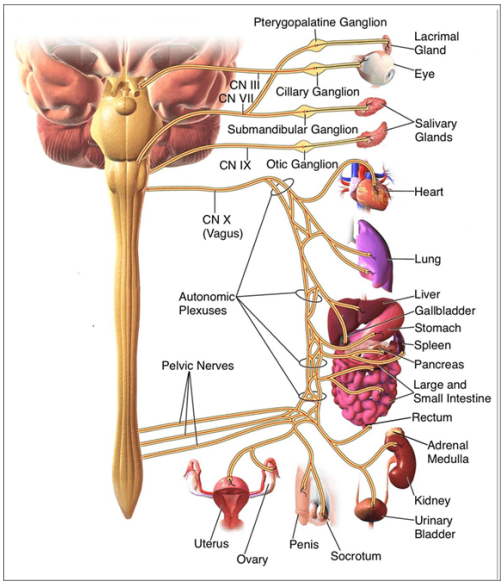


Figure 6.16.2: **Organization of the Parasympathetic Division of the Autonomic Nervous System.**[5] Originating from the brainstem and sacral region of the spinal cord, preganglionic neurons of the parasympathetic division project to terminal ganglia located near or within target organs. Within these terminal ganglia, preganglionic fibers synapse directly with postganglionic neurons. Postganglionic fibers then extend to innervate various target tissues, including smooth muscle, cardiac muscle, and glands, to regulate functions such as digestion, urination, and sexual arousal.

Summary of the Autonomic Nervous System

The autonomic nervous system (ANS) links the CNS to the body's internal organs through preganglionic neurons and ganglia. Its two main divisions — the sympathetic and parasympathetic divisions — generally work in opposition, but this opposition is best seen as complementary. Think of the **sympathetic system as the accelerator** and the **parasympathetic system as the brake**: one prepares the body for quick responses ("fight or flight"), while the other promotes rest, recovery, and routine functions ("rest and digest").

Importantly, the ANS does much more than just prepare us for emergencies or relaxation. Everyday activities — such as standing up without fainting or the beat-to-beat regulation of heart rate — depend on the constant, balanced interplay of both systems. In short, the sympathetic and parasympathetic divisions are always working together, adjusting organ function moment by moment to maintain **homeostasis**.

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6.17: Agonists and Antagonists of the ANS

Agonists and antagonists are types of drugs that interact with the autonomic nervous system (ANS) to either mimic or block its actions.

Master this section and you'll be able to

- Distinguish between the effects of an agonist versus an antagonist in the autonomic nervous system.

What Are Agonists and Antagonists of the ANS?

By learning which neurotransmitters control the autonomic nervous system (ANS), scientists have been able to design drugs that **either mimic their effects or block them.**

Agonists are drugs that **activate** receptors in the ANS, essentially copying or boosting the effects of the body's own neurotransmitters. For example, **Albuterol inhalers** (for asthma) act as beta-2 agonists, causing airway muscles to relax and ease breathing. Beta-2 receptors are tiny "signal switches" found mostly on the smooth muscle cells of the lungs and some blood vessels. When activated, they cause these smooth muscles in the bronchi to relax, which leads to **bronchodilation**, helping to open the airways and improve airflow.

These drugs are often called **sympathomimetics** (if they stimulate the sympathetic nervous system) or **parasympathomimetics** (if they mimic the parasympathetic system).

Antagonists are drugs that **block** or **inhibit** the action of neurotransmitters at ANS receptors, stopping or reducing the system's normal effects. For example, a **beta blocker** (like metoprolol) acts as a **sympathetic antagonists,** preventing adrenaline from making the heart beat too fast or too hard. They slow down the heart rate and reduce blood pressure.

This type of antagonistic drug can be called **sympatholytics** (blocking sympathetic effects) or **parasympatholytics** (blocking parasympathetic effects).

In summary, **agonists "turn on" a response in the ANS, while antagonists "turn off" or block that response**. This allows healthcare providers to carefully control body functions in many common medical situations.

Acetylcholine (Cholinergic) Agonists and Antagonists

The **vagus nerve** (a major parasympathetic nerve) helps slow the heart by releasing the neurotransmitter **acetylcholine (ACh)**. ACh binds to special receptors on pacemaker cells in regions of the heart that control heart rhythm — specifically the **sinoatrial (SA)** and **atrioventricular (AV)** nodes. (We will discuss these nodes in more detail soon.)

Because ACh activates these receptors, it is considered a **cholinergic agonist**, meaning it turns on cholinergic (ACh-sensitive) pathways. Drugs that mimic this effect by binding directly to the ACh receptors are called **direct-acting cholinergic agonists**. Agents targeting ACh receptors may target **either the nicotinic or muscarinic receptors** for ACh. Drugs acting as cholinergic agonists are used less often than **cholinergic antagonists** because they can have widespread side effects. Still, there are a few important ones, such as **Pilocarpine** – used in eye drops to treat **glaucoma** (it causes the pupil to constrict, which helps drain fluid from the eye and lower intraocular pressure).

Sometimes, however, doctors want to **block the parasympathetic effects** on the body. This can be done with drugs called **cholinergic antagonists**. These drugs attach to the same receptors that ACh normally binds to, but instead of activating them, they **block them**, preventing ACh from doing its job.

A classic example of a **cholinergic antagonist** is **atropine**, a natural chemical found in plants like deadly nightshade. Eye doctors

sometimes use atropine in eye drops to make your pupils get really big (dilated) during an exam. Atropine works as a **muscarinic antagonist** — blocking the subgroup of acetylcholine (ACh) receptors called muscarinic receptors. By blocking ACh's normal action on the eye muscles, atropine prevents the pupil from constricting, leaving it wide open so the doctor can clearly see the back of your eye, including the retina and optic nerve. Because your pupils stay wide open, they cannot adjust to bright light. When you leave the doctor's office you may notice that your eyes feel **extra sensitive to light**. The focusing muscle in your eye is also temporarily blocked, which is why **things look blurry up close** for a few hours after the exam.

By blocking muscarinic receptors, atropine reduces parasympathetic influence in other parts of the body as well. For example, it can raise heart rate and speed up signal conduction through the SA and AV nodes in the heart. Although atropine is useful in medicine when given carefully, it can be **toxic at high doses**.

Adrenaline (Adrenergic) Agonists and Antagonists

While cholinergic drugs act on acetylcholine receptors, **adrenergic drugs** target receptors that respond to **norepinephrine and epinephrine** (the sympathetic neurotransmitters).

- **Adrenergic agonists** activate adrenergic receptors and mimic the effects of the sympathetic nervous system. For example, **albuterol** is a β_2 agonist that relaxes airway muscles, making it easier to breathe during asthma attacks. **Epinephrine**, which stimulates both α- and β-receptors, is used in emergencies like anaphylaxis to raise blood pressure, open airways, and increase heart rate.
- **Adrenergic antagonists** block adrenergic receptors and reduce sympathetic effects. **Beta-blockers**, as their name suggests, block the action of epinephrine and norepinephrine on β-receptors. They are commonly used to manage cardiac arrhythmias, slow the heart rate, and lower blood pressure. A common example is metoprolol. **Alpha-blockers**, which act on a different subset of adrenergic receptors, cause blood vessels to relax and help reduce hypertension. An example is prazosin.

In short, adrenergic agonists act like pressing the gas pedal harder, while adrenergic antagonists act like easing off the gas to slow things down.

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7: SPECIAL SENSES

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7.1: General and Special Senses

Sensory receptors are the body's detectors, turning touch, sights, sounds, and other stimuli into signals the brain can understand.

Master this section and you'll be able to

- Identify the difference between general senses and special senses, and give examples of each.
- Classify sensory receptors based on their structure, location, and function.
- Match each type of sensory receptor (chemoreceptor, mechanoreceptor, thermoreceptor, photoreceptor, nociceptor) with the stimulus it detects and the sense it supports.

What Are Agonists and Antagonists of the ANS?

General senses include ***somatosensation*** (touch, pressure, vibration, temperature, pain) and ***visceral senses*** (signals from internal organs, often below the level of conscious awareness).

A **general sense** is one that is spread throughout the body, with receptor cells located in many organs and tissues. Examples include mechanoreceptors in the skin, muscles, and blood vessel walls. General senses contribute to touch, proprioception (awareness of body position), kinesthesia (awareness of movement), and visceral sensations that are especially important for autonomic functions.

Special senses are tied to specific organs: ***taste*** *(gustation),* ***smell*** *(olfaction),* ***hearing*** *(audition),* ***balance*** *(equilibrium), and* ***vision***. These are consciously perceived and linked to the somatic nervous system, though some also influence automatic (autonomic) functions.

The body detects different kinds of stimuli using special cells called **sensory receptors**. These receptors convert (or ***transduce***) incoming signals, like light or sound, into the electrical signals used by the nervous system.

Structural Classification of Sensory Receptors

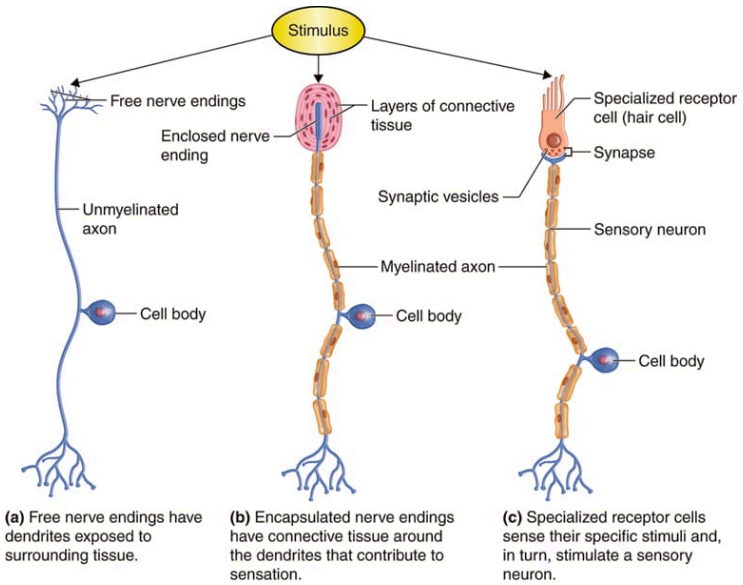


Figure 7.1.1: **Receptor Classification by Structure of Cell Type.** Sensory receptors can be classified on the basis of their structure. Sensory neurons can have either free nerve endings on their dendritic side such as in a or encapsulated endings where dendrites are covered by connective tissue such as in b. In c, hair cells in the inner ear are examples of specialized receptor cells. *(Image Credit: "Structural Receptor Classification" by Cenveo is licensed under CC BY 3.0(opens in new window)).*

Structural classification looks at what the receptor cell looks like or where it is located:

Receptor Types Based on Structure or Location

Structure or Location	Description	Examples / Function
Free nerve endings	Bare nerve tips	Detect pain, temperature, touch
Encapsulated endings	Nerve tips wrapped in a capsule of connective tissue	Detect pressure and vibration
Specialized receptor cells	Distinct cells that respond to specific stimuli	Eye (light), Ear (sound, balance)
Exteroceptors	Located near body surface	Detect outside stimuli such as touch, sound, light
Interoceptors	Located inside organs	Monitor internal conditions (*e.g.*: blood pressure, O_2 levels)
Proprioceptors	Found in muscles, tendons, joints, inner ear	Provide awareness of body position and movement

Functional Classification of Sensory Receptors

A third way to classify receptors is by **how they convert (transduce) stimuli into changes in membrane potential**. Stimuli come in three general types:

- **Chemicals** such as ions or molecules that bind to receptor proteins or diffuse across membranes.
- **Physical changes** in the environment, such as pressure or vibration, that alter membrane potentials.
- **Electromagnetic energy**, like visible light, which is detected by receptors in the eye.

Humans detect only visible light, but other animals sense stimuli humans cannot sense — for example, snakes detect infrared heat, bees see ultraviolet light, and migratory birds use magnetic receptors to navigate.

Receptors can therefore also be grouped functionally by the **specific type of stimulus they detect**:

Receptor Types Based on Function

Receptor Type	Stimulus Detected	Examples / Role
Chemoreceptors	Chemicals	Taste (gustation), smell (olfaction)
Mechanoreceptors	Pressure, vibration, stretching, sound	Touch, proprioception, hearing, balance
Thermoreceptors	Temperature	Detect heat and cold
Photoreceptors	Light	Vision (rods and cones in the retina)
Nociceptors	Pain	Detect harmful or damaging stimuli

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7.2: Introduction to the Eye and Vision

Vision begins as light enters the eye, travels through its specialized structures, and is transformed into signals the brain can interpret as images.

Master this section and you'll be able to

- Identify the major parts of the eye.
- Trace the pathway of light through the major structures of the eye.
- Differentiate between the function of the rods and cones.
- Follow the signal as it travels from the eye to the brain.

Our **eyes** act like the body's cameras, capturing light and converting it into electrical signals that the brain interprets as images. **Vision**, or sight, is our ability to detect light and perceive the world around us. The eye is the specialized sensory organ that gathers and focuses light to form images, but the eye alone is not enough for us to see. The brain is equally essential, processing and making sense of the information the eyes provide.

Each eye is a complex organ made of specialized structures that work together to focus light, detect color and movement, and adjust to different lighting conditions. Vision is not just about "seeing" — it is about how the brain interprets what the eyes collect, allowing us to read, recognize faces, drive, or admire a sunset. Because of its importance, the eye has evolved multiple protective features, like **eyelids**, **eyelashes**, and **tears**, to keep it safe from injury and infection. Studying the anatomy and physiology of the eye helps us understand not only how sight works, but also what can go wrong when diseases or injuries interfere with the visual system.

The image below appears at first glance to be just a pattern of colored tiles, but hidden within it are some three-dimensional shapes. Can you see the shapes? What are they? This figure is an example of a stereogram, which is a two-dimensional picture that reveals a three-dimensional object when viewed correctly, or more likely when viewed in a special way (by slightly crossing or relaxing the eyes). Stereograms demonstrate binocular vision by showing how our brain uses input from both eyes to create depth perception.

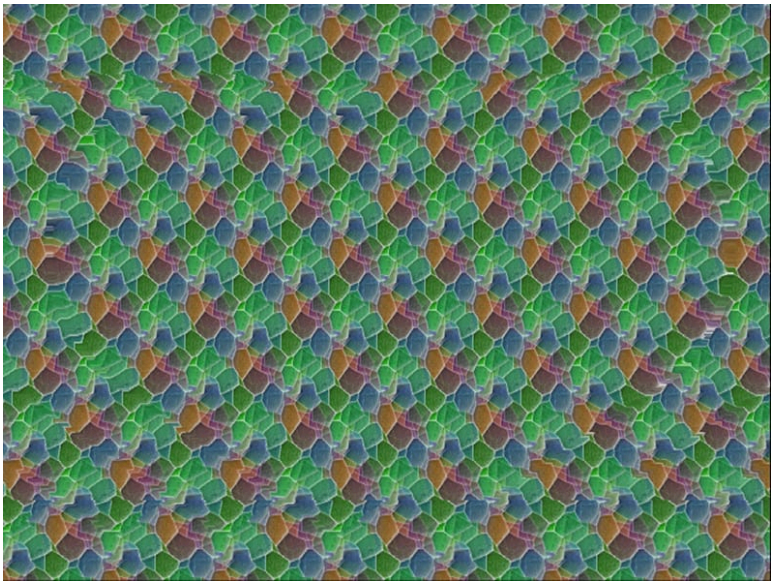


Figure 7.2.1: **Seeing is Believing.** This is a stereogram — a type of optical illusion where a hidden three-dimensional image or shape appears if you focus your eyes in a certain way (usually by relaxing your gaze as if looking "through" the picture).

If you have trouble seeing the 3-D shapes in there try to follow these instructions:

- Have the image close to your nose so it is blurry.
- Relax your eyes and pretend you are looking *through* the picture.
- Slowly move your head away while keeping your eyes unfocused.
- When the repeating patterns “double,” keep relaxing — the 3D shapes will pop out.

If a person cannot see the hidden image, no panic, maybe they are just not doing it quite right. In some people, however it could indicate that there is a problem with **binocular vision,** or they may rely more heavily on one eye (a condition called **suppression**). They may also have a condition like **strabismus** (eye misalignment) or **amblyopia** (“lazy eye”), which prevents the brain from combining images from both eyes effectively. In short, not being able to see stereograms often points to difficulties in how the two eyes and the brain work together to perceive depth.

Overview of Eye Anatomy

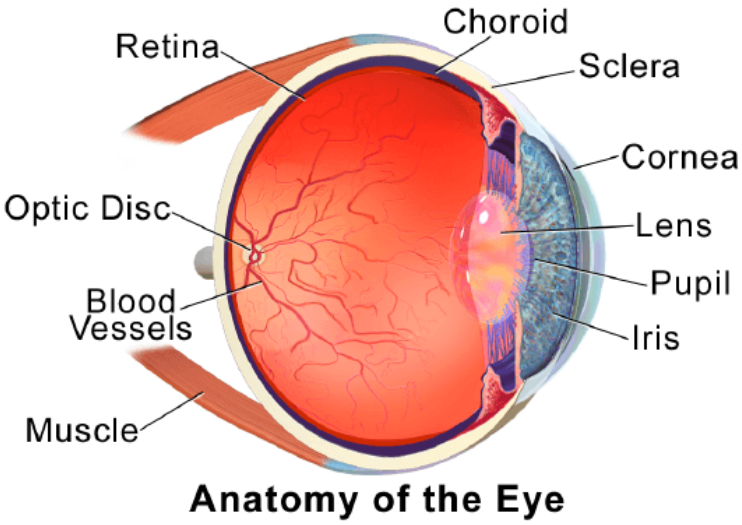


Figure 7.2.1: **Basic Anatomy of the Human Eye in Cross-Section.** You can see the three layers of the eyeball, the sclera (cornea at the front), choroid, and retina. Lens, pupil, iris, optic disc, option nerve (not labeled), blood vessels, and eye muscles are also visible. Trace the path of light through the eye as you read about in the five steps described in the text below.

First Look: An Introduction to How the Eye Works

Seeing works a lot like photography. Light first enters the eye, which acts like a camera lens, bending and focusing the rays onto the retina at the back of the eye. The retina works like film or a digital sensor, capturing the image and converting it into electrical signals. These signals travel along the optic nerve to the brain, which develops the “photo” into the final picture we actually perceive.

Imagine light going on an obstacle course — dodging through clear windows, squeezing through doorways, and bending around curves — before finally landing on a screen at the back of your eye where the picture of the world is formed. Let's take a quick look at it step by step:

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 can change shape to refract the light so that it is focused perfectly on the **retina** at the back of the eye as an inverted image. This focusing mechanism is called **accommodation**.

4) The **retina** contains photoreceptor cells of two types, called **rods** and **cones**. Rods, which are found 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 electrical and chemical 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.

The optic nerves from both eyes meet and cross over to the other side 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.

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7.3: Vision Begins Here - The External Structures of the Eye

The accessory structures of the eye — from tear-producing glands to protective eyelids and precise extraocular muscles — work together to protect, clean, and move the eyeball so vision can be clear and accurate.

Master this section and you'll be able to

- Identify the accessory structures of the eye and explain how they protect and support vision.
- List the six extraocular muscles and describe their function.
- Describe the components and function of the lacrimal apparatus, including how tears are produced, distributed, and drained.



Vision is the remarkable sense that lets us turn light stimuli into the colorful, detailed world we see. Each eye sits snugly in a **bony orbit of the skull**, a built-in fortress that protects the delicate eyeball while anchoring the muscles and soft tissues that keep it moving. On the outside, the eyelids act like protective curtains, complete with eyelashes that serve as little “dust filters” to keep intruders out.

The inside of each eye lid is lined by the **palpebral conjunctiva**, a smooth membrane that continues onto the white of the eye (the **sclera**), creating a seamless connection between the eyelids and the eyeball. To keep everything clean and comfortable, the l**acrimal gland** — tucked just beneath the outer edge of the eye — acts like a built-in sprinkler system. It produces tears that sweep across the surface of the eye, flowing toward the inner corner where they drain away. With every blink, this tear film washes away dust and debris, keeping your windows to the world clear and functional.

Accessory Structures of the Eye

The eyes come with built-in support systems essential for protecting, lubricating, and supporting the eyeball. These components are sometimes called the ocular adnexa.

- **Eyebrows:** Positioned above the eye, they help keep sweat and debris from getting into the eye and contribute to facial expression.
- **Eyelids and Eyelashes:** The eyelids (palpebrae) are folds of skin that can close to shield the eye from injury, excess light, and dehydration. Eyelashes trap dust and other tiny particles.
- **Conjunctiva:** A clear **mucous membrane** that lines the inner surface of the eyelid and part of the eye surface, aiding in lubrication.
- **Lacrimal Apparatus:** This includes **tear glands** (lacrimal glands) and **ducts** that produce and drain tears, keeping the eye moist, clean, and free from infection.
- **Orbit and Extraocular Muscles:** The bony socket (orbit) provides protection, while the muscles around the eye (extraocular muscles) allow smooth movement of the eyeball in all directions.

Lacrimal Apparatus

The lacrimal apparatus is the system responsible for producing and draining tears. It includes the **lacrimal gland**, which secretes lacrimal fluid (tears), and the **lacrimal drainage system**, which channels the tears into the nasal cavity. The drainage system consists of the **puncta,** canaliculi, **lacrimal sac, and nasolacrimal duct**.

Although **tears** are about 98% water, they also contain several other important components, including:

- **Salts (electrolytes):** They help maintain proper pH and osmotic balance.
- **Proteins, including lysozyme:** Lysozyme is an enzyme that damages bacterial cell walls, causing the bacteria to burst and die. It acts as a natural defense and is found in many of your body's secretions, such as tears, saliva, and mucus. Each time you blink, a fresh layer of tears spreads lysozyme across your eye, helping to protect it from infection.
- **Antibodies (IgA):** Antibodies are special proteins your immune system makes to recognize and fight germs. There are different types of antibodies, and one important class is called **IgA** (short for *immunoglobulin A*). IgA antibodies are found mostly in body secretions that cover surfaces exposed to the outside world — such as **tears, saliva, mucus, and even breast milk**. You can think of IgAs as a **frontline guard** since they patrol your eyes, mouth, nose, and gut, where germs are most likely to sneak in.
- **Mucins:** Large, sticky proteins — they are the "**slime-makers**" of your body. Mucins are coated with many sugars, which help them hold onto water and give mucus its thick, gel-like consistency. In the eyes, mucins help tears cling to the cornea, keeping it lubricated, nourished, and protected from pathogens. In the nose, mouth, and airways, mucins trap dust, microbes, and other particles so the body can clear them out.

The **drainage system** of the lacrimal apparatus acts like a clever plumbing network for your tears. Tiny openings at the inner corner of your eyelids, called **puncta**, collect tears from the surface of the eye. From there, the tears flow through small channels known as the **canaliculi** into the **lacrimal sac**, a small chamber that briefly holds them. Finally, the **nasolacrimal duct** carries the tears into the nasal cavity — which is why you get a runny nose when you cry.

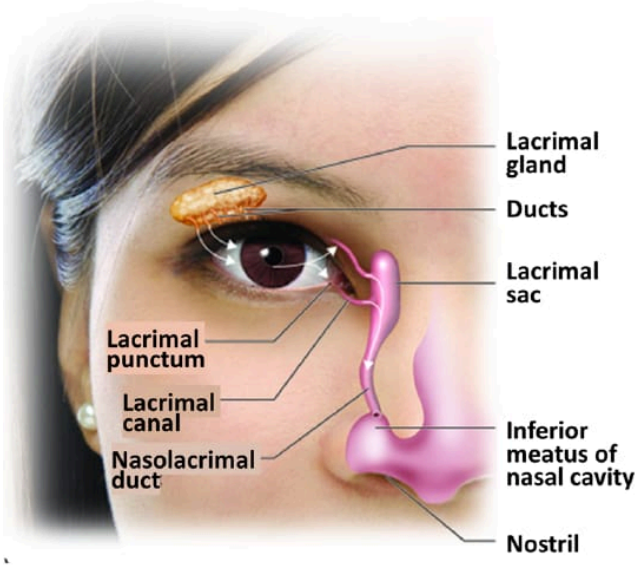


Figure 7.3.1: **The Lacrimal Apparatus.** The lacrimal gland produces tears, which flow across the eye surface through ducts. Tears drain medially through the lacrimal puncta into the lacrimal canaliculi, then collect in the lacrimal sac. From there, they travel through the nasolacrimal duct and empty into the inferior meatus of the nasal cavity near the nostril.

Extraocular Muscles

The eye sits within a protective bony socket called the **orbit**, which not only shields it but also provides attachment points for the extraocular muscles. These **six small muscles** precisely control eye movements so that both eyes can align and track together. Four of them — the **superior, inferior, medial, and lateral rectus muscles** — move the eye mainly up, down, inward, and outward. The other two, the **superior and inferior oblique muscles**, fine-tune movements like rotation and allow the eye to look diagonally. Coordinated action of these muscles is essential for focusing on objects and for depth perception. Several cranial nerves control the movement of the eyeball, and they all **originate from the brainstem** (midbrain and pons), making the orbit and its contents a highly organized system for vision.

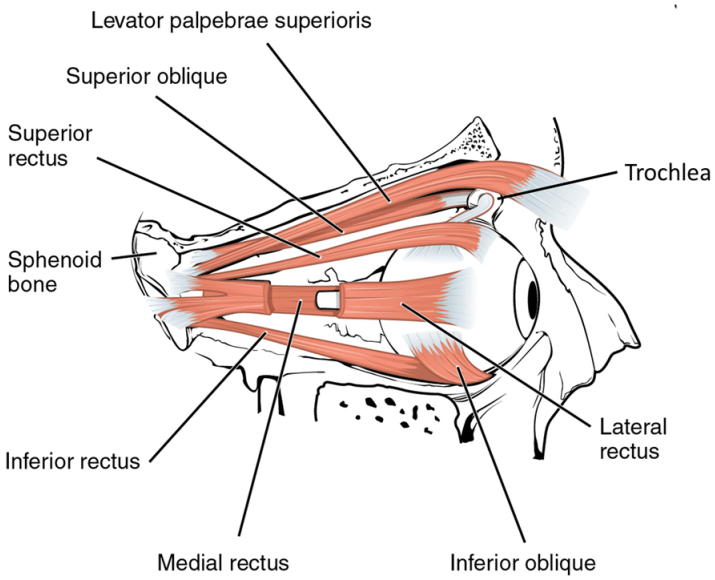


Figure 7.3.1: **Lateral View of the Right Eye Showing the Six Extraocular Muscles and Their Points of Attachment.** The four rectus muscles (superior, inferior, medial — not visible here — and lateral) run straight from the common tendinous ring at the back of the orbit to the sclera of the eye. The two oblique muscles (superior and inferior) attach at angles to allow for rotation of the eyeball. The superior oblique passes through a pulley-like structure called the trochlea before attaching to the eye. These muscles work together to produce precise movements of the eyeball in all directions.

Here is a brief description of the main actions for each of the six extraocular muscles:

- **Superior rectus:** Moves the eye upward (elevation).
- **Inferior rectus:** Moves the eye downward (depression).
- **Medial rectus:** Moves the eye inward toward the nose (adduction).
- **Lateral rectus:** Moves the eye outward, away from the nose (abduction).
- **Superior oblique:** This muscle passes through a pulley-like structure (trochlea) near the top of the eye and **pulls the top of the eyeball down and a little outward**. You can think of it as helping you **look down and out**.
- **Inferior oblique:** This muscle runs under the eye and pulls the bottom of the eyeball upward and outward. It helps you look **up and out**. Together, these oblique muscles fine-tune your eye movements, especially when you need to look diagonally or keep your eyes steady while tilting your head.

Each muscle works in coordination with the other muscles to allow precise and smooth eye movements in all directions.

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7.4: Inside the Eye — Tunics and Cavities

The eyeball is a layered, fluid-filled organ whose tunics and chambers work together to protect the eye, control light entry, and convert light into visual signals for the brain.

Master this section and you'll be able to

- Identify the structures of the eye ball.
- Distinguish between the three tunics of the eye, and describe their main structures and function.
- Compare the anterior and posterior cavities of the eye.

Layers of the Eyeball

Think of the eye like a baseball or an onion — it has layers that surround and protect what is inside. The human eye is a round, hollow organ about the size of a large marble (roughly 2.5 cm across). It rests in the bony orbit of the skull, cushioned by fat tissue that works like “packing peanuts,” keeping it in place and preventing it from knocking against the bone.

For even more protection, the eyeball has three distinct coats, called **tunics**. These tunics form the wall of the eye, each with its own role in support, nourishment, or vision:

1. Fibrous Tunic (Outer Layer)

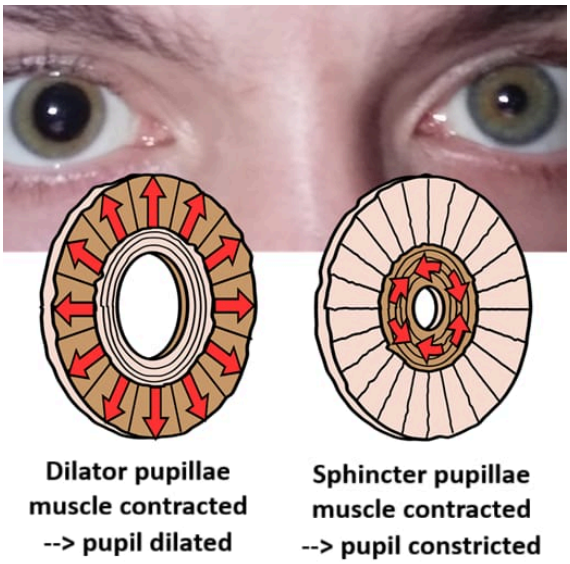
The **fibrous tunic** is the tough outer coat (like the shell of a baseball).This tough outer coat includes two parts:

- **Sclera** – the “white of the eye.” It is made of strong connective tissue that gives the eyeball its shape and provides attachment points for the eye muscles. Humans are unusual in showing so much sclera; in most animals (like cats or dogs) it is barely visible.
- **Cornea** – the clear “window” at the front of the eye. Its curved surface bends (refracts) incoming light to help focus images. If the cornea’s shape is off, vision becomes blurry.

2. Vascular Tunic (Middle Layer)

The **vascular tunic** is the middle coat, full of blood vessels and color (like a padded jacket that provides both support and shade). This layer contains blood vessels and pigment. It has three parts:

- **Choroid** – a dark, blood-rich layer at the back of the eye. The pigment absorbs stray light so it does not bounce around inside the eye.
- **Ciliary body** – a muscular ring connected to the lens by tiny fibers. When the ciliary muscles contract or relax, they change the lens shape to help focus near or far.



- **Iris** – the colored part of the eye (blue, green, brown, etc.). In the center is the **pupil**, a hole that lets light in. Think of the pupil like the aperture of a camera: it automatically becomes smaller in bright light and larger in darker settings, all thanks to tiny muscles in the iris and signals from the nervous system.
  Tiny muscles in the iris control the pupil size depending on light conditions.
  - In bright light, the **sphincter pupillae**, a circular muscle, contracts to make the pupil smaller. This constriction is controlled by the **parasympathetic nervous system** through the oculomotor nerve (cranial nerve III). Constricting the pupil protects the retina from too much light and helps sharpen focus.
  - In dim light, the **dilator pupillae** muscle, which pulls the pupil outward, contracts to widen the opening. This dilation is managed by the **sympathetic nervous system**, the body's "fight or flight" branch. By allowing more light to enter the eye, dilation improves vision in darkness and also enhances alertness.

  Anisocoria is when the pupils are unequal in size. It may be harmless (physiologic anisocoria — typically < 1 mm difference), but it can also result from nerve damage, eye trauma, medications, or medical conditions such as Horner's syndrome.

3. Neural Tunic (Inner Layer: Retina)

The **neural tunic** (the **retina**) is the innermost tunic. Its purpose is to convert light into nerve signals, which are then carried to the brain by the optic nerve (like the film in a camera or the sensor in a digital camera). It "records" images and has two parts:

- **Pigmented layer** – right underneath the choroid is the **retinal pigment epithelium** (RPE), an additional thin layer of dark cells that absorb stray light and prevents light scattering inside the eye, thereby supporting photoreceptor health.
- **Neural layer** – contains the **photoreceptors** (**rods** and **cones**) that detect light. This layer also includes other neurons (bipolar and ganglion cells) that process visual information and transmit it to the brain via the optic nerve.

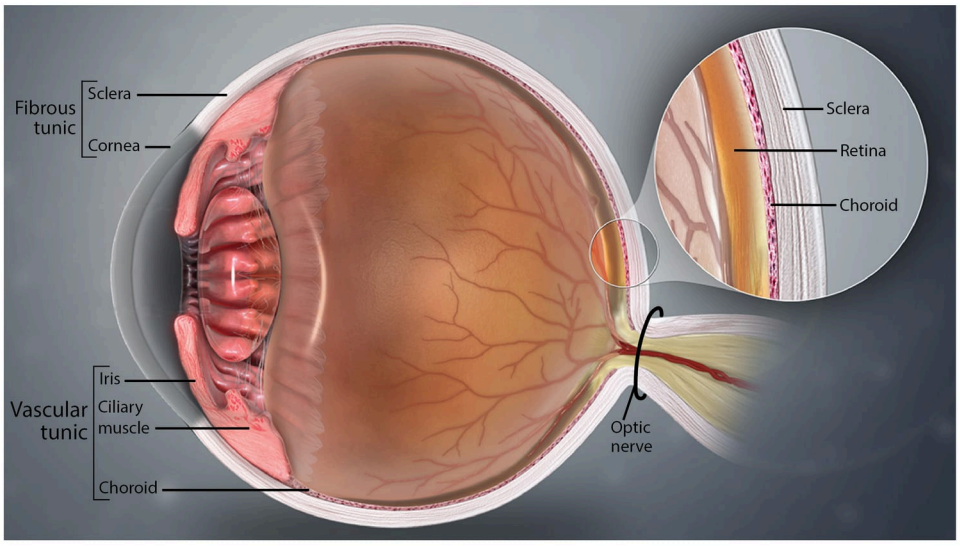


Figure 7.4.1: **Tunics of the Eye.** The wall of the eye is composed of three layers. From superficial to deep they are 1) fibrous tunic, 2) vascular tunic, and 3) neural tunic (also called the retina). *(Image credit: "Eye Structure - Tunics" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

Cavities and Chambers

The interior of the eye is divided into two cavities that are filled with circulating fluids: the **anterior cavity** and the **posterior cavity**. The anterior cavity is the space between the cornea and lens that is further divided into **anterior and posterior chambers** by the iris. These chambers are filled with a watery fluid called the **aqueous humor**. The posterior cavity is the space between the lens and the the retina that is filled with a thicker fluid called the **vitreous humor**. The vitreous humor has a similar consistency to the white part of an egg.

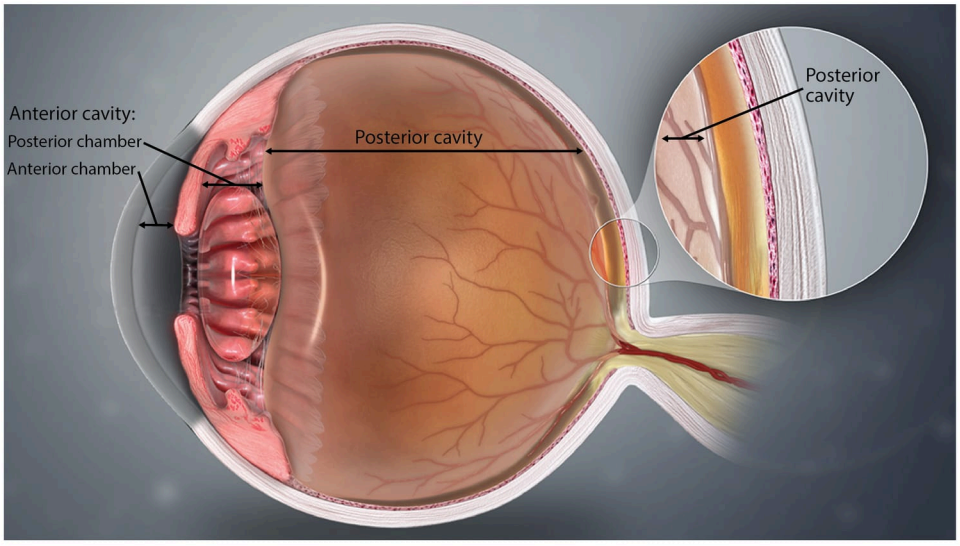
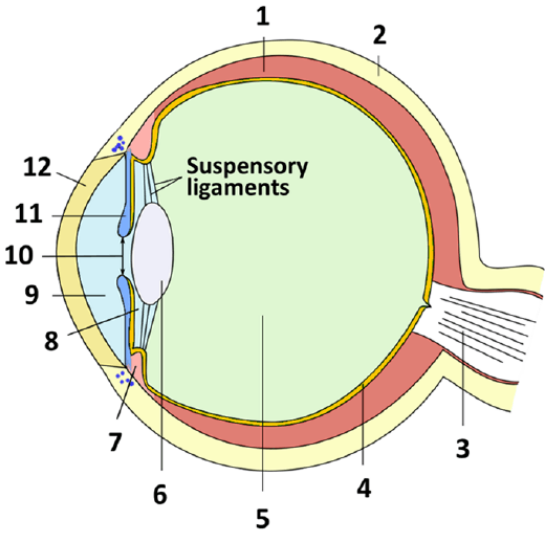


Figure 7.4.2: **Cavities of the Eye.** The interior of the eye is divided into two fluid filled cavities: the anterior cavity is anterior to the lens and the posterior cavity is posterior to the lens. *(Image credit: "Eye Structure - Cavities" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*



Can you put a name to every number?

Answers

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7.5: The Retina — Gateway to Vision

The retina is the light-sensitive layer at the back of the eye, containing specialized photoreceptors — rods and cones — that convert light into neural signals, enabling both color vision in bright light and black-and-white vision in dim light.

Master this section and you'll be able to

- Identify and compare the two types of photoreceptors.
- Trace the direction of light and neural signal transmission within the retina.

Anatomy of the Retina

As you have already learned, the front of the eye consists of the **cornea**, **pupil**, **iris**, and **lens**. The cornea is the transparent, outermost part of the eye. It covers the pupil and iris and serves as the first site of **light refraction**. The pupil is the opening in the iris that allows light to enter the eye. The iris is the colored portion of the eye that surrounds the pupil and, through its intrinsic muscles, controls pupil size to regulate the amount of light entering the eye. The lens lies directly behind the pupil and iris. It further refracts light to focus images onto the retina. Proper focusing requires the lens to change shape by stretching or relaxing, a process known as **accommodation**.

The **retina** is the light-sensitive layer that lines the back of the eye. It contains the **photoreceptors**, specialized cells that respond to light. The retina curves around the back of the eye like a bowl. At the center of this bowl is the **fovea**, the area of highest visual acuity, where the sharpest images are formed. The **optic nerve** extends from the back of the eye to the brain, carrying visual information from the retinal cells. At the point where the optic nerve exits the eye, there are no photoreceptors because the axons of the retinal neurons converge there. This region is known as the **optic disc** and corresponds to the **blind spot** in our visual field.

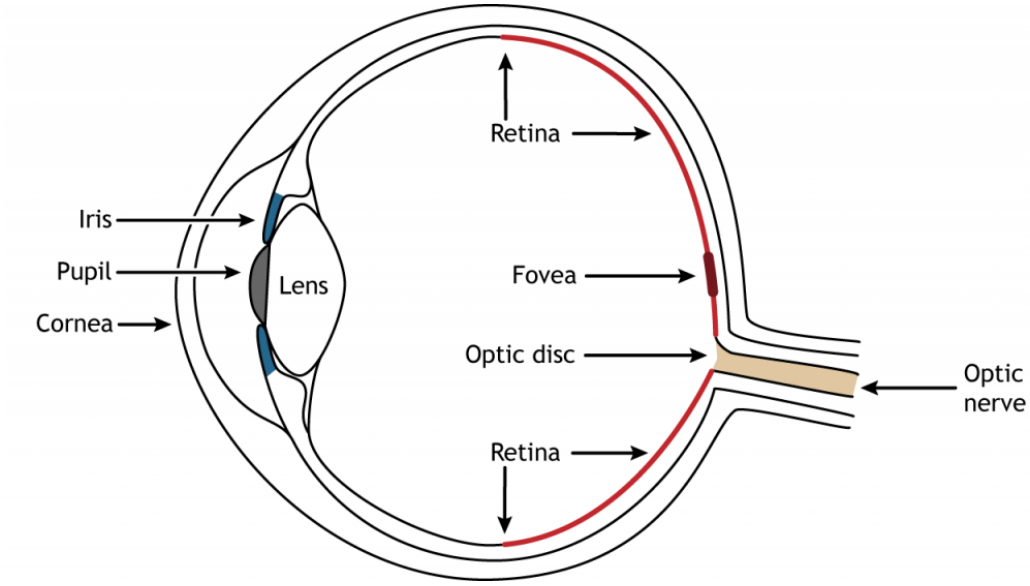


Figure 7.5.1: **Cross Section of the Eye.** The visible regions of the eye include the cornea, pupil (gray region), and iris (blue region). The lens sits behind the pupil and iris. The retina (red line) is located along the back of the eye. The fovea (dark red section) is a small portion of the retina where visual acuity is highest, and the optic disc is located where the optic nerve (tan region) leaves the eye. Details about the functions of each region are in the text. 'Eye Anatomy' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Retinal Cells

The retina is made up of several different types of cells. The most famous ones are the **photoreceptors**, specifically the **rods** and the **cones**. The photoreceptors synapse on bipolar cells, and the bipolar cells synapse on the **ganglion cells**. Horizontal and amacrine cells allow for communication laterally between the neurons.

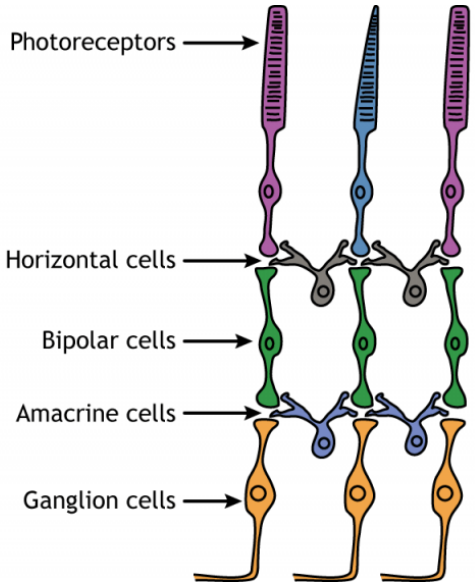


Figure 7.5.2: **The Five Cell Types in the Retina.** 'Retinal Neurons' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.Direction of Information

When light enters the eye and strikes the retina, it must pass through all the neuronal cell layers before reaching and activating the photoreceptors. The photoreceptors then initiate the synaptic communication back toward the ganglion cells. The axons of the ganglion cells then combine to become the optic nerve.

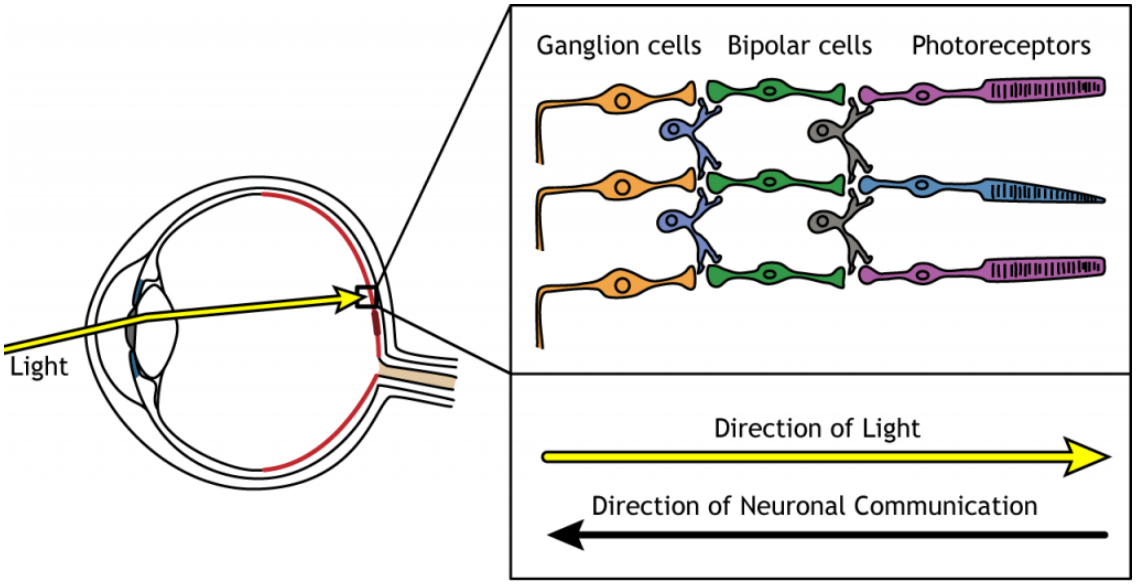


Figure 7.5.3: **Light Passing Through the Eye Ball.** When light enters the eye and reaches the retina, it must pass through the ganglion and bipolar cell layers before reaching the rods and the cones. The neuronal communication travels in the opposite direction from the photoreceptors toward the ganglion cells. 'Light in the Retina' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Photoreceptors

The **rods** and **cones** are specialized **photoreceptors** that respond to light.

Lighting conditions, such as those at night, determine which type of photoreceptor is most active. **Cone photoreceptors** are less sensitive to dim light and function best in bright, daylight conditions *(photopic vision)*. They enable us to see fine detail and color. Humans have three types of cones, each sensitive to a different range of wavelengths corresponding roughly to blue, green, and red light. The brain combines signals from these cones to produce the full spectrum of color vision.

The **cones** are clustered together in a small circular region at the very back of the eye. This region is in line with the center of the cornea and the lens and is called the macula lutea or simply the macula. In the center of the macula is a slightly depressed area that contains a very high concentration of cones. This central area is called the **fovea centralis** or simply the **fovea**. The fovea provides the sharpest vision. It is specialized for detecting fine detail and color in bright light. When you look directly at something — such as reading text or recognizing a face — the image is focused on the fovea, which is why it is called the **area of highest visual acuity**.

Objects immediately surrounding the center of the field of view are focused on the outer regions of the macula. Since the cones are less concentrated there, these objects are seen with less visual acuity but still are seen in color.

In very dim lighting *(scotopic vision)*, the cones become inactive, and vision relies mainly on **rod photoreceptors**, which are far more sensitive to low light but cannot detect color. Rods are much more numerous and are distributed throughout the retina, especially toward its periphery. They allow us to see in dim light, but only in shades of gray. This is why our night vision lacks fine detail and color perception.

In summary: **Cones** provide sharp, detailed color vision in bright light (daytime vision), while rods enable vision in dim light but only in black and white (night vision).

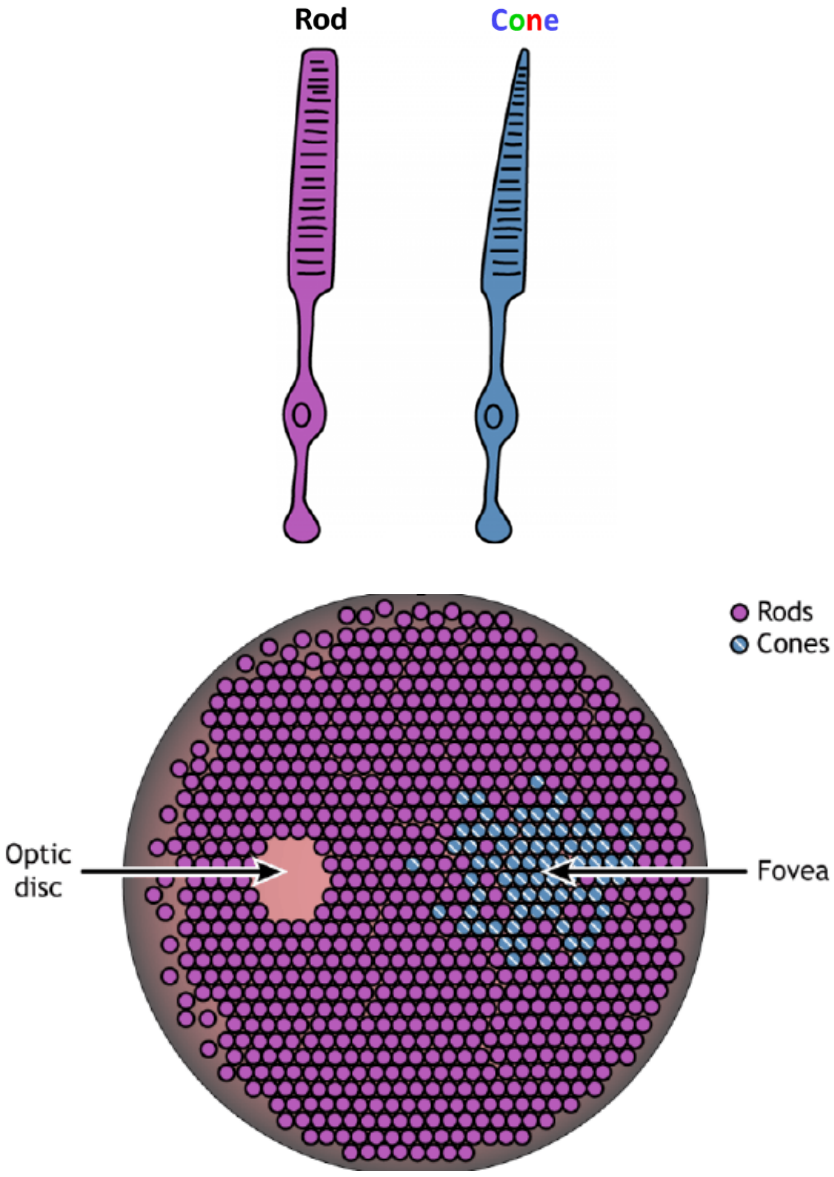


Figure 7.5.4: **Rods and Cones.** a) These two light receptor cells have different physical appearances and play separate roles in visual processing. b) Rods and cones are also differently distributed across the retina. Cones are located at the fovea. Rods are located everywhere else. The optic disc lacks all photoreceptors since the optic nerve fibers are exiting the eye at this location. 'Rod and Cone' and 'Retinal Receptor Density' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

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7.6: Focusing Light for Sight

Refraction and accommodation work together to focus light precisely on the retina.

Master this section and you'll be able to

- Define refraction and describe how it helps focus light on the retina.
- Explain how accommodation allows the eye to focus on objects at different distances.
- Identify how age-related changes in the lens affect accommodation (presbyopia).

Refraction and Accommodation

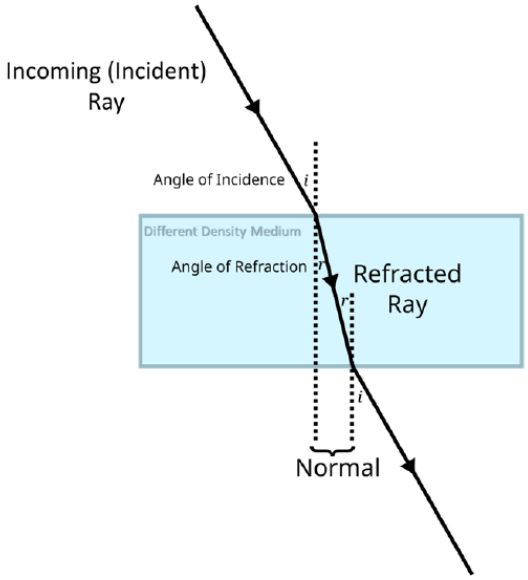
Refraction and accommodation are the **two key optical processes** that make clear vision possible.

- **Refraction** ensures that light rays entering the eye are **bent (focused)** so they converge precisely on the retina, forming a sharp image. Without correct refraction, the light rays would focus either in front of or behind the retina, leading to blurred vision conditions such as **myopia (nearsightedness)** or **hyperopia (farsightedness)**.
- **Accommodation** allows the eye to **adjust its focus** when shifting between near and far objects. This flexibility keeps images clear as the distance to the object changes. Without proper accommodation, as happens with **presbyopia** or **lens rigidity**, close-up vision becomes blurry.

Together, these processes act like a **built-in camera system**:

- Refraction corresponds to how the lens of a camera bends light to create an image.
- Accommodation is like adjusting the camera's focus to make that image sharp at different distances.

Understanding these mechanisms helps explain not only how **normal vision** works but also **why vision problems occur** and how corrective lenses or surgery can restore proper focus.



Refraction

Refraction is the **bending of light rays** when they pass from one transparent substance into another with a different density. This

bending occurs because **light travels at different speeds** in different materials. Refraction is what allows the eye to **focus light rays onto the retina** and form a clear image. *See image on the right.*

Light entering the eye passes through **four transparent structures**, each with a different **refractive index** (a measure of how much the material bends light):

1. **Cornea**
2. **Aqueous humor**
3. **Lens**
4. **Vitreous humor**

The **cornea** provides about **~ 70%** of the eye's total refraction because it has the **largest difference in refractive index** between air and corneal tissue.

The **lens** fine-tunes the remaining ~ **30%**, allowing the eye to focus on objects at varying distances through **accommodation**.

Aqueous and vitreous humor bend the light only slightly as it passes through them, and their impact on refraction can be neglected. Their main optical role is to maintain the shape of the eye and provide a smooth pathway for light to reach the retina without distortion.

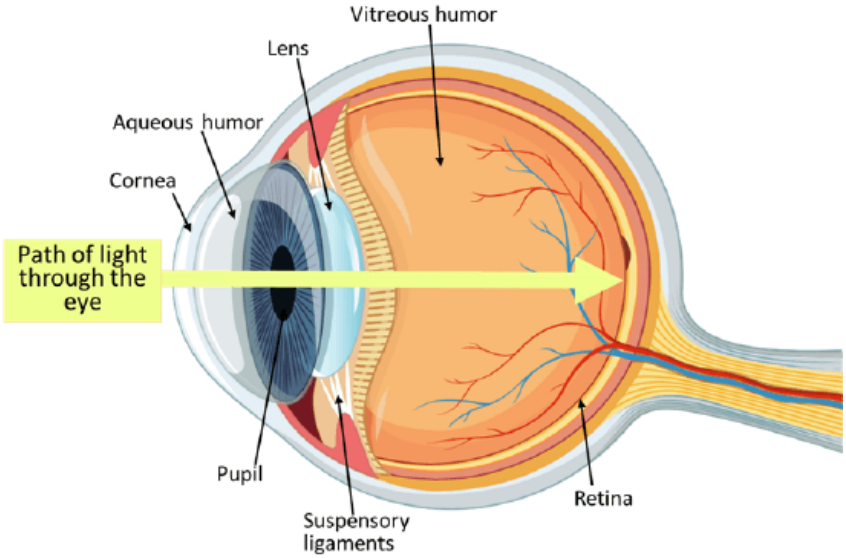


Figure 7.6.1: **Path of Light Through the Eye.**

By the way: the image on the retina is actually inverted and reversed left-to-right, but the brain corrects this so we perceive it normally.



Example: When you place a ball point pen in a glass of water, it looks bent at the surface where water and air meet. This is refraction in action — the same physical principle that helps your eyes focus light. *See image on the left.*

Accommodation

Accommodation is the process by which the eye adjusts the shape of its lens to focus light rays, allowing clear vision of objects at different distances — especially those that are close.

It involves:

- **The ciliary muscle** (also called the *ciliary body*) — a circular band of muscle cells that contract, pulling the edges of the muscle inward.
- **The lens**, which changes shape to become thicker (more curved) or thinner (flatter).

Figure 7.6.2: **Accommodation of the Lens with Distant and Near Vision.**

When the eye is in a **resting or relaxed state** — such as when focusing on **distant objects** — the ciliary muscles relax. This causes the **suspensory ligaments** (also called **zonular fibers**) to tighten, pulling on the lens and flattening it. Because the suspensory ligaments are under tension, they keep the lens relatively thin and less curved. A flatter lens bends (refracts) light less, which is ideal for focusing distant light rays onto the retina.

When you shift your focus to something **nearby**, the opposite occurs: the ciliary muscles contract, reducing tension on the suspensory ligaments. This allows the elastic lens to become thicker and more curved as it recoils into its natural, rounded shape. The increased curvature bends light more strongly, bringing nearby objects into sharp focus on the retina.

During accommodation, two other changes occur to enhance near vision:

- The **pupils constrict**, reducing light scatter and improving focus.
- The **eyes converge** (turn slightly inward) to align on the near object.

With age, the lens gradually becomes less flexible — a condition called **presbyopia** — making it harder to focus on nearby objects.

Summary

Changes in muscle activity, ligament tension, and lens shape during distant or near vision.

Visual State	Muscle Activity	Ligament Tension	Lens Shape	Function
Resting (distant focus)	Ciliary muscles relax	Suspensory ligaments tighten	Lens flattens	Focuses distant light rays
Near focus (accommodation)	Ciliary muscles contract	Suspensory ligaments loosen	Lens thickens and rounds	Focuses nearby light rays

This dynamic adjustment happens automatically, allowing the retina to receive sharply focused images at different distances without conscious effort.

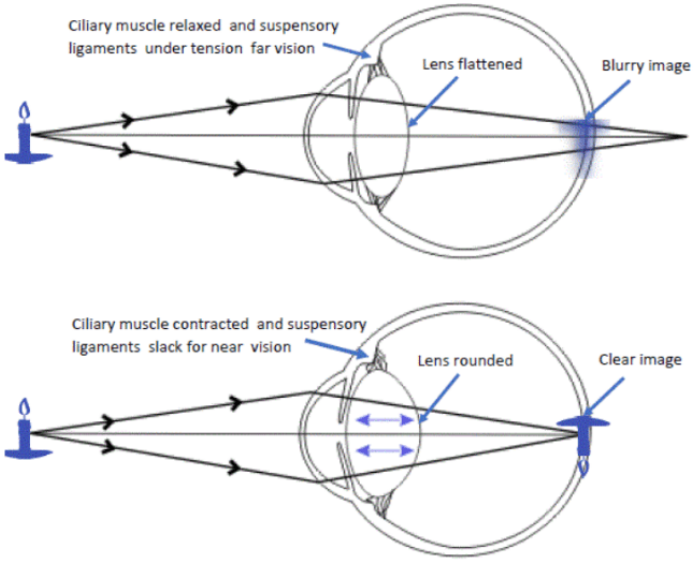


Figure 7.6.3: **Accommodation to Near Objects.** Contraction of the ciliary muscle releases the tension in the suspensory ligaments, allowing the lens to become rounder. The rounder lens bends the light from the near object more, focusing it on the retina for a clear image. (Copyright 2020: Augustine G. DiGiovanna, Ph.D., Salisbury University, Maryland. Used with permission.)

Key Takeaways

- **Refraction:** The bending of light as it passes from one medium to another with a different density. In the eye, refraction occurs mainly as light passes through the cornea and lens.
- **Accommodation:** The lens changes shape to adjust focus for near and far vision.
- **Cornea and lens teamwork:** The cornea does most of the bending; the lens fine-tunes the image.
- **Presbyopia:** Age-related loss of lens flexibility that reduces near-vision clarity.

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7.7: Common Visual Defects and Eye Pathologies

Vision relies on the precise coordination of the eye's structures and neural pathways, and disruptions at any point can lead to disorders ranging from simple refractive errors to serious diseases that impair sight.

Master this section and you'll be able to

- Explain how disruptions in the eye's structure or function can lead to refractive errors or other visual disorders.
- Differentiate between common refractive errors and more serious eye diseases that can impair vision.

Healthy vision requires three basic components: formation of retinal images, stimulation of rods and cones, and nerve impulse conduction to the brain. Malfunction of any of these can disrupt vision. Eye disorders range from common refractive errors that can be treated with the use of eyeglasses, contact lenses, or surgery to more serious conditions such as glaucoma, macular degeneration, and ocular inflammation and infection.

A. Eye Disorders due to Refractive Errors

Remember what "refraction" means? If not reread the previous page.

When the shape of the eye or the curvature of the cornea or lens prevents light from focusing exactly on the retina, a **refractive error** occurs. This causes blurred or distorted vision.

In the previous section, you also learned about accommodation, and how the **ciliary muscle** controls the shape of the lens to keep vision clear at different distances.:

- When viewing **distant objects**, the ciliary muscle **relaxes**, pulling on the suspensory ligaments and flattening the lens.
- When viewing **near objects**, the ciliary muscle **contracts**, loosening the suspensory ligaments and allowing the lens to become **more rounded (convex)**.

The lens is the only **adjustable** part of the eye's refractive system, allowing a smooth transition between near and far vision.

When the shape of the eye or the curvature of the cornea or lens prevents light from focusing exactly on the retina, a **refractive error** occurs. This causes blurred or distorted vision.

Refractive errors can be corrected with **glasses, contact lenses, or surgery**, which adjust how light focuses on the retina. The four main types are:

1. **Myopia (Nearsightedness)** – Close objects are clear, but distant objects are blurry. Light focuses **in front of the retina** because the eyeball is **too long** or the lens is **too curved**.
2. **Hyperopia (Farsightedness)** – Distant objects are clear, but close objects are blurry. Light focuses **behind the retina** because the eyeball is **too short** or the lens is **too flat**.
3. **Astigmatism** – Light focuses on **multiple points** instead of one, causing distorted or blurred vision. This happens when the **cornea or lens** has an **irregular shape** (often more like a football than a baseball).
4. **Presbyopia** – A natural age-related change where the lens becomes **thicker and less elastic**, reducing the ability to focus on close objects. It typically begins around age 45 and is often corrected with reading glasses.

1) Myopia (Nearsightedness)

Myopia (my-Ō-pē-ă), or **nearsightedness**, is a common vision condition in which **near objects appear clear, but distant**

objects look blurry.

This happens because **light rays entering the eye are focused in front of the retina** instead of directly on it. As a result, the image that reaches the retina is out of focus.

There are two main reasons this occurs:

1. **The eyeball has grown too long** from front to back.
2. The **cornea or lens bends (refracts) light too strongly.**

These problems make light focus in front of the retina, instead of on it, causing blurriness.

Correction:
Myopia can be corrected with **concave (diverging) lenses** in glasses or contact lenses. These lenses **spread out the light rays slightly before they enter the eye,** moving the focal point back so it lands directly on the retina.

Analogy:
Think of it like a camera that's focusing too close — the image from far away looks blurry because the focus point is in front of the film or sensor. Adjusting the lens (or adding corrective lenses) brings that image back into sharp focus.



Figure 7.7.1: **Simulated Vision With Myopia.** Nearsightedness usually becomes apparent between ages 6 and 14. It is corrected with glasses, contacts, or LASIK surgery.

2) Hyperopia (Farsightedness)

Hyperopia (hī-pĕr-Ō-pē-ă)**, or farsightedness**, is a common vision condition in which **distant objects appear clear, but nearby objects look blurry.**

This happens because **light rays entering the eye are focused *behind* the retina** instead of directly on it. As a result, the image formed on the retina is out of focus when viewing close objects.

There are two main reasons this occurs:

1. **The eyeball is too short** from front to back.
2. The **cornea or lens does not bend (refract) light strongly enough.**

These issues cause light rays to converge behind the retina, producing blurry vision for nearby objects.

Correction:
Hyperopia can be corrected with **convex** (converging) lenses in glasses or contact lenses. These lenses **bend the light rays slightly inward before they enter the eye**, moving the focal point forward so it lands directly on the retina.

Analogy:

Think of it like a camera that's focused too far away — close-up images look blurry because the focus point is *behind* the film or sensor. Adjusting the focus (or adding corrective lenses) brings near objects into sharp detail.



Figure 7.7.2: **Simulated Vision With Hyperopia (or Presbyopia).** A person holds a product label close to their eyes, attempting to read the fine print. In hyperopia, near objects such as text on a label appear blurry because light rays from close objects are focused behind the retina.

3) Presbyopia

When hyperopia occurs in middle-aged and older adults, it is referred to as **presbyopia** (prez-bī-Ō-pē-ă). Presbyopia happens because the **lens of the eye gradually loses flexibility** with age. When we are young, the lens easily changes shape to focus on close objects — remember **accommodation**? Over time, the lens gets harder and less flexible, and even though the ciliary muscles contract in an attempt to try to increase lens curvature, the lens is too stiff to bulge up. Thus close vision becomes difficult. As a result, light from nearby objects is focused *behind* the retina instead of directly on it, making close-up vision blurry. This is why many adults begin holding reading material farther and farther away as they reach their 40s or 50s.

Correction:
Presbyopia can be corrected with **convex (converging) lenses**, such as reading glasses, bifocals, or progressive lenses. These lenses help bend light rays more sharply so that near objects come into focus on the retina.

Analogy:
Think of it like a camera whose zoom or focus ring has become stiff with age — it can still take sharp pictures of distant scenes, but struggles to focus on close-up details until a lens adjustment helps compensate.

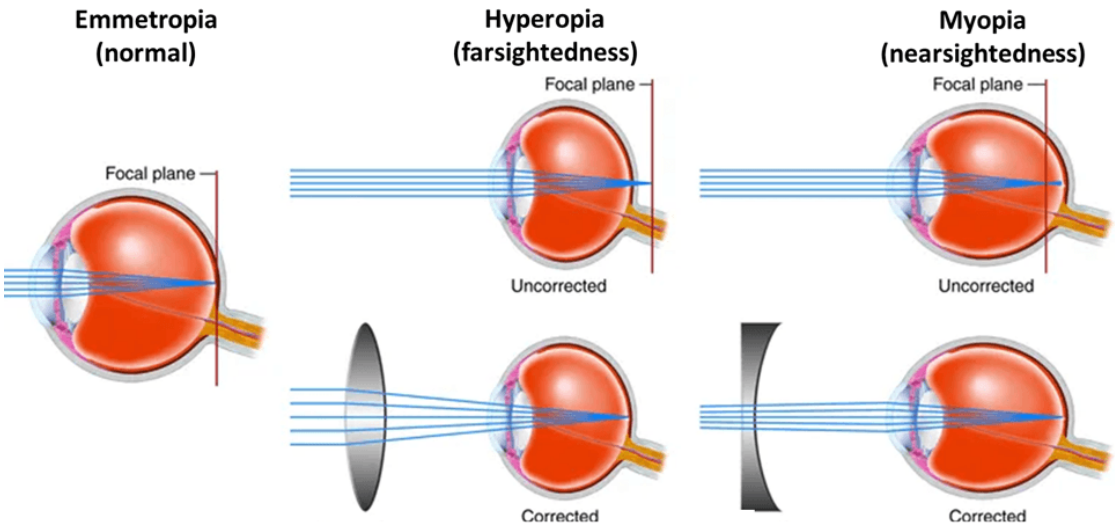


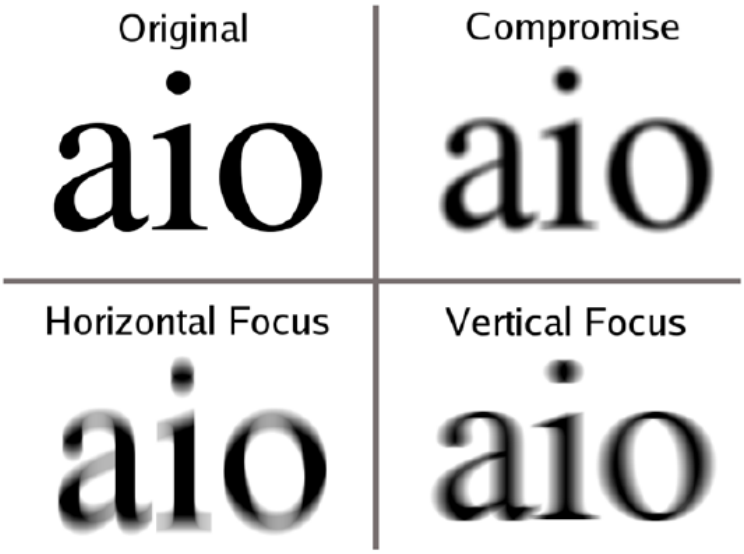
Figure 7.7.3: **Emmetropia, Hyperopia, and Myopia.** A normal eye focuses light directly on the retina, forming a clear image. In farsightedness, light focuses **behind** the retina and needs a **convex lens** to bring the focal point forward. In nearsightedness, light focuses **in front of** the retina and requires a **concave lens** to move the focal point back onto it.

4) Astigmatism

Astigmatism (ă-STIG-mă-tizm) is a common vision condition in which images appear blurry or distorted at all distances. It is due to the **irregular shape** and therefore curvature **of the cornea or lens.** This uneven curvature causes **light rays to focus at multiple points**, either in front of or behind the retina, rather than converging at a single sharp point. As a result, vision can appear wavy, fuzzy, or unevenly focused.

Correction:
Astigmatism can be corrected with **cylindrical lenses** in glasses or contact lenses that compensate for the uneven curvature of the cornea or lens. In some cases, **refractive surgery** (such as LASIK) can reshape the cornea to produce a single, clear focal point.

Analogy:
Think of it like taking a photo through a slightly warped window. Because the surface bends light unevenly, parts of the image come into focus while others look stretched or blurred. Corrective lenses are purposefully crafted with complex and precise shapes tailored to neutralize the particular irregularities of the specific cornea or lens that needs to be corrected to restore clear vision accurately.



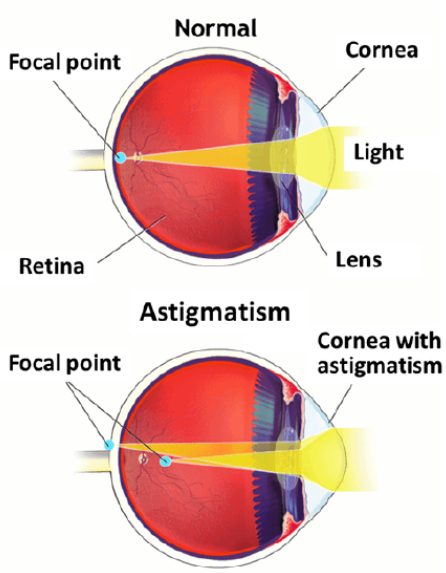


Figure 7.7.4: **Astigmatism**. The image on the left demonstrates simulated vision with astigmatism causing a blur. the image on the right shows two cross-sectional diagrams of the eye comparing normal vision (top) and astigmatism (bottom). In the normal eye, light rays converge to a single point on the retina. In the astigmatic eye, the cornea's uneven curvature causes light rays to focus at different points, resulting in a blurred image.

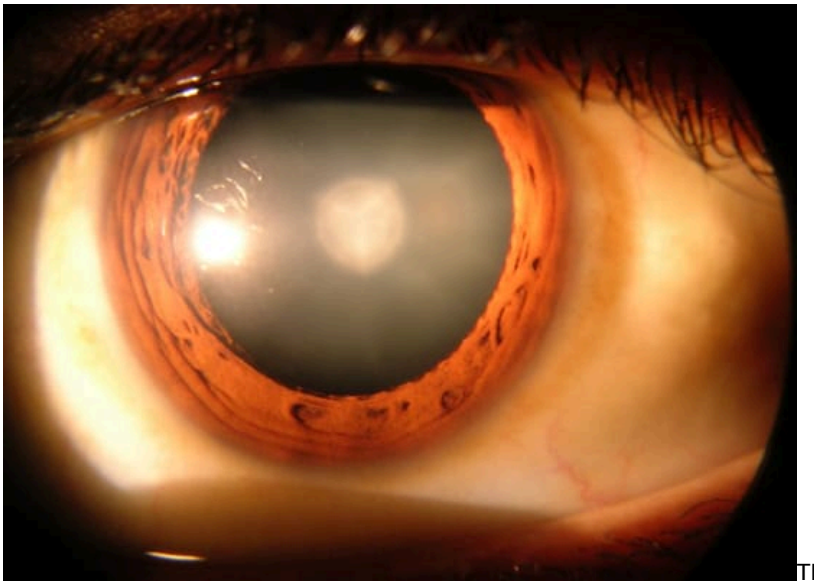
Link to Learning: Refractive Errors

The American Academy of Ophthalmology has a video entitled "Vision Loss and Refractive Error," presented by the University of Wisconsin Department of Ophthalmology and Visual Sciences. It discusses topics such as myopia, hyperopia, astigmatism, and presbyopia.

B. Cataracts

A **cataract** *(KAT-ă-rakt)* is a condition in which the **lens of the eye becomes cloudy**, making it harder for light to pass to the retina. Because the lens needs to be transparent to focus light, this cloudiness leads to **gradual vision loss**.

Cataracts usually **develop slowly** over time and can affect **one or both eyes**.



The image on the right shows a magnified view of a cataract seen on examination with a slit lamp. Cataracts develop when the normal balance between water and proteins in the lens is disrupted. As a result, some **lens proteins change shape and begin to clump together, forming cloudy aggregates.** These protein clumps scatter light as it passes through the lens, reducing clarity and causing blurred or dim vision. Over time, the lens becomes increasingly opaque, interfering with normal vision.

Cataracts are **especially common in older adults**. In fact, **more than half of Americans aged 80 years or older** either have cataracts or have already undergone cataract surgery. Cataracts are the **leading cause of blindness worldwide**. In 2020, they accounted for **nearly 40 percent of global blindness** and **more than one quarter of all visual impairment**.

Although cataract surgery is **highly effective**, many people — particularly in **developing nations** — lack access to timely and affordable treatment. As a result, the clouding of the lens may continue to worsen, leading to **severe vision impairment or complete blindness** that could otherwise be prevented.

The condition typically develops gradually, with symptoms that may include:

- Faded or yellowed colors
- Blurred or double vision
- Halos around lights
- Difficulty seeing at night

As cataracts worsen, everyday activities such as **reading, driving, and recognizing faces** can become difficult. Reduced vision can also increase the **risk of falls** and may contribute to **social withdrawal or depression**, especially in older adults.

Cataract surgery is a common and highly effective procedure. During surgery, the clouded natural lens is removed and replaced with a clear, artificial lens (called an *intraocular lens*), restoring vision in most patients.

YouTube Video

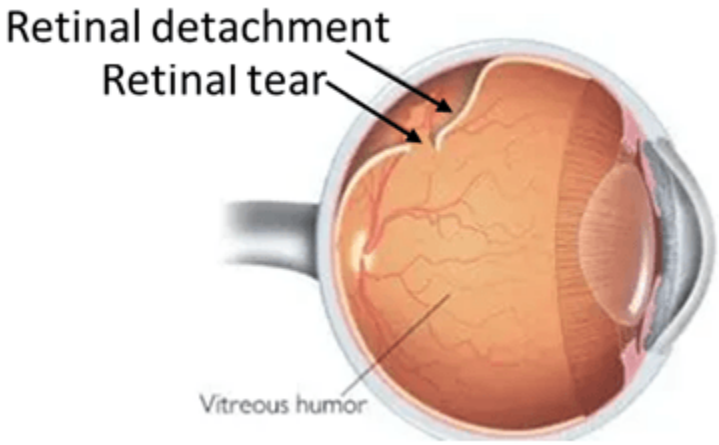
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C. Retinal Detachment

Retinal detachment is a vision-threatening **medical emergency** in which the thin light-sensitive neural layer lining the back of the eye (the retina), separates from the retinal pigment epithelium (RPE) and its underlying blood supply in the choroid.

Under normal conditions, the retina depends on the close contact with these underlaying layers,for oxygen, nutrients, and waste removal so photoreceptors can function properly. When the retina peels away, often compared to wallpaper lifting off a wall, photoreceptors lose access to this support, leading to impaired vision and, if not treated promptly, permanent retinal damage and vision loss.



Tear-related Retinal Detachment

The most common form of retinal detachment occurs when a tear or hole in the retina allows fluid from the vitreous humor to leak underneath, lifting the retina away from its support layer. This is called a **tear-related retinal detachment**.

This type of retinal detachment occurs most often in **older adults**, especially those over age 50. As people age, the vitreous gel inside the eye becomes more liquid and may pull away from the retina, a process called **posterior vitreous detachment.** This pulling can create a small tear in the retina, allowing fluid to slip underneath and lift the retina away from its support layer.

Besides old age, the risk is higher in people with **high myopia (nearsightedness)** because their eyes are longer, which stretches and thins the retina, making it easier to tear. Persistent long term risks for retinal detachment is also associated with cataract surgery and following eye trauma.

Tractional Retinal Detachment

In contrast, **tractional retinal detachment** occurs when the retina is pulled away from the back of the eye by scar tissue rather than by a tear. In poorly managed diabetes, a process called **fibrovascular change** occurs, in which abnormal new blood vessels and scar-like fibrous tissue grow on the surface of the retina. This condition is known as **diabetic retinopathy**.

Over time, the fibrous scar tissue contracts and tightens, creating traction that gradually pulls the retina away from its normal position. Unlike tear-related retinal detachment, there is no initial hole or tear in the retina. As the retina is lifted, fluid can leak underneath the still-intact retina, further separating it from the underlying layers. Tractional retinal detachment most often occurs in patients with long-standing and poorly controlled diabetes.

Typical warning signs for retinal detachment **include flashes of light**, a **sudden increase in floaters**, and the **sensation of a dark curtain or shadow moving across part of the visual field**. These symptoms matter because they signal acute retinal disturbance, and rapid evaluation can prevent involvement of the macula, the region responsible for sharp central vision.

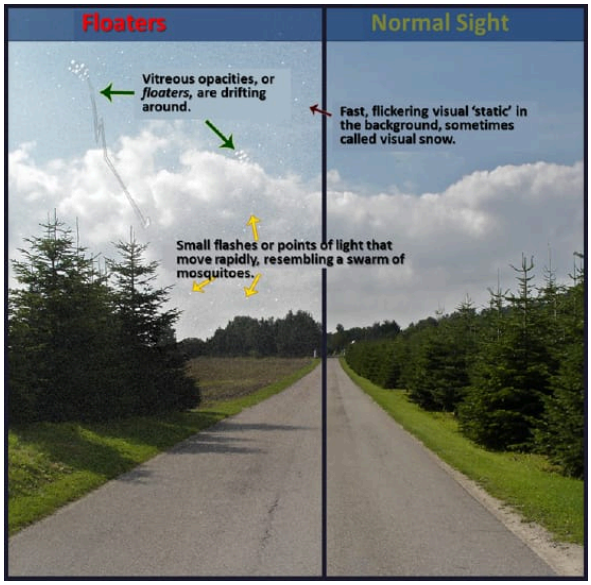
⚠️ When to Worry: Retinal Detachment Red Flags

Retinal detachment is **painless**! Visual changes are the key warning signs! The **3 Fs** are a classic, easy-to-remember way to recognize early warning signs of retinal detachment. These symptoms often appear suddenly and should be treated as an eye emergency, because only early detection can preserve vision.

The 3 Fs:

1. **Flashes:** Brief flashes or flickers of light, often described as lightning streaks or camera flashes. They are most noticeable in dim light or when moving the eyes, and they are caused by the vitreous gel pulling on the retina and stimulating retinal cells.
   Clinical note: Flashes suggest **retinal traction**, which can precede a tear or detachment.

2. **Floaters**: New or suddenly increased dark spots, specks, strings, or cobweb-like shapes in vision. These shapes move as the eyes move and may drift out of view. They occur when vitreous gel changes or when small amounts of blood or debris enter the vitreous humor.
   Important distinction: Occasional floaters can be normal, but **a sudden shower of floaters** is concerning.



1. **Field Loss** (Curtain or Shadow): A dark shadow, curtain, or gray veil moving across part of the visual field. It can start in the peripheral vision and spread toward the center. It indicates that the retina has already begun to detach. This is the most serious of the 3 Fs and often means vision loss is actively occurring.



Any combination of flashes, new floaters, or visual field loss is an **ophthalmologic emergency.**

D. Color Blindness (Color Vision Deficiency)

Color blindness, also called color vision deficiency, is a condition in which a person has difficulty distinguishing between certain colors. The **most common** type **affects red and green color perception.**

Color blindness often runs in families and is usually **inherited** as a **genetic condition.** However, it can also develop later in life due to damage to the eye, optic nerve, or brain.

There is no cure for color blindness. That said, special glasses or contact lenses can help some people better tell colors apart. Most individuals with color blindness learn visual strategies to adapt and are able to participate fully in everyday activities such as school, work, and driving.

X-Linked Recessive Disorders in Humans

Color blindness provides a classic example of an X-linked recessive genetic disorder. Other well-known X-linked recessive conditions include hemophilia type A and hemophilia type B.

Because males have only one X chromosome, they only need to inherit one recessive mutated gene on the X chromosome to show the disorder. For this reason, X-linked recessive disorders are **much more common in males.**

Females have two X chromosomes. To express an X-linked recessive disorder, a female must inherit the recessive gene from both parents, which is much less common.

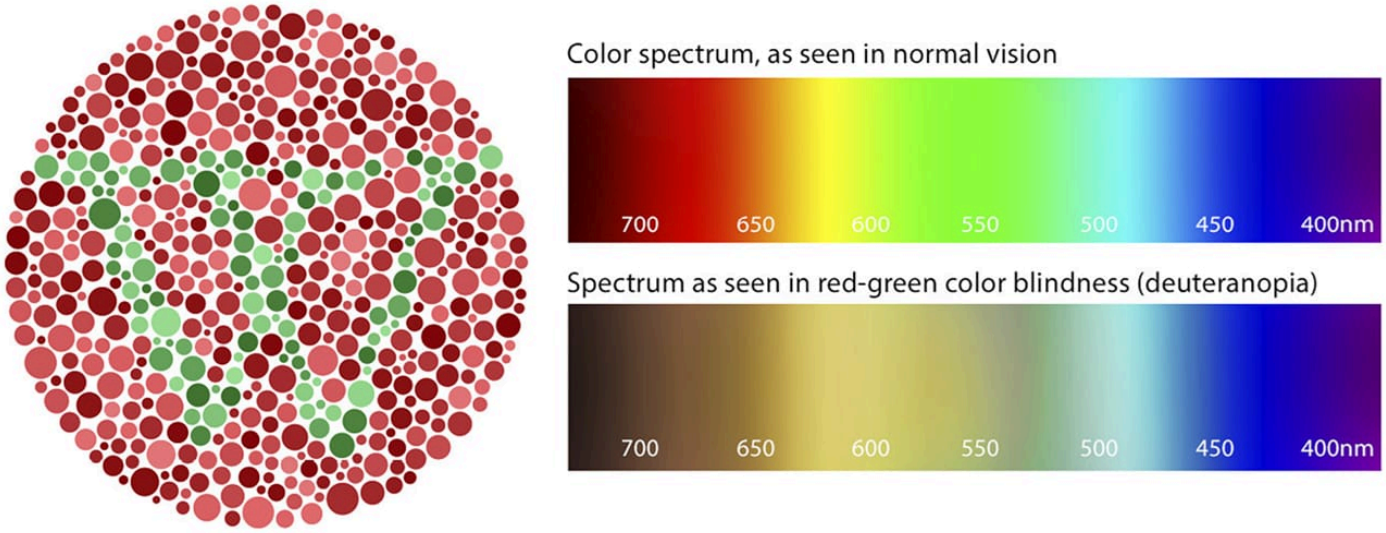


Figure 7.7.5: **Color Blindness.** Approximately 9% of males have some degree of red-green color blindness (deuteranopia) and cannot read the letter in the circular Ishihara color test at the left. The bottom color spectrum on the right simulates the spectrum as seen by people with red-green color blindness.

Recessive Carriers

Females who inherit one recessive X-linked allele and one normal dominant allele are called **carriers**. Carriers typically do not show symptoms of the disorder.

In some cases, carrier females may show very mild symptoms due to random inactivation of one X chromosome in each cell. Even if unaffected, carrier females can pass the recessive gene to their children.

- A son has a 50% chance of being affected
- A daughter has a 50% chance of being a carrier

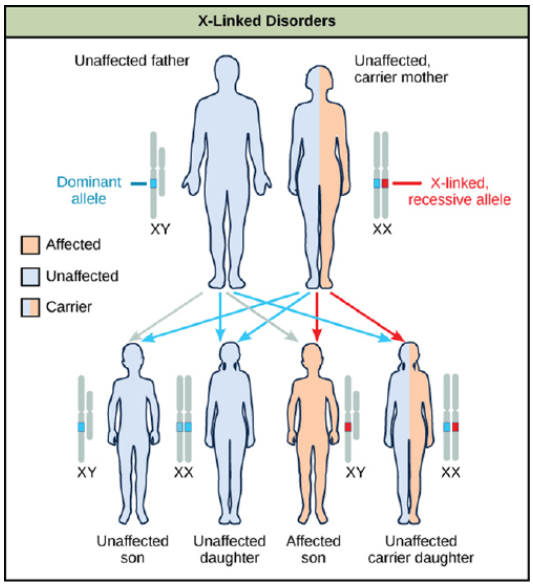


Figure 7.7.6: **Color Blindness.** X-linked recessive inheritance. An unaffected father (XY) and an unaffected carrier mother (XX) are shown, where the mother carries one normal (dominant) X allele and one recessive X-linked allele. Because males have only one X chromosome, sons who inherit the recessive allele are affected, while sons who inherit the normal allele are unaffected. Daughters inherit two X chromosomes, so those who receive one recessive allele are carriers but typically unaffected, and those who receive two normal alleles are unaffected. This pattern explains why X-linked recessive disorders are more common in males than in females.

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7.8: The Ear and the Process of Hearing

Hearing is the process by which the ear captures sound waves, amplifies them, and transforms them into electrical signals that the brain interprets as sound.

Master this section and you'll be able to

- Identify the main parts of the outer, middle, and inner ear and describe how each contributes to hearing.
- Explain how vibrations in the ear are turned into electrical signals the brain can understand.
- Describe how different sound frequencies activate specific parts of the cochlea to create the perception of pitch.

Hearing: How the Ear Turns Sound into Signals

Hearing, or **audition**, is our ability to turn sound waves from the environment into electrical signals the brain can understand. This amazing process depends on the intricate design of the ear. Let's take a look at the anatomy of the ear:

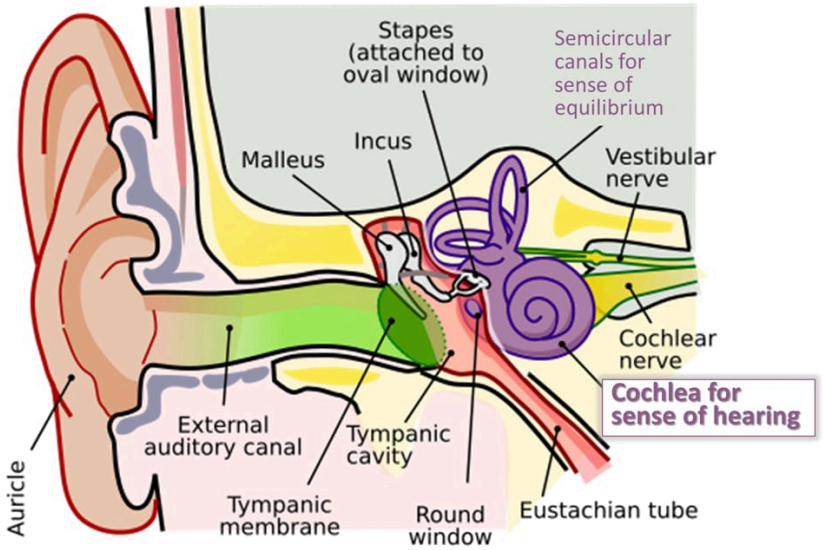


Figure 7.8.1: **Diagram of the Anatomy of the Human Ear.** Green is outer ear; red is middle ear; purple is inner ear. tructures of the Ear The external ear contains the auricle, ear canal, and tympanic membrane. The middle ear contains the ossicles and is connected to the pharynx by the Eustachian tube. The inner ear contains the cochlea, which is responsible for audition.

The Outer Ear: Catching and Channeling Sound

The large, visible part on the side of your head is called the **auricle** (or **pinna**). In animals like cats, the pinna can swivel to capture sounds from different directions, but in humans it mainly acts as a funnel, channeling sound waves into the external **auditory canal,** which ends at the **tympanic membrane** — better known as the **eardrum** — which vibrates when hit by sound waves. In adults, the auditory canal is approximately 2.5 centimeters long. Together, the auricle, auditory canal, and eardrum make up the external or outer ear.

The Middle Ear: Amplifying Vibrations

Next comes the middle ear, a small air-filled space containing three tiny bones called the **ossicles**: the **malleus** (hammer), **incus** (anvil), and **stapes** (stirrup). These bones form a delicate chain that transfers vibrations from the eardrum to the inner ear, where

sound is converted into nerve impulses.

The malleus is attached to the tympanic membrane and connects with the incus, which in turn articulates with the stapes. The stapes rests against the **oval window**, a thin membrane that separates the air-filled middle ear from the fluid-filled inner ear. When the stapes vibrates against the oval window, it transfers sound energy — originally air pressure waves — into the inner ear, where the vibrations become **fluid waves** and are ultimately **transduced into neural signals** that the brain can interpret as sound.

The **Eustachian tube** connects the middle ear to the **pharynx (throat)** and plays a vital role in keeping the air pressure inside your middle ear balanced with the air pressure outside. Without this pressure equalization, the tympanic membrane could not vibrate properly, and your hearing would become muffled or distorted. The tube usually stays closed, but it briefly opens when you **swallow, yawn, or change altitude** — that familiar "pop" you feel in your ears when you go up the mountain in a gondola, for example, is the sound of air pressure equalizing on both sides of the eardrum.

The Inner Ear: Translating Vibrations into Sound

The inner ear is where the magic of hearing truly happens. Here, mechanical vibrations are transformed into electrical signals that your brain interprets as sound.

This region is housed deep within the **temporal bone** and contains a maze of fluid-filled passages known as the **bony labyrinth**. Within it lies the **cochlea**, a spiral-shaped structure that resembles a snail shell. Inside the cochlea, sound vibrations create pressure waves in the fluid, bending tiny hair cells located along a specialized membrane called the **organ of Corti**. These hair cells act as sensory receptors, converting mechanical movement into **neural signals** that travel along the **cochlear branch of the vestibulocochlear nerve (cranial nerve VIII)** to the brain.

Different frequencies of sound activate different regions of the cochlea: high-pitched sounds stimulate hair cells near the base, while low-pitched sounds reach the apex. The brain then assembles all this information into the rich experience we call hearing.

Although the inner ear also contains the **vestibular system**, which is responsible for balance, we will focus here only on the **cochlea and the process of hearing**.

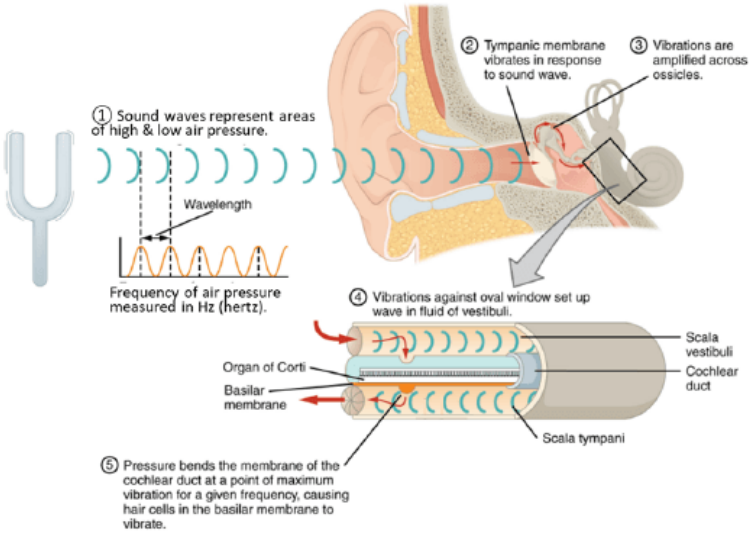


Figure 7.8.2: **Transmission of Sound Waves to Cochlea.** A sound wave causes the tympanic membrane to vibrate. This vibration is amplified as it moves across the malleus, incus, and stapes. The amplified vibration is picked up by the oval window causing pressure waves in the fluid of the scala vestibuli and scala tympani. The complexity of the pressure waves is determined by the changes in amplitude and frequency of the sound waves entering the ear.

Cochlea and Organ of Corti

A cross-sectional view of the cochlea shows that the **scala vestibuli** and **scala tympani** run on either side of the **cochlear duct.** As sound waves travel through the fluid of the scala vestibuli and scala tympani, they cause the basilar membrane to vibrate at specific spots depending on the **frequency** of the sound. **High-pitched** sounds cause vibrations near the **base** of the cochlea, while **low-pitched** sounds activate regions near the **apex** (tip).

The **organ of Corti** contains specialized sensory cells called **hair cells**, named for the **hair-like projections** (stereocilia) that extend from the top (apical) surface of each cell *(see Figure below)*. These **stereocilia** are arranged in rows from tallest to shortest, forming a staircase-like pattern. Fine **protein fibers** connect the tips of neighboring stereocilia, linking them so that when one moves, the others move as well.

The stereocilia extend upward to touch the **tectorial membrane**, a gelatinous structure that lies above them and is attached along one edge to the organ of Corti. When sound waves move through the **scala vestibuli** and **scala tympani**, they cause the **basilar membrane** beneath the hair cells to vibrate. This motion makes the tectorial membrane slide across the tops of the stereocilia, bending them either **toward** or **away** from the tallest row.

When the stereocilia bend **toward** the tallest member of the array, the tension in the protein links increases, pulling open tiny **ion channels** in the hair cell membrane. This causes the hair cell to **depolarize**, generating an electrical signal that travels through the **afferent nerve fibers** to the brain. When the stereocilia bend **away** from the tallest member, the tension decreases and the ion channels close, stopping the signal. Even when no sound is present, the stereocilia stand slightly bent, maintaining a small amount of tension that keeps the hair cell just slightly **depolarized**—ready to respond instantly to the next vibration.

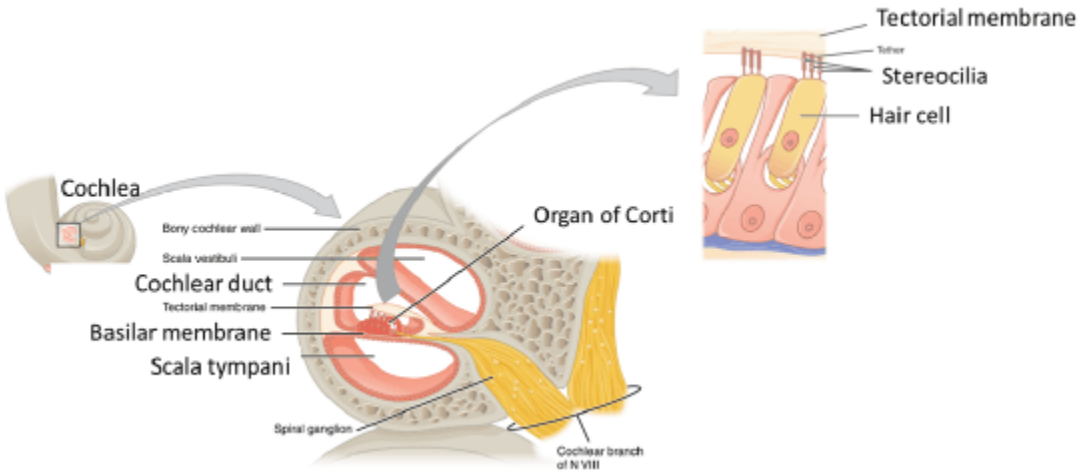


Figure 7.8.3: **Organ of Corti.** Inside the cochlear duct lies the **organ of Corti**, the sensory structure responsible for converting mechanical sound vibrations into electrical signals that the brain can interpret. It rests on the **basilar membrane**, which separates the cochlear duct from the **scala tympani**. The **hair cells** within the organ of Corti act as **mechanoreceptors**. Each hair cell has an array of **stereocilia** extending from its apical surface. When these stereocilia bend in response to vibrations, the mechanical movement is transformed into an **electrical signal** that travels along the auditory nerve to the brain, where it is perceived as sound.

Analogy:
Think of the cochlea like a **tiny, spiral piano** rolled up inside your inner ear. Each location along the basilar membrane acts like a different piano key, tuned to a particular pitch. When a sound wave of a certain frequency enters the ear, it “strikes” the matching key inside the cochlea, sending a signal to your brain that you perceive as a specific tone.

Interactive Link

YouTube Video

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Watch this video to learn more about how the structures of the ear convert sound waves into a neural signal by moving the “hairs,” or stereocilia, of the cochlear duct. Specific locations along the length of the duct encode specific frequencies, or pitches. The brain interprets the meaning of the sounds we hear as music, speech, noise, etc. Which ear structures are responsible for the amplification and transfer of sound from the external ear to the inner ear?

Frequency Mapping Along the Cochlea

As mentioned above, each region of the **basilar membrane** vibrates only in response to a specific **sound frequency**. Because the **tectorial membrane** moves only where the basilar membrane moves, the **hair cells** in that region also respond only to sounds of that particular frequency.

As the frequency of a sound changes, different groups of hair cells are activated along the length of the cochlea. This organization allows the cochlea to **encode sound frequencies** across the full range of human hearing — from about **20 to 20,000 Hz (Hertz)**, where *Hertz* refers to the number of vibration cycles per second.

Low-frequency sounds (around **20 Hz**) stimulate hair cells near the **apex** or tip of the cochlea, while high-frequency sounds (around **20,000 Hz or 20 kHz**) activate hair cells near the **base** of the cochlea, close to the **oval** and **round windows** *(see Figure below)*.

Most sounds we hear are complex mixtures of many frequencies and intensities (determined by the **amplitude** of the sound wave). Because each region of the cochlear duct is tuned to a specific frequency, the cochlea effectively separates these components — **much like a prism separates white light into a spectrum of colors**.

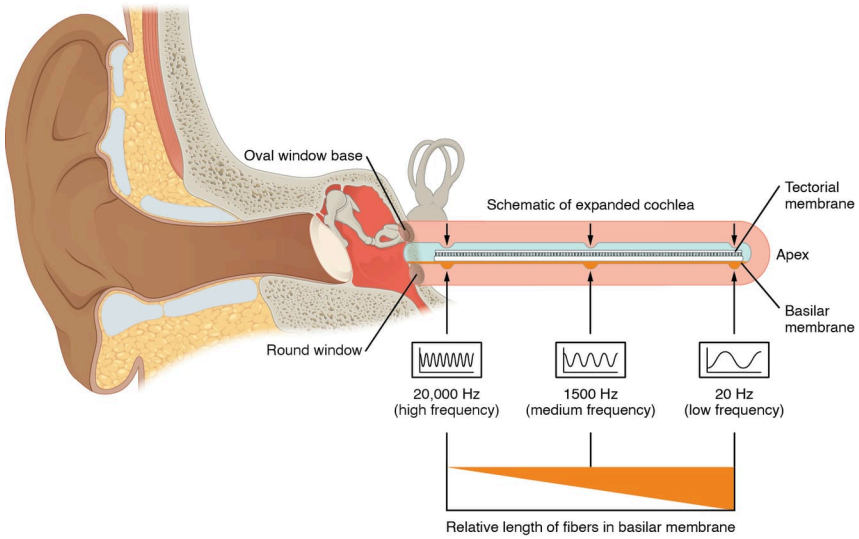


Figure 7.8.4: Frequency Coding in the Cochlea The standing sound wave generated in the cochlea by the movement of the oval window deflects the basilar membrane on the basis of the frequency of sound. Therefore, hair cells at the base of the cochlea are activated only by high frequencies, whereas those at the apex of the cochlea are activated only by low frequencies.

Interactive Link

YouTube Video

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View this YouTube Video online

Watch this animation to learn more about the inner ear and to see the cochlea unroll, with the base at the back of the image and the apex at the front. Specific wavelengths of sound cause specific regions of the basilar membrane to vibrate, much like the keys of a piano produce sound at different frequencies. Based on the animation, where do frequencies—from high to low pitches—cause activity in the hair cells within the cochlear duct?

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7.9: Hearing Impairments

Hearing loss occurs when sound transmission or inner ear function is disrupted, reducing the brain's ability to interpret sound and maintain balance.

Master this section and you'll be able to

- Explain how disruptions to normal sound transmission or sensory cell function in the ear lead to different types of hearing loss.

Hearing Loss and Ear Problems

About one third of people aged 70 and older experience some degree of hearing loss. As you have learned, hearing relies on a series of steps that transform sound waves in the air into electrical signals the brain can interpret. These signals travel from the inner ear to the brain through the auditory nerve. For normal hearing to occur, all the parts of the ear — from the tympanic membrane to the cochlea — must be healthy and working properly.

Age-related hearing loss (presbycusis) develops gradually in most individuals as they get older. Typically, lower-pitched sounds remain easier to hear, while higher-pitched sounds and normal conversation — especially in noisy environments — become harder to understand. Many people benefit from hearing aids, which help amplify sound and improve communication.

Hearing loss can also result from **causes other than aging.** For instance, a buildup of earwax in the ear canal can block sound waves and cause temporary conductive hearing loss. Exposure to very loud sounds — either suddenly, such as an explosion, or repeatedly over time, like loud music or machinery — can permanently damage the sensory hair cells in the cochlea. Once these hair cells are destroyed, they do not regenerate, leading to irreversible hearing loss.

Another common symptom is **tinnitus**, or "ringing in the ears," which can be triggered by loud sound exposure or by certain medications (for example, high doses of aspirin or some diuretics) that are toxic to the ear's sensory cells. In addition to hearing loss, damage to parts of the inner ear can also cause balance problems, dizziness, or vertigo due to **vestibular dysfunction**, which leads to impairments in the sense of equilibrium.

A 2025 survey by the **Royal National Institute for Deaf People (**RNID(opens in new window)) found that hearing problems from loud music are surprisingly common — **58% of Gen Z respondents (ages 18–28)** reported experiencing tinnitus, temporary hearing loss, or both after music exposure. While these effects may start as temporary, repeated exposure can make them permanent.

In short, **loud sound damages the cochlear hair cells and their nerve connections (synapses)**. The more often these cells are overstimulated, the higher the risk of **permanent noise-induced hearing loss** and **chronic tinnitus**, both of which can seriously impact communication, learning, and quality of life.

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8: ENDOCRINE SYSTEM

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8.1: Overview of the Endocrine System

The nervous and endocrine systems both use chemical messengers to signal target cells, but while the nervous system transmits signals rapidly through neurons, the endocrine system uses ductless glands that release hormones carried long distances through the bloodstream.

Master this section and you'll be able to

- Describe how homeostasis is maintained through the coordinated actions of the nervous and endocrine systems.
- Compare and contrast the mechanisms of communication in the nervous and endocrine systems.
- Produce a brief overview of the endocrine system.
- Analyze how the structural and functional differences between endocrine and exocrine glands contribute to their distinct roles in regulating body processes.

Homeostasis and Its Regulators

As you learned at the beginning of the course, the body — despite external changes — must maintain a stable internal environment through a continuous and dynamic process called **homeostasis**. Homeostasis is not a fixed state; it is an active process of constant monitoring and adjustment to maintain internal conditions within a narrow, healthy range. This self-regulating process relies on **feedback loops** (primarily negative feedback) to adapt to changing environmental or internal conditions, keeping variables such as **body temperature, fluid balance, and blood glucose** within normal limits to ensure survival.

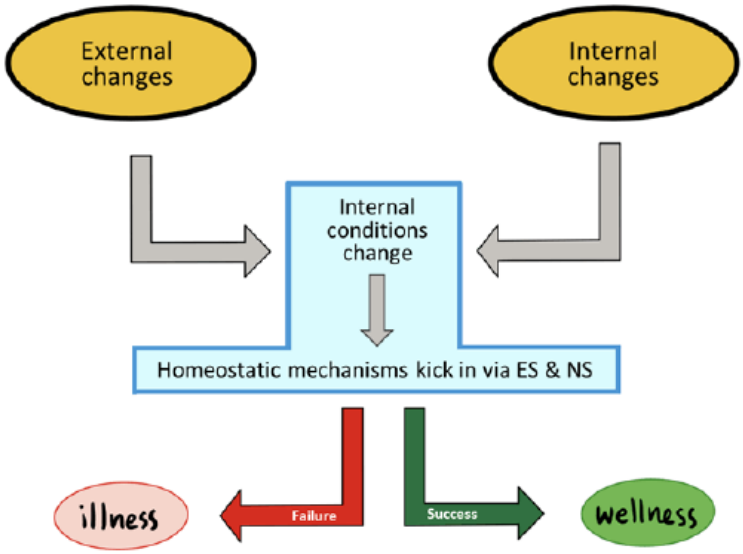


Figure 8.1.1: **Homeostasis Review.** Flowchart showing how external and internal changes alter internal conditions. Homeostatic mechanisms via the endocrine and nervous systems respond; success leads to wellness, failure leads to illness.

Coordination Between the Nervous and Endocrine Systems

The **nervous system** and **endocrine system** are the two primary control systems that regulate and maintain homeostasis, but they differ in how they communicate and how quickly their effects occur.
Both systems use **chemical messengers** to signal target cells, yet their signaling speed and duration of action are distinct.

Nervous System

The **nervous system** responds rapidly to stimuli by generating **electrical impulses (action potentials)** that travel along neurons. When these impulses reach the synaptic terminals, they trigger the release of **neurotransmitters**, which are the chemical messengers of the nervous system.
These neurotransmitters act on nearby target cells — such as muscles, glands, or other neurons — producing effects that are **almost instantaneous but short-lived**.
A classic example is the **withdrawal reflex**: when you touch something hot, sensory neurons rapidly transmit the signal to the spinal cord, which immediately activates motor neurons to contract your arm muscles and pull away.

Endocrine System

In contrast, the **endocrine system** communicates more slowly but with longer-lasting effects. It uses **hormones**, chemical messengers produced and secreted by **endocrine glands**, such as the pituitary, thyroid, or adrenal glands. These hormones travel through the **bloodstream or interstitial fluid** to reach distant **target cells** that have specific receptors for each hormone.

Because hormones must be synthesized, secreted, transported, to then interact with receptors, endocrine responses take **seconds to hours** to occur. However, their effects can last **minutes, hours, or even days**.
For example, **growth hormone** secreted by the **anterior pituitary gland** promotes protein synthesis and tissue growth over an extended period during childhood and adolescence.

Summary

- The **nervous system** acts quickly and locally, using **electrical impulses** and **neurotransmitters** to produce short-term responses.
- The **endocrine system** acts more slowly, using **hormones** to coordinate long-term processes such as growth, metabolism, and reproduction.
- Together, these systems maintain **homeostasis** by ensuring that internal conditions remain balanced despite external or internal fluctuations.

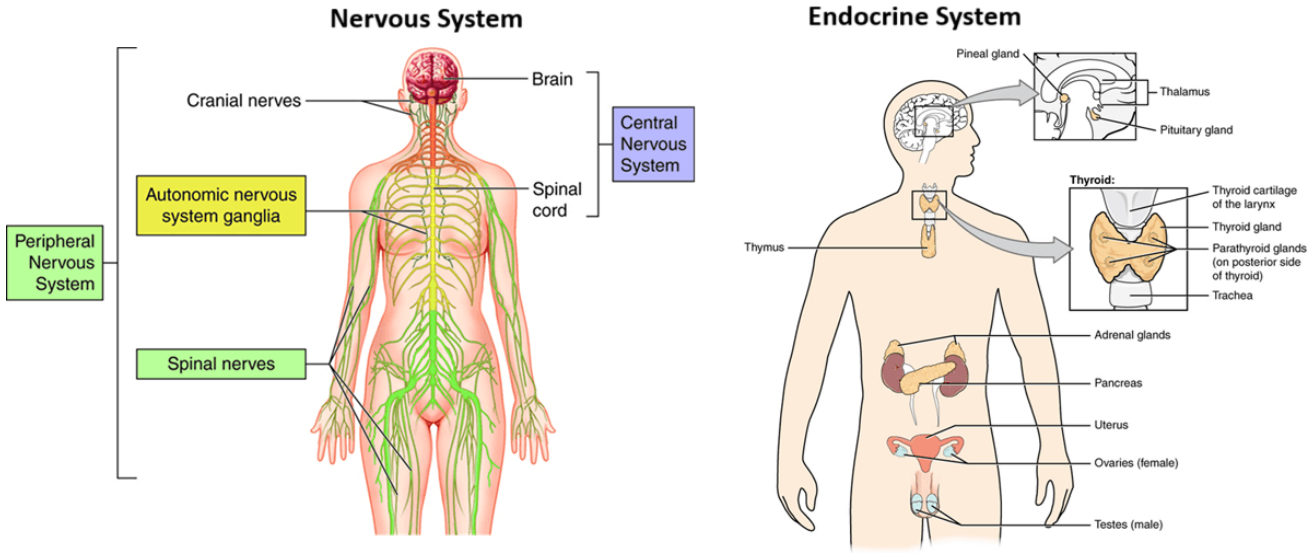


Figure 8.1.2: **Nervous and Endocrine Systems.** The nervous and endocrine systems are the body's two main control systems

that maintain homeostasis.
Left: The nervous system includes the brain, spinal cord (CNS), and nerves and ganglia (PNS). It communicates through rapid electrical impulses and neurotransmitters to produce quick, coordinated responses. *Right:* The *endocrine system* consists of ductless glands that secrete hormones directly into the bloodstream. These hormones act more slowly but produce longer-lasting effects on target organs throughout the body.

Comparison of Signaling Mechanisms, Response Characteristics, and Functions of the Nervous and Endocrine Systems

Feature	Nervous System	Endocrine System
Type of Signal	Electrical impulses (action potentials) and neurotransmitters	Chemical messengers (hormones)
Speed of Response	Very fast (milliseconds)	Slower (seconds to hours)
Duration of Effect	Short-lived	Long-lasting
Distance to Target	Acts on nearby target cells at synapses	Acts on distant target cells via the bloodstream
Primary Structures Involved	Brain, spinal cord, nerves	Endocrine glands (e.g., pituitary, thyroid, adrenal)
Examples of Functions	Reflexes, muscle contraction, sensory perception	Growth, metabolism, reproduction, fluid balance
Example of Stimulus Response	Touching a hot surface → arm withdraws	Growth hormone released → promotes tissue growth

The Endocrine System: The Body's Long-Distance Messenger Network

The **endocrine system** is like the body's **slow but steady postal service** — sending chemical messages (hormones) through the bloodstream to coordinate body functions over time. Unlike the nervous system, which delivers lightning-fast "text messages" to nearby cells, endocrine signals travel farther, work more gradually, and often produce effects that last much longer.

Endocrine glands are *ductless*, meaning they release hormones directly into the **circulatory system**, where the blood carries them to distant target organs and tissues. These hormones regulate vital processes such as growth, metabolism, stress response, and reproduction.

For example, the **pineal gland**, a small structure tucked deep in the brain, secretes **melatonin**, a hormone that helps regulate your **sleep–wake cycle**. When it gets dark, melatonin levels rise, signaling that it is time to sleep — nature's way of dimming the lights inside your body.

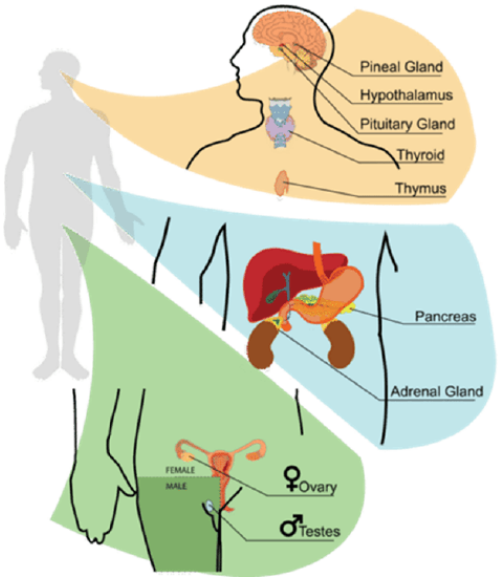
Endocrine glands are richly supplied with blood vessels, ensuring hormones can quickly enter circulation. The glands' secretory cells are packed with **vacuoles or granules** that store hormones until it is time for release. Although endocrine signaling is **slower to start** than nerve impulses, its effects are **more sustained**, influencing body functions over minutes, hours, or even years. Think of growth or puberty — both are orchestrated by long-term hormonal signals.

"To Duct or Not to Duct?" — The Difference Between Endocrine and Exocrine Glands

Both **endocrine and exocrine glands** are specialized structures that produce and secrete substances essential for body function and regulation. Endocrine glands release hormones directly into the bloodstream, allowing them to travel to distant target organs and coordinate long-term processes.

In contrast, exocrine glands secrete their products — such as sweat, saliva, or digestive enzymes — through ducts onto body

surfaces or into body cavities, where they perform a local function.



Key Endocrine Glands

Major endocrine glands include the:

- **Pituitary gland** – often called the ***"master gland"*** because it controls several other glands
- **Pineal gland** – regulates sleep through melatonin
- **Thyroid gland** – controls metabolism and energy use
- **Adrenal glands** – manage stress responses through hormones like cortisol and adrenaline
- **Hypothalamus** – links the nervous and endocrine systems, controlling pituitary output
- **Ovaries and testes** – produce sex hormones that regulate reproduction and secondary sex characteristics

Other organs such as the **kidneys, liver, pancreas, and heart** also have **secondary endocrine functions**, releasing hormones that help regulate blood pressure, red blood cell production, and glucose levels.

Figure 8.1.3: **The Endocrine System and Its Major Glands.** The major endocrine glands are distributed throughout the body. These ductless glands release hormones into the bloodstream to regulate growth, metabolism, reproduction, and homeostasis.

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8.2: Hormones

Hormones are classified by their chemical structure, which determines how they travel, bind to receptors, and trigger specific responses in target cells.

Master this section and you'll be able to

- Identify the two major hormone classes by chemical structure and explain how structure affects their solubility, transport, and action on target cells.
- Compare and contrast intracellular and cell membrane hormone receptors.
- Explain how target cell sensitivity is regulated through upregulation and downregulation.
- Discuss what BPA is and the concerns its use has created.

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

Hormones of the human body can be divided into two main chemical groups: **amino acid–derived hormones** (amines, peptides, and proteins) and **lipid-derived hormones** (steroids). These chemical differences determine how hormones travel in the bloodstream, whether they bind to receptors on the cell surface or inside the cell, and how they influence target cell function.

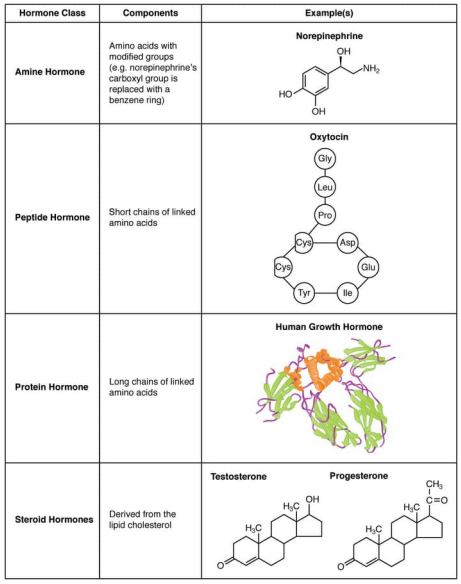


Figure 8.2.1: **Chemical Subdivisions of Hormones.**

Amine, Peptide and Protein Hormones

Hormones made from amino acids fall into three main types: **amine**, **peptide**, and **protein** hormones.

- **Amine hormones** are small molecules made from single modified amino acids, usually **tryptophan** or **tyrosine**. For example, **melatonin**, which is synthesized from tryptophan in the pineal gland, helps regulate the sleep–wake cycle, while the **thyroid hormones (T_3 and T_4)** and the **catecholamines** (epinephrine, norepinephrine, etc.), which are derived from tyrosine, help regulate metabolism.

- **Peptide hormones** are composed of chains of amino acids, typically ranging from 2 to ~ 50 aa in length, though longer chains — called **polypeptides** — can contain even more. Examples of peptide hormones are **insulin** and **glucagon**, both regulating blood sugar levels, working in opposition to each other.

- **Protein hormones** are longer amino acid chains, with lengths typically exceeding 51 amino acids. One such example is the **growth hormone (GH)**, which stimulates cell growth and repair.

Most amine, peptide, and protein hormones are **hydrophilic** (water-loving) and therefore **water-soluble**, allowing them to travel easily through the bloodstream but preventing them from crossing cell membranes. An exception is the **thyroid hormones (T3 and T4)**, which are **hydrophobic (lipid-soluble)** and can enter target cells directly to influence gene expression.

Lipid-Derived (Steroid) Hormones

The primary hormones derived from lipids are the **steroid hormones**, which are synthesized from **cholesterol**. Examples include the reproductive hormones **testosterone** and **estrogens**, produced by the gonads (testes and ovaries), as well as **aldosterone** and **cortisol**, secreted by the adrenal glands. Aldosterone helps regulate salt and water balance (osmoregulation), while cortisol influences metabolism and the body's response to stress.

Like cholesterol, steroid hormones are **hydrophobic** (water-hating), thus **fat-soluble** and **not soluble in water**. Because blood is water-based, these lipid-derived hormones must travel through the bloodstream bound to **transport proteins**. Once they reach their target cells, steroid hormones can **easily cross the cell membrane** and bind to receptors inside the cell — often in the cytoplasm or nucleus — where they directly influence gene expression and protein synthesis.

In the figure below, you can see seven of the most well-known hormones and the glands where they are produced.

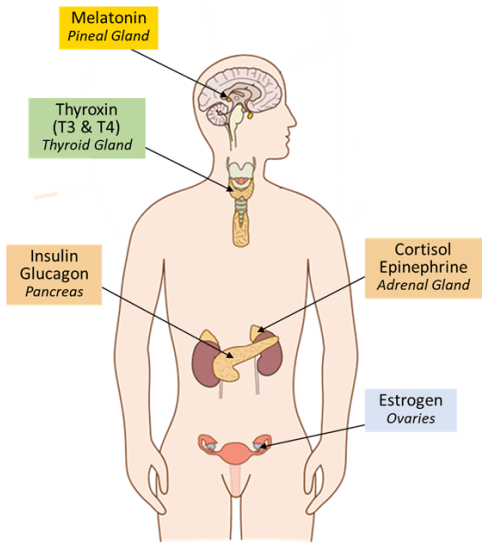


Figure 8.2.2: **Some Endocrine Glands and Their Hormones.** The **pineal gland** (in the brain) releases *melatonin*, which regulates sleep–wake cycles. The **thyroid gland** (in the neck) produces *thyroxine* (T_3 and T_4), which controls metabolism. The **pancreas** secretes *insulin* and *glucagon* to regulate blood glucose levels. The **adrenal glands** (above the kidneys) release *cortisol* and *epinephrine*, important for stress response and metabolism. The **ovaries** produce *estrogen*, which regulates female reproductive functions.

Below is the table that lists these important human hormones, their sources, chemical classifications, and main functions in regulating homeostasis.

Hormone Examples

Hormone	Source Gland	Type of Hormone	Main Function
Insulin	Pancreas (β-cells)	**Peptide**	Lowers blood glucose by promoting cellular uptake of glucose and glycogen formation.

Hormone	Source Gland	Type of Hormone	Main Function
Glucagon	Pancreas (α-cells)	**Peptide**	Raises blood glucose by stimulating glycogen breakdown and glucose release from the liver.
Cortisol	Adrenal cortex	**Steroid**	Regulates metabolism and the stress response by increasing blood glucose and reducing inflammation.
Epinephrine (Adrenaline)	Adrenal medulla	**Amine (Catecholamine)**	Triggers "fight-or-flight" responses: increases heart rate, blood pressure, and energy availability.
Thyroxine (T_4)	Thyroid gland	**Amine (Iodinated Tyrosine derivative)**	Controls metabolic rate, growth, and development.
Estrogen	Ovaries (and adrenal cortex)	**Steroid**	Promotes development of female reproductive organs and secondary sexual characteristics.
Melatonin	Pineal gland	**Amine (Tryptophan derivative)**	Regulates sleep–wake cycles and responds to changes in light and darkness.

Pathways of Hormone Action

Hormones deliver their messages by binding to **specific receptors**, which are proteins located either on the **cell membrane** or **inside the cell**. Each receptor is designed to recognize and bind only to hormones with a matching molecular shape, ensuring that signals are highly specific. When a hormone binds to its receptor, it triggers a series of **signaling events** that lead to the target cell's response. The same type of receptor may be found in different tissues, but the resulting effects can vary depending on the cell type and its internal machinery.

Once activated, the target cell can respond in several ways. These responses may include **stimulating protein synthesis**, **activating or inhibiting enzymes**, **changing cell membrane permeability**, **altering cell growth or division rates**, or **initiating secretion of cellular products**. Importantly, a **single hormone** can produce **different effects** in the same cell type depending on which signaling pathways are engaged.

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

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

Pathways Involving Intracellular Hormone Receptors

Intracellular receptors (intra = inside; cellular = cell) are located **within the cell**, either in the **cytosol** or **nucleus**. To reach these receptors, a hormone must be able to **cross the cell membrane**. **Steroid hormones**, which are derived from cholesterol, can easily diffuse through the lipid bilayer because they are **lipid-soluble**. **Thyroid hormones**, which are also lipid-soluble but more complex in structure, enter the cell through **specific carrier-mediated transport mechanisms**.

Once inside the cell, the hormone binds to its receptor to form a **hormone–receptor complex**. For **steroid hormones**, this binding may occur in the cytosol or directly in the nucleus. The complex then attaches to a specific segment of DNA, regulating the transcription of certain genes. In contrast, **thyroid hormones** bind directly to receptors that are already attached to DNA. In both cases, the interaction between the hormone–receptor complex and DNA initiates **gene transcription** into **messenger RNA (mRNA)**, which then moves to the cytoplasm and directs **protein synthesis** by ribosomes, ultimately altering cell function.

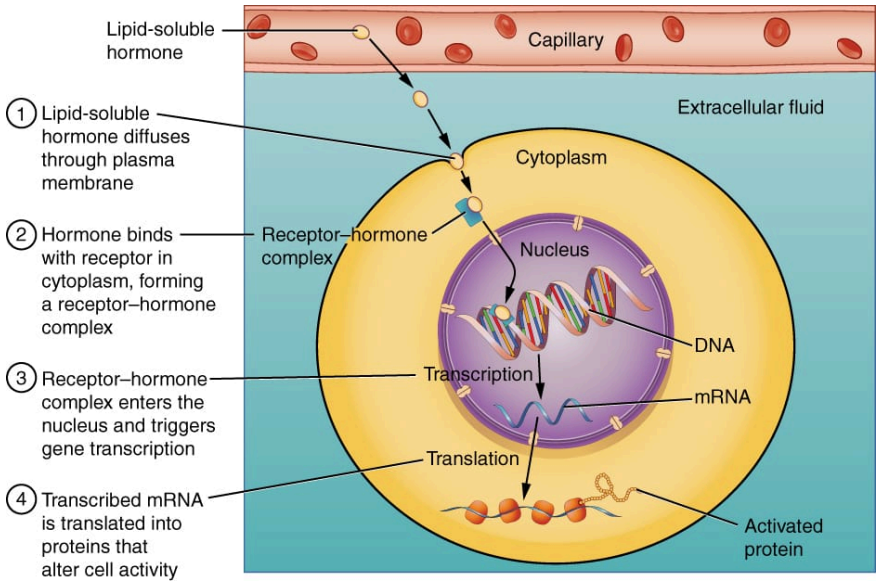


Figure 8.2.3: **Binding of Lipid-Soluble Hormones.** A steroid hormone directly initiates the production of proteins within a target cell. Steroid hormones easily diffuse through the cell membrane. The hormone binds to its receptor in the cytosol, forming a receptor–hormone complex. The receptor–hormone complex then enters the nucleus and binds to the target gene on the DNA. Transcription of the gene creates a messenger RNA that is translated into the desired protein within the cytoplasm.

Pathways Involving Cell Membrane (Extracellular) Hormone Receptors

Hydrophilic (water-soluble) hormones cannot diffuse through the lipid bilayer of the cell membrane, so they must bind to **receptors located on the cell's surface**. With the exception of the **thyroid hormones**, which are lipid-soluble, all **amino acid–derived hormones** interact with receptors that sit on the **extracellular (outer) surface** of the membrane.

Because these hormones cannot enter the cell directly, they act as **first messengers**, triggering a **signaling cascade** inside the cell through **second messengers** such as cyclic AMP (cAMP), calcium ions, or other signaling molecules. These second messengers activate specific enzymes and proteins within the cell, ultimately leading to the **targeted cellular response** — such as changes in metabolism, secretion, or membrane permeability — without directly altering gene transcription.

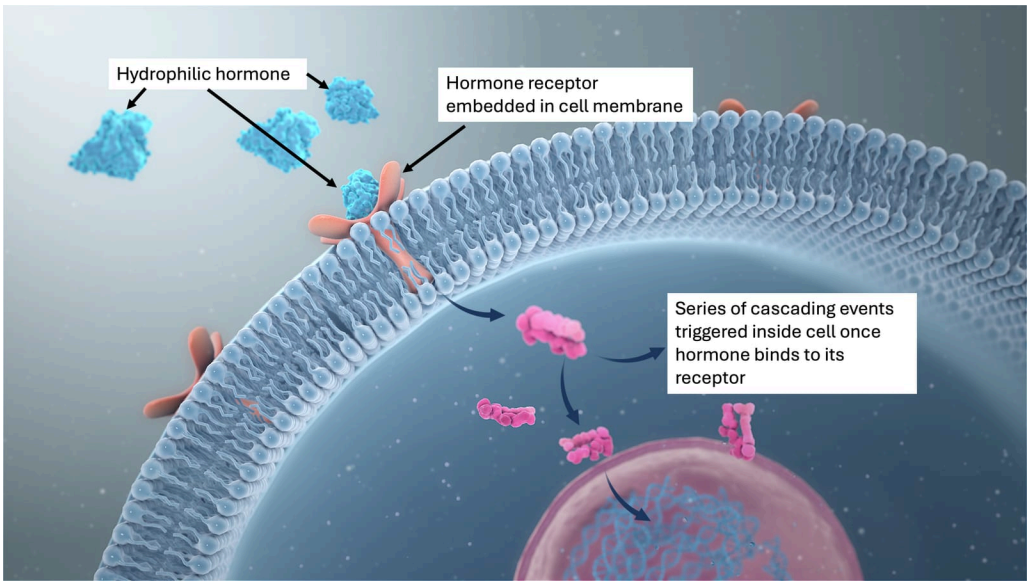


Figure 8.2.4: **Hydrophilic Hormones.** Because hydrophilic (water-soluble) hormones cannot cross the cell membrane, they bind to **receptors on the cell surface**. When the hormone attaches to its receptor, it triggers a **cascade of intracellular signaling events** that amplify the message within the cell. These signaling pathways ultimately lead to specific cellular responses, such as activating or inhibiting enzymes, altering membrane permeability, or stimulating protein synthesis and other metabolic processes. *(Image credit: "Signal Transduction" by Harmony Folse is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

Factors Affecting Target Cell Response

For a hormone to trigger a response, the **target cell** must have specific **receptors** that recognize and bind to that hormone. However, the **strength and duration** of the response can vary depending on several factors.

When hormone levels in the bloodstream remain **high for an extended period**, target cells may **decrease** the number of available receptors — a process known as **downregulation** — to reduce their sensitivity and prevent overstimulation. Conversely, when hormone levels are **chronically low**, cells may **increase** the number of receptors through **upregulation**, making them more responsive to the hormone. In addition to changing receptor number, cells can also adjust the sensitivity of existing receptors, fine-tuning their response to maintain balance and effective communication within the endocrine system.

Everyday Connection

Bisphenol A (BPA): A Hormone Impersonator in Everyday Life

You have probably seen the phrase **"BPA free"** on water bottles or food containers — but what exactly is BPA, and why the concern? **Bisphenol A (BPA)** is a chemical used to make hard plastics and epoxy resins found in many everyday items: food and drink cans, plastic storage containers, water bottles, baby bottles and "sippy" cups, dental sealants, and even the lining of water pipes. Because these plastics can leach small amounts of BPA into food and liquids, scientists have begun to ask an important question: *Is this chemical affecting our hormones?*

Research suggests that BPA is an **endocrine disruptor** — a substance that interferes with the body's hormonal communication system. BPA can **mimic the hormone estrogen** and **block the actions of androgens** (male hormones), which can throw off normal hormone signaling, especially during early development. Studies have linked BPA exposure in **fetuses, infants, and young children** to possible effects on the **brain, behavior, and prostate gland**. In adults, high BPA exposure has been associated with **thyroid disruption**, **fertility problems**, and **changes in metabolism**.

While the **FDA** currently considers low-level exposure to BPA generally safe, ongoing research continues to raise concerns. As a precaution, many U.S. companies have **removed BPA** from baby bottles, sippy cups, and food packaging. **Canada and the European Union** have gone a step further, banning BPA entirely from baby products.

To minimize exposure, consumers are advised to:

- Choose **“BPA-free”** containers and packaging.
- **Avoid plastics labeled with recycling codes 3 or 7**, which may contain BPA.
- **Do not microwave or heat food in plastic containers** — use glass, ceramic, or paper instead.

BPA’s story is a powerful reminder that the endocrine system is **highly sensitive** — even small chemical imbalances can have widespread effects on growth, reproduction, and health.

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8.3: Review of the Negative Feedback Loop

Negative feedback loops maintain homeostasis by detecting changes, like temperature shifts, and triggering responses that restore balance.

Master this section and you'll be able to

- Explain how negative feedback loops maintain homeostasis by detecting and reversing changes that move the body away from normal conditions.
- Describe how the hypothalamus and thermoreceptors work together to regulate body temperature and maintain thermal homeostasis.

As you learned in Section 1.9 (Maintaining Balance — Homeostasis and the Power of Negative Feedback), negative feedback loops are the primary mechanism the body uses to maintain homeostasis. They are called “negative” because they work to reverse a change, bringing the system back to its normal balance.

Negative Feedback and Homeostasis

Negative feedback is essential for keeping the body in balance and maintaining good health. These homeostatic feedback loops help the body regulate itself by reversing any changes that move conditions away from normal. For example, when a body system becomes too active and produces too much of a certain protein or hormone, the negative feedback system steps in to slow or stop that production. This prevents levels from getting too high and brings them back to normal. In this way, negative feedback loops help keep the body’s internal environment within the physiological limits. An example of a negative feedback loop is shown in the figure below.

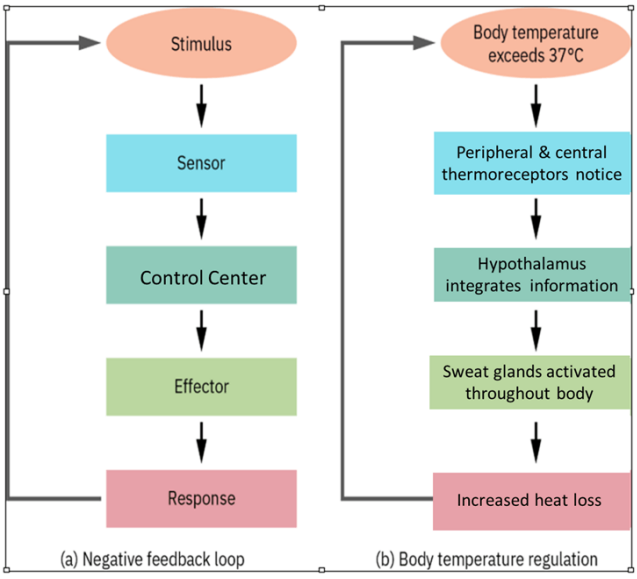


Figure 8.3.1: **Negative Feedback Loop and Body Temperature Regulation.** (a) A negative feedback loop maintains homeostasis by detecting a change, sending it to a control center, and triggering an effector response that reverses the change. (b) When body temperature rises above 37°C, the brain activates sweat glands to increase heat loss and restore normal temperature. (Credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license) Homeostatic Response System

The body’s homeostatic response system is always working to keep things balanced, even when internal or external factors try to

push it off course. This system maintains a stable internal environment so that the body can function properly.

The hypothalamus acts as the body's thermostat, setting the normal temperature and keeping this set point steady through homeostasis. The body contains special nerve cells called **thermoreceptors** that detect changes in temperature. Some thermoreceptors, called **peripheral thermoreceptors**, are located in the skin and sense surface temperature. Others, called **central thermoreceptors**, are found in the internal organs (viscera), spinal cord, and hypothalamus itself, where they monitor the body's core temperature. Together, these thermoreceptors send information to the hypothalamus, which then integrates all the temperature data and creates responses to keep the body temperature within a healthy range.

In a healthy individual, the core body temperature is about **37 ± 0.5 °C (98.6 ± 0.9 °F)**. When temperature rises above or falls below this range, the hypothalamus detects the change and acts as the control center. It sends signals to effectors — such as sweat glands or muscles — to counteract the disturbance and restore balance (Figure 8.3.1). In this way, the homeostatic response system allows the body to adjust to changing conditions and remain stable.

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8.4: The Major Endocrine Organs

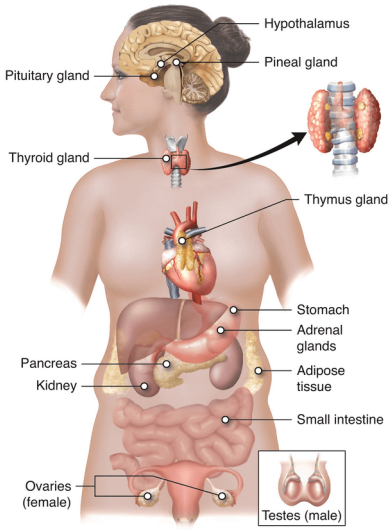
The endocrine system is made up of glands that release hormones — such as insulin, cortisol, and thyroxine — to regulate growth, metabolism, reproduction, and overall body balance.

Master this section and you'll be able to

- Identify the major endocrine glands of the human body and describe the primary hormones they secrete and their main functions.

The Major Endocrine Organs — Your Body's Chemical Command Centers

As you have already learned, the **endocrine system** is sending chemical messages (hormones) through the bloodstream to keep everything running smoothly — from your metabolism and growth to reproduction and stress response. Each **endocrine gland** has a specialty, but together they form a powerful team that keeps your body in balance (homeostasis). Here is a list of all the important endocrine glands that you might want to be aware of:



Back View

🧠 Hypothalamus

The brain's command hub for hormones! It bridges the nervous and endocrine systems, collecting information about the body's internal state (like temperature or stress) and telling the **pituitary gland** what to do.

🎛️ Pituitary Gland — The "Master Gland"

No cape required, but this tiny gland at the brain's base controls many others. It releases hormones that influence growth, reproduction, and the activity of other endocrine glands like the thyroid, adrenals, and gonads.

The hypothalamus and pituitary gland work like the ultimate management duo — monitoring the body and adjusting hormone output body-wide as needed

🌙 Pineal Gland

Deep inside your brain, the pineal gland acts like your internal nightlight timer. It releases **melatonin**, which helps you fall asleep and stay in sync with the day–night cycle.

🦋 Thyroid Gland

This butterfly-shaped gland in your neck controls how fast your body uses energy. Its hormones, such as **thyroxine (T_4)**, regulate metabolism, growth, and temperature.

🫀 Parathyroid Glands

These four tiny glands on the back of the thyroid act as calcium managers, releasing **parathyroid hormone (PTH)** to keep blood calcium levels just right — crucial for muscles and nerves.

⚡ Adrenal Glands

Perched on top of your kidneys, they are your body's stress-response powerhouses. They produce **adrenaline (epinephrine)** for quick "fight-or-flight" reactions and **cortisol** to help manage long-term stress, metabolism, and blood pressure.

🍽️ Pancreas

A multitasker! The pancreas works both as an endocrine and exocrine organ. As an **endocrine gland**, it releases **insulin** and **glucagon** to regulate blood sugar levels.

♀ Ovaries

In females, the ovaries release **estrogen** and **progesterone**, which regulate the menstrual cycle, pregnancy, and the development of female characteristics — and they also release eggs for fertilization.

♂ Testes

In males, the testes produce **testosterone**, which drives sperm production and male physical traits.

Fun Fact: Hormone Helpers

Other organs also moonlight as hormone producers! The **heart**, **thymus**, **kidneys**, and **digestive tract** secrete hormones that support specialized functions — like blood pressure control or red blood cell production.

When Things Go Off Balance

If a gland produces too much or too little hormone, it can cause **endocrine disorders** such as **diabetes**, thyroid disease, or **adrenal insufficiency**. Maintaining the right hormonal "mix" is vital for health and homeostasis.

The major hormones of the human body and their effects are identified in the following Table:

Major Endocrine Glands, the Hormones they Secrete, and their Primary Physiological Effects

Endocrine gland	Associated hormones	Effect
Pituitary (anterior)	Growth hormone (GH)	Promotes growth of body tissues
Pituitary (anterior)	Prolactin (PRL)	Promotes milk production
Pituitary (anterior)	Thyroid-stimulating hormone (TSH)	Stimulates thyroid hormone release
Pituitary (anterior)	Adrenocorticotropic hormone (ACTH)	Stimulates glucocorticoid release by adrenal cortex
Pituitary (anterior)	Follicle-stimulating hormone (FSH)	Stimulates gamete (egg or sperm) production
Pituitary (anterior)	Luteinizing hormone (LH)	Stimulates androgen production by gonads
Pituitary (posterior)	Antidiuretic hormone (ADH; aka vasopressin)	Stimulates water reabsorption by kidneys
Pituitary (posterior)	Oxytocin	Stimulates uterine contractions during childbirth
Thyroid	Thyroxine (T_4), triiodothyronine (T_3)	Stimulate basal metabolic rate
Thyroid	Calcitonin	Reduces blood Ca^{2+} levels
Parathyroid	Parathyroid hormone (PTH)	Increases blood Ca^{2+} levels
Adrenal (cortex)	Aldosterone	Increases blood Na^{+} levels
Adrenal (cortex)	Cortisol, corticosterone, cortisone	Increase blood glucose levels, involved in stress response
Adrenal (medulla)	Epinephrine, norepinephrine	Stimulate fight-or-flight response
Pineal	Melatonin	Regulates sleep cycles
Pancreas	Insulin	Reduces blood glucose levels
Pancreas	Glucagon	Increases blood glucose levels
Testes	Testosterone	Stimulates development of male secondary sex characteristics and sperm production
Ovaries	Estrogens and progesterone	Stimulate development of female secondary sex characteristics and prepare the body for childbirth

CONNECTIONS: Endocrinology

Endocrinology is the branch of medicine that focuses on the **endocrine system**.

Endocrinologists are physicians who specialize in diagnosing and treating disorders of these hormonal systems. Their patients generally have **hormone imbalances** such as **thyroid disease or diabetes mellitus.**
When surgery is needed — for example, to remove a tumor or an overactive gland — **endocrine surgeons** perform the procedure to restore hormonal balance.

Patients are usually referred to an endocrinologist when symptoms or blood tests suggest that a gland is producing **too much or too little hormone**. To confirm the diagnosis, the endocrinologist may order additional lab tests, sometimes stimulating or suppressing gland activity before measuring hormone levels in the blood.

Treatment depends on the underlying cause:

- **Lifestyle modifications** (such as improving diet, increasing physical activity, or managing stress) can help in conditions like **type 2 diabetes**.
- **Medications** may be needed when the body cannot regulate hormones on its own—for instance, **thyroid hormone replacement** or **growth hormone therapy**.
- **Long-term monitoring** ensures that hormone levels remain within healthy ranges.

As people age, certain hormone levels naturally decline. Endocrinologists help patients evaluate the **risks and benefits of hormone replacement therapy (HRT)**, especially for reproductive hormones such as estrogen or testosterone. The goal is to support overall well-being while minimizing side effects.

Beyond patient care, endocrinologists also play a crucial role in **medical research**. They study how hormones interact with cells and organs, explore the causes of endocrine disorders, and develop new treatments to restore balance in the body's complex hormonal systems.

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8.5: Pituitary Gland and Hypothalamus

The hypothalamus–pituitary complex acts as the body's hormonal command center, linking the nervous and endocrine systems to regulate hormone production and maintain homeostasis.

Master this section and you'll be able to

- Describe the structure and function of the hypothalamus–pituitary complex, including how it links the nervous and endocrine systems.
- Compare the anterior and posterior pituitary glands in regards to hormone production, storage, and release, and how each is regulated by the hypothalamus.

The hypothalamus–pituitary complex serves as the **command center of the endocrine system**. It secretes hormones that either act directly on target tissues or regulate the hormone production of other endocrine glands. This complex also bridges the **nervous and endocrine systems**, translating neural signals into hormonal messages. In many cases, sensory information processed by the nervous system must pass through the hypothalamus–pituitary complex before it can trigger hormonal responses that maintain homeostasis.

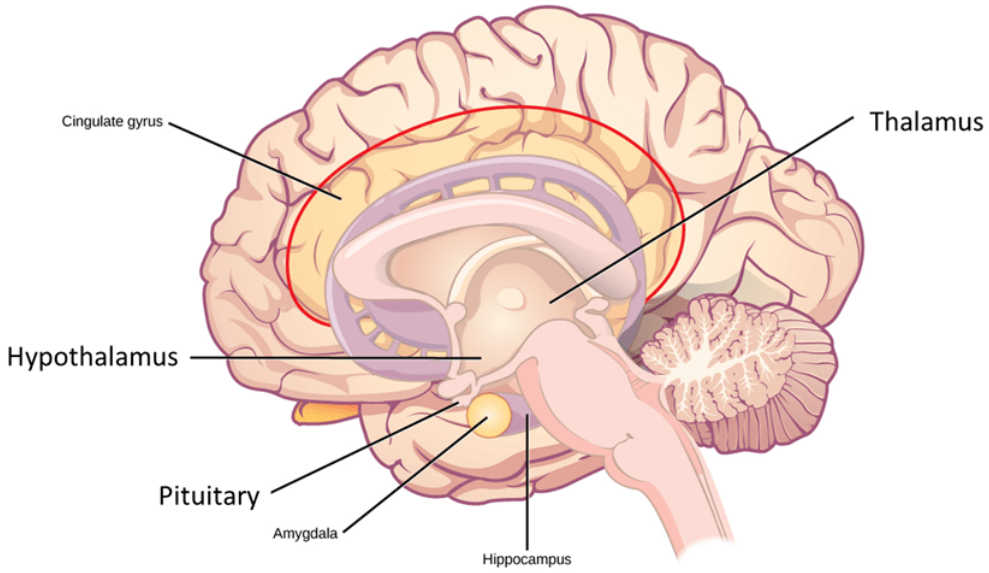


Figure 8.5.1: **Hypothalamus–Pituitary Complex.** The hypothalamus region of the brain lies inferior and anterior to the thalamus. The pituitary gland consists of an anterior and posterior lobe, with each lobe releasing different hormones in response to signals from the hypothalamus. *(Image credit: "Hypothalamus and Pituitary Gland" by Jennifer Lange and Justin Greene is licensed under CC BY-NC-SA 4.0.)*

Hypothalamus

The **hypothalamus** is part of the brain located just below the thalamus. It plays a major role in linking the **nervous system** and the **endocrine system** by controlling the **pituitary gland**. The pituitary hangs below the hypothalamus by a thin stalk called the infundibulum and sits in a small bony cavity of the skull called the **sella turcica**. The hypothalamus produces several hormones and controls when the pituitary releases its own.

Posterior Pituitary

The posterior pituitary is actually part of the brain, not a true gland. It is made of nerve fibers that come from special neurons in

the hypothalamus. These neurons make two hormones: **oxytocin** and **antidiuretic hormone (ADH), also known as vasopressin**. The hormones travel down the axons to the posterior pituitary, where they are stored. When the hypothalamus sends the appropriate signal, the posterior pituitary releases these hormones into the bloodstream.

Anterior Pituitary

The **anterior pituitary** develops from tissue in the roof of the mouth during early growth and later moves toward the brain. Unlike the posterior pituitary, the anterior pituitary **makes its own hormones**. However, it does not act on its own — it is controlled by the **hypothalamus**. The hypothalamus sends **releasing hormones** to tell the anterior pituitary to release hormones, and **inhibiting hormones** to tell it to stop. These hypothalamic hormones reach the anterior pituitary through a special group of blood vessels called the **hypophyseal portal system**. This system forms a direct connection between the hypothalamus and the anterior pituitary, allowing hormones to travel quickly and directly without going through the whole bloodstream.

Six hormones are synthesized in the anterior pituitary. These are the growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin. Of the hormones of the anterior pituitary, TSH, ACTH, FSH, and LH are collectively referred to as tropic hormones (trope- = “turning”) because they turn on or off the function of other endocrine glands.

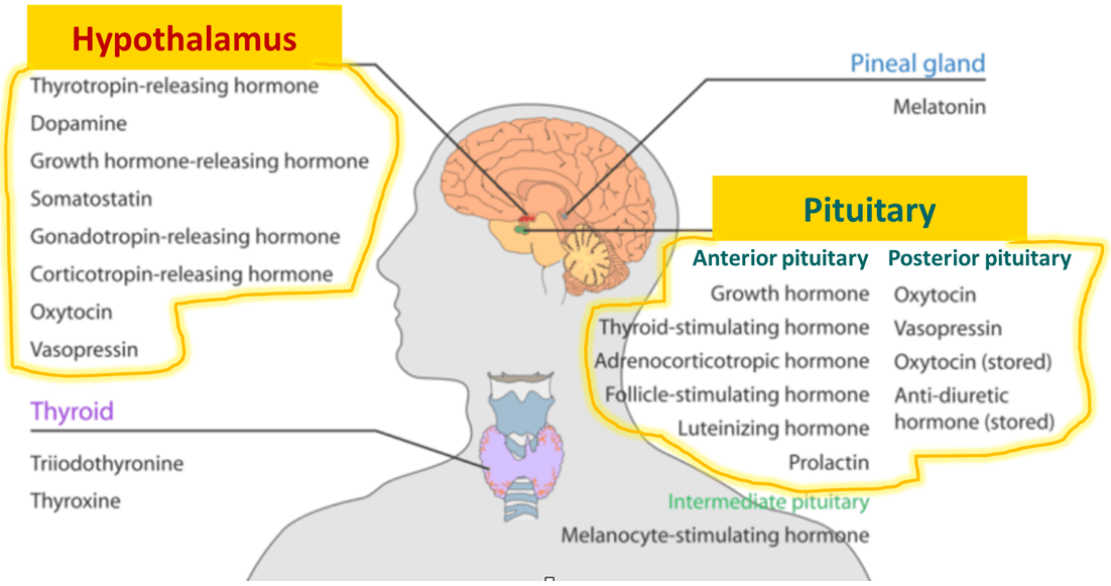


Figure 8.5.2: **Hypothalamus and Pituitary Hormones.** The hypothalamus produces releasing (and inhibiting) hormones like TRH, dopamine, GHRH, somatostatin, GnRH, CRH, oxytocin, and vasopressin. The pituitary releases GH, TSH, ACTH, FSH, LH, prolactin, oxytocin, and ADH.

Hormones Released by the Anterior and Posterior Pituitary Glands and their Primary Physiological Effects

Pituitary lobe	Associated hormones	Effect
Anterior	**Growth hormone (GH)**	Promotes growth of body tissues
Anterior	**Prolactin (PRL)**	Promotes milk production from mammary glands
Anterior	**Thyroid-stimulating hormone (TSH)**	Stimulates thyroid hormone release from thyroid
Anterior	**Adrenocorticotropic hormone (ACTH)**	Stimulates hormone release by adrenal cortex
Anterior	**Follicle-stimulating hormone (FSH)**	Stimulates gamete production in gonads

Pituitary lobe	Associated hormones	Effect
Anterior	**Luteinizing hormone (LH)**	Stimulates androgen production by gonads
Posterior	**Antidiuretic hormone (ADH) / Vasopressin**	Stimulates water reabsorption by kidneys
Posterior	**Oxytocin**	Stimulates smooth muscle contractions in male and female reproductive tracts and uterine contractions during childbirth

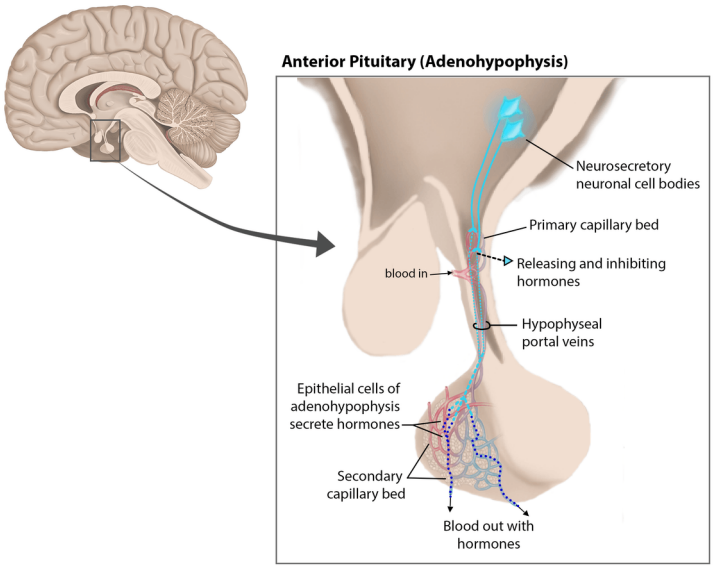


Figure 8.5.3: **Anterior Pituitary Gland.** The anterior pituitary manufactures six hormones. Neurosecretory cells in the hypothalamus produces separate hormones that stimulate or inhibit hormone production in the anterior pituitary. Hormones from the hypothalamus travel by neuron axons to the primary capillary bed of the hypophyseal portal system located in the infundibulum. The hormones move through hypophyseal portal veins in the infundibulum to the secondary capillary bed in the anterior pituitary. Hormones produced in the anterior pituitary are released into the bloodstream via the secondary capillary bed. *(Image credit: "Anterior Pituitary" by Jennifer Lange and Justin Greene is licensed under CC BY-NC-SA 4.0.)*

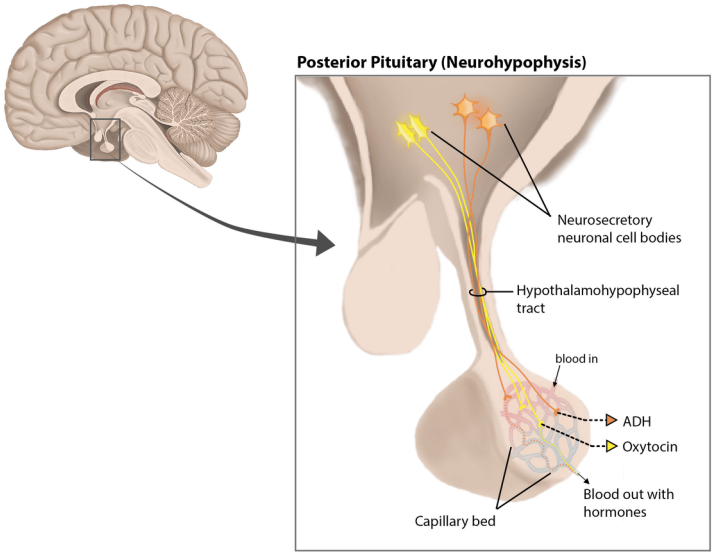


Figure 8.5.4: **Posterior Pituitary Gland.** Neurosecretory cells in the hypothalamus release **antidiuretic hormone** (ADH, a.k.a.:vasopressin) and **oxytocin** (OT). The hormones move through the axons in the hypothalamohypophyseal tract that run through the infundibulum to their axon terminals located in the posterior lobe of the pituitary gland. These hormones are stored or released into the bloodstream via the capillary bed in the posterior pituitary gland. *(Image credit: "Posterior Pituitary" by Jennifer Lange and Justin Greene is licensed under CC BY-NC-SA 4.0.)*

Concept Review

The hypothalamus–pituitary complex is located in the diencephalon of the brain. The hypothalamus and the pituitary gland are connected by a structure called the infundibulum, which contains vasculature and nerve axons. The pituitary gland is divided into two distinct structures with different embryonic origins. The posterior lobe houses the axon terminals of hypothalamic neurons. It stores and releases into the bloodstream two hypothalamic hormones: oxytocin (OT) and antidiuretic hormone (ADH). The anterior lobe is connected to the hypothalamus by the vasculature of the hypophyseal portal system in the infundibulum and produces and secretes six hormones. Their secretion is regulated, however, by releasing and inhibiting hormones from the hypothalamus. The six anterior pituitary hormones are: growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL). Figure 8.5.4 is a summary of the pituitary hormones and their principal effects.

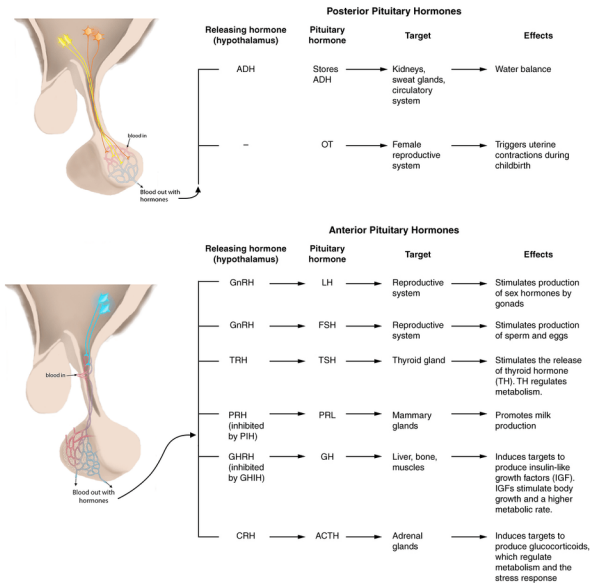


Figure 8.5.5: **Major Pituitary Hormones.** Major pituitary hormones and their target organs and effects. *(Image credit: "Major Pituitary Hormones" by Jennifer Lange and Justin Greene is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*

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8.6: Thyroid Gland

The thyroid gland produces hormones (T_3, T_4, and calcitonin) that regulate metabolism, growth, development, body temperature, and calcium balance through a tightly controlled feedback system involving the hypothalamus and pituitary gland.

Master this section and you'll be able to

- Describe the location and anatomy of the thyroid gland.
- Identify the hormones produced by the follicular cells and the parafollicular cells of the thyroid.
- Describe the synthesis, secretion, and regulation of the thyroid hormones (T_3 and T_4), emphasizing the hypothalamic–pituitary–thyroid (HPT) feedback loop.
- Explain how thyroid hormones influence metabolism, body temperature, and fetal development.

Thyroid Gland Anatomy

The **thyroid gland**, a butterfly-shaped organ, is located anterior to the trachea, just inferior to the larynx (Figure 8.6.1). The medial region, called the isthmus, is flanked by **wing-shaped left and right lobes**. Each of the thyroid lobes has a pair of parathyroid glands embedded on its posterior surface. The tissue of the thyroid gland is composed mostly of **thyroid follicles** lined with simple cuboidal epithelium (Figure 8.6.2). The follicles are made up of a central cavity filled with a sticky fluid called **colloid**. Surrounded by a wall of epithelial follicle cells, the colloid is the center of thyroid hormone production, and that production is dependent on the essential and unique component of thyroid hormones: **iodine**.

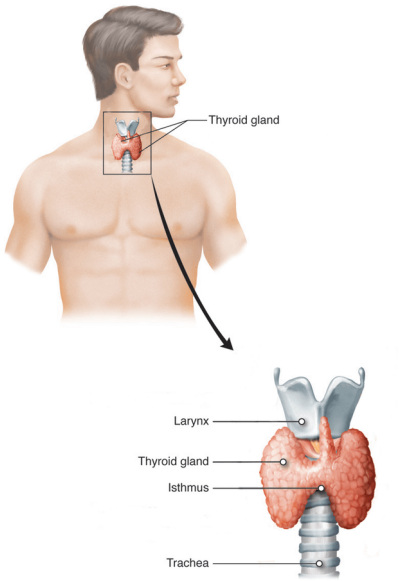
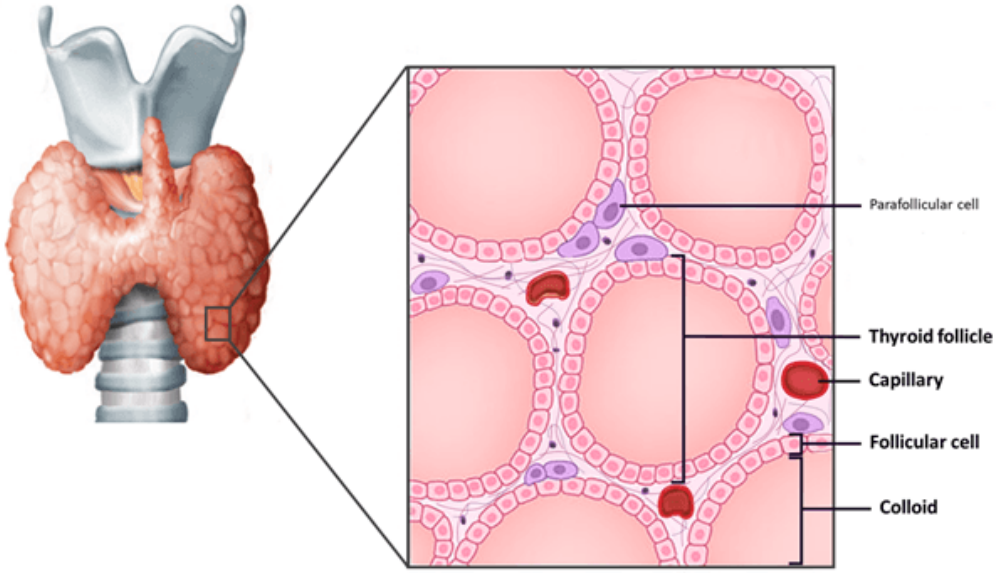


Figure 8.6.1: **Thyroid Gland.** The thyroid gland is located in the neck, wrapping around the front of the trachea just below the thyroid cartilage of the larynx. *(Image Credit: "Thyroid Gland Location" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of original by "KnowledgeWorks - Drawing Thyroid gland and its vascularisation - English labels".)*



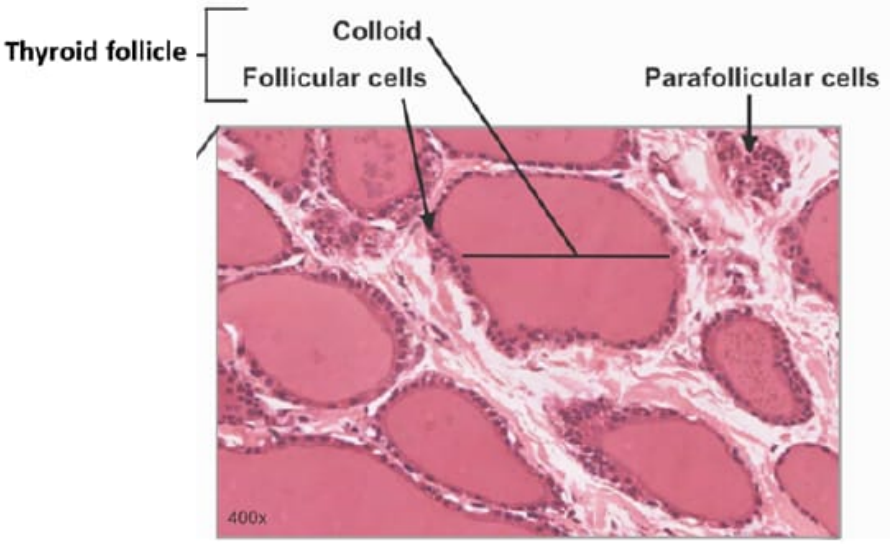


Figure 8.6.2: **Thyroid Follicles.** Each spherical thyroid follicle contains an external layer of epithelial follicular cells surrounding the colloid. Parafollicular cells are scattered in the connective tissue surrounding the follicles. *(Image Credit: "Thyroid Follicles" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Includes modification of original by "KnowledgeWorks - Drawing Thyroid gland and its vascularisation - English labels".) Image on the right:* **Thyroid Gland Histology.** Visibly, the thyroid gland is dominated by the colloid of the follicles. Higher magnification is needed to clearly see the follicular cells and the parafollicular cells. *(Image credit: "Thyroid Gland Histology" by Jennifer Lange and modified by Barbara Zingg is licensed under CC BY-NC-SA 4.0. Micrograph from Digital Histology is licensed under CC BY-NC-SA 4.0.)*

Thyroid Hormones (T_3 and T_4)

The thyroid gland makes two main hormones — **thyroxine (T_4)** and **triiodothyronine (T_3)** — which help control how fast your body uses energy (metabolism). Their production is controlled by **thyroid-stimulating hormone (TSH)** from the anterior pituitary gland.

Inside the thyroid, **follicular cells** make a large protein called **thyroglobulin**, which serves as the "starter material" for these hormones. **Iodide** (the form of iodine in your blood) is pulled into these cells from the bloodstream through **iodide trapping**, a process that concentrates iodine about 30-fold inside the gland — iodine is essential for thyroid hormone production.

An enzyme called **thyroperoxidase** attaches iodine to tyrosine amino acids within thyroglobulin, forming **monoiodotyrosine**

(MIT) and **diiodotyrosine (DIT)**.

- Two DIT molecules combine to make **T_4 (thyroxine)**.
- One MIT and one DIT combine to make **T_3 (triiodothyronine)**.

When the body needs thyroid hormones, the follicular cells break down the stored thyroglobulin, releasing **T_3** and **T_4** into the bloodstream.
Although most hormone released is **T_4**, tissues convert much of it into the more active **T_3**. Think of T_4 as a *storage form* and T_3 as the *active form* that actually drives metabolism, growth, and energy use in cells.

As with the steroid hormones, thyroid hormones are lipophillic and can cross the cell membrane and bind to intracellular receptors, which act alone as transcription factors or in association with other factors to modulate DNA transcription.

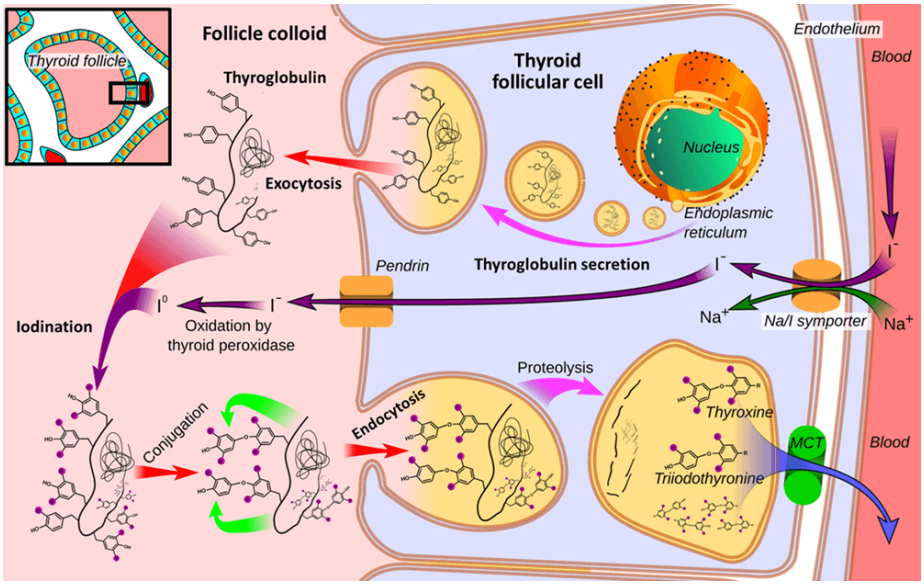


Figure 8.6.3: **Thyroid hormone production and secretion.** Diagrammatic representation of thyroid hormone synthesis in a thyroid follicle.

Control of Thyroid Hormone Release

The production of **thyroxine (T_4)** and **triiodothyronine (T_3)** is regulated by a **feedback system** that begins in the **hypothalamus**. The hypothalamus releases **thyrotropin-releasing hormone (TRH)**, which stimulates the **anterior pituitary gland** to secrete **thyroid-stimulating hormone (TSH)**. TSH then acts on the **thyroid gland**, prompting it to produce and release T_3 and T_4. These hormones increase metabolism, support growth and development, and influence many body systems. When T_3 and T_4 levels rise, they inhibit TRH and TSH release through **negative feedback**, maintaining hormonal balance.

Thyroid hormones also provide negative feedback to the hypothalamus and anterior pituitary gland. When thyroid levels in the blood are elevated TSH and TRH production is reduced. Excessive TRH can also inhibit the production of further TRH.

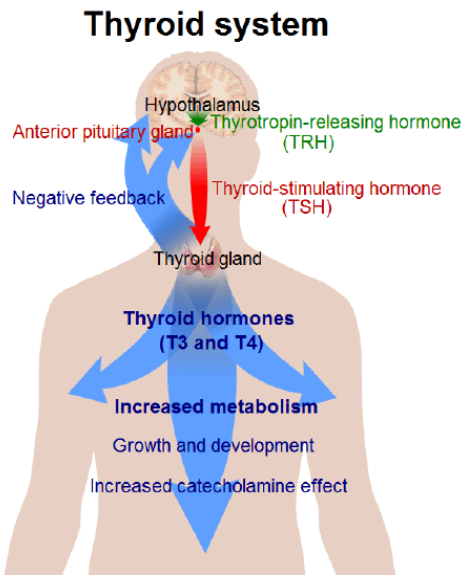


Figure 8.6.4: **The thyroid works under the control of the hypothalamus** and **anterior pituitary gland.**

The hypothalamus releases **TRH (thyrotropin-releasing hormone)**.

TRH stimulates the **anterior pituitary** to release **TSH (thyroid-stimulating hormone)**.

TSH travels through the bloodstream to the thyroid gland, stimulating the release of **T_3 and T_4**.

As you learned in your study of homeostasis, the thyroid system also operates through a **negative feedback loop**: when levels of T_3 and T_4 rise, they signal the hypothalamus and anterior pituitary to reduce the release of TRH and TSH, helping maintain hormonal balance.

Effects of Thyroid Hormones on the Body

1) Effect on Metabolism

The thyroid hormones **T_3 (triiodothyronine)** and **T_4 (thyroxine)** control the **body's overall metabolic rate** — how quickly cells use energy from food. They increase the metabolism of **carbohydrates, fats, and proteins**, helping regulate growth, development, and energy balance. These hormones also enhance the effects of catecholamines (like epinephrine).

2) Effect on Body Temperature

Thyroid hormones also help regulate **body temperature** by influencing **blood vessel dilation** and **heat production.**

- In **hyperthyroidism** (overactive thyroid), metabolism speeds up — patients often feel hot and may have an elevated body temperature.
- In **hypothyroidism** (underactive thyroid), metabolism slows down — patients may feel cold and have a lower body temperature.

3) Role in Fetal Development

Thyroid hormones are **essential for brain development in the fetus**. They guide the growth and organization of nerve cells, supporting normal brain maturation before and after birth. Insufficient thyroid hormone during pregnancy can cause serious developmental problems.

Not Just Thyroxine — Calcitonin: The Thyroid's Other Hormone

The thyroid gland also secretes a hormone called **calcitonin** that is produced by the parafollicular cells (also called clear cells or C cells) that stud the tissue between distinct follicles (Figure 8.6.2 and Figure 8.6.3). Calcitonin is released in response to a rise in blood calcium levels.

The hormones secreted by the thyroid gland are summarized in the table below:

Thyroid Hormones, Their Sources, Targets, and Primary Physiological Effects

Hormone	Chemical Type	Produced By	Main Target(s)	Primary Function(s)
Thyroxine (T_4)	Amine (iodinated tyrosine)	Thyroid follicular cells	Most body cells	Increases metabolic rate; supports growth, development, and energy production. Serves as a *storage* form that is converted to T_3 in tissues.
Triiodothyronine (T_3)	Amine (iodinated tyrosine)	Thyroid follicular cells	Most body cells	Active form of thyroid hormone; regulates metabolism, oxygen use, and heat production; influences heart rate and protein synthesis.
Calcitonin	Peptide	Parafollicular (C) cells	Bone (osteoclasts) and kidneys	Lowers blood calcium levels by inhibiting bone resorption and increasing calcium excretion by the kidneys.

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8.7: Disorders of Thyroid Function- Hypo- and Hypersecretion

Low iodine or autoimmune diseases can disrupt normal thyroid hormone production, causing either hypothyroidism hyperthyroidism.

Master this section and you'll be able to

- Describe how inadequate dietary iodine impairs T_3/T_4 synthesis and leads to elevated TSH and goiter.
- Compare iodine deficiency hypothyroidism to autoimmune thyroiditis (both: Hashimoto's thyroiditis and Graves disease).
- Differentiate hypothyroidism from hyperthyroidism by relating hormone levels to key clinical signs.

Iodine Deficiency

As you have learned, dietary iodine is essential for the production of the thyroid hormones **T_3 (triiodothyronine)** and **T_4 (thyroxine)**, which regulate metabolism, growth, and development. To prevent deficiency, many countries fortify table salt with iodine, creating **iodized salt** — the primary source of iodine in most modern diets. The U.S. began salt iodization in 1924, and this simple public health measure continues to protect millions of people worldwide from thyroid disorders.However, natural food sources of iodine vary greatly depending on the amount of iodine in local soil and water. **Seafood**, such as fish and shrimp, are rich in iodine, but people living far from the ocean often have limited access to these sources.

Iodine-deficiency hypothyroidism is now uncommon in countries that iodize salt, so in places such as the United States and Western Europe most cases are autoimmune — Hashimoto's thyroiditis — rather than dietary. It remains a significant problem where iodized salt is not reliably available, especially in Central and Eastern sub-Saharan Africa, South Asia (India, Nepal, Pakistan), and inland or mountainous regions with iodine-poor soils and highly local diets. Globally, hundreds of millions consume too little iodine, and a smaller but still substantial subset develop goiter or hypothyroidism as a result.

When the body lacks iodine, the thyroid gland cannot make enough T_3 and T_4. In response, the **pituitary gland** releases extra **thyroid-stimulating hormone (TSH)**, which overstimulates the thyroid and causes it to enlarge — forming a **goiter**, an enlargement of the thyroid gland.



Figure 8.7.1: ***Goiter.*** *A goiter is the abnormal enlargement of the thyroid gland. (Image credit: "Goiter"(opens in new window) by Almazi is licensed under CC BY 4.0)*

Furthermore, iodine deficiency can have other serious effects on health and development. In **children**, it can cause **stunted**

growth and **delayed physical and mental development.** In fact, iodine deficiency is the leading preventable cause of intellectual disability worldwide. **Adults** may experience **reduced fertility** and complications during pregnancy, and infants born to iodine-deficient mothers face a higher risk of mortality. One of its most severe outcomes is **congenital hypothyroidism** (also called **cretinism**), which results from maternal iodine deficiency during pregnancy and can lead to lifelong cognitive impairment, short stature, and sometimes hearing or speech difficulties.

Other Types of Hypothyroidism

Hypothyroidism is a condition in which the thyroid gland produces insufficient thyroid hormone. In regions where iodine deficiency is rare, the most common cause of hypothyroidism is **Hashimoto's thyroiditis**, an **autoimmune** disorder in which the immune system attacks the thyroid, leading to chronic inflammation and gradual loss of function. Other causes include surgical removal of the thyroid and certain medications that interfere with hormone synthesis.

When thyroid activity decreases, **metabolic processes slow down**. Typical symptoms include fatigue, weight gain despite normal eating, cold intolerance, dry skin and hair, constipation, slow heart rate, and sometimes depression or slowed thinking. In people who menstruate, periods may become heavy or irregular. Laboratory findings usually show **low T_3 and T_4 levels with elevated TSH**, as the pituitary gland increases stimulation in an attempt to boost thyroid output. This persistent stimulation can cause the thyroid to enlarge, forming a **goiter**.

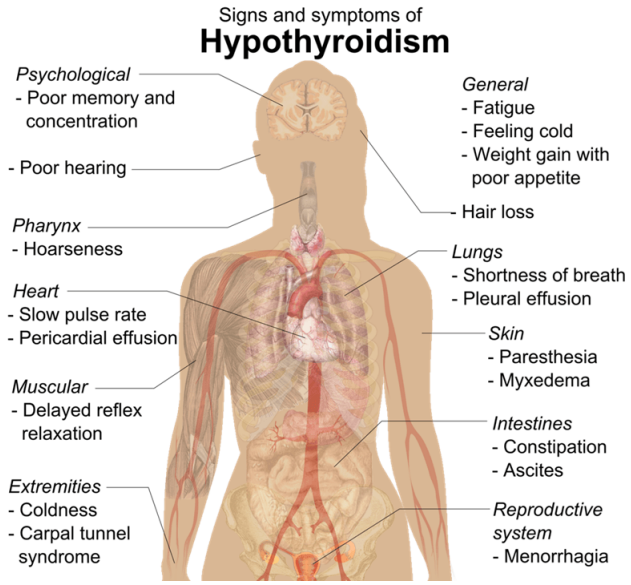
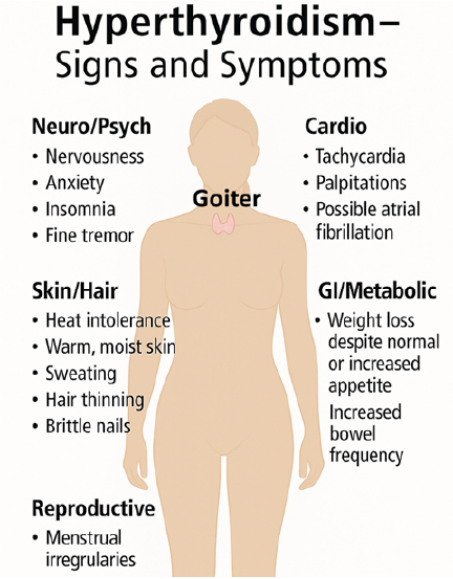


Figure 8.7.2: **Hypothyroidism can affect nearly every organ system because thyroid hormones regulate metabolism, growth, and energy balance.** The image highlights common systemic effects: slowed brain function; fatigue and cold intolerance due to reduced metabolism; slowed heart rate and poor circulation; constipation from reduced digestive motility; muscle weakness; and menstrual irregularities or infertility. In children, hypothyroidism can impair growth and development, while in adults it leads to generalized slowing of body processes. *(Image credit: "Human endocrine system with target organs" by Mikael Häggström, licensed under CC0/public domain via Wikimedia Commons.)*



Hyperthyroidism

Hyperthyroidism is the opposite of hypothyroidism: the thyroid produces and releases too much hormone. The most common cause is **Graves disease**, another **autoimmune** disorder in which **antibodies overstimulate the thyroid so it enlarges and secretes excess T_3 and T_4.** Other causes include autonomously functioning thyroid nodules or, less commonly, a pituitary tumor that produces too much TSH. Because metabolism is accelerated, patients may show unintentional weight loss, heat intolerance, excessive sweating, nervousness or irritability, insomnia, rapid or irregular heartbeat, and more frequent bowel movements. In Graves disease, inflammation behind the eyes can cause **exophthalmos** (bulging eyes). Laboratory findings typically show **elevated T_3 and T_4** with **low TSH**, because the pituitary tries to turn down the signal.

Both thyroid disorders are important clinically because their symptoms can mimic depression, anxiety, menopause, or normal aging. *In summary:*

- **Hypothyroidism slows body processes,**
- **Hyperthyroidism speeds them up.**

Figure 8.7.3: **Hyperthyroidism**. Amongst the typical signs and symptoms — besides exophthalmos — are: anxiety, tremor, tachycardia, heat intolerance, weight loss, goiter.

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8.8: Meet the Pancreas — Dual Roles in Digestion and Hormone Control

The endocrine pancreas consists of clusters of islet cells that secrete the hormones insulin and glucagon, which work together to regulate and maintain stable blood glucose levels throughout the body.

Master this section and you'll be able to

- Describe the location and structure of the pancreas, and the morphology and function of the pancreatic islets.
- Compare and contrast the functions of insulin and glucagon.
- Differentiate between Type 1 and Type 2 diabetes mellitus.

Location and Structure

The **pancreas** is a long, slender organ located **behind the lower half of the stomach** in the **retroperitoneal space** (Figure \PageIndex1{8{.}8{.}\eatSpaces{1} \endSpaces}\PageIndex1). It stretches from the **duodenum** on its right side to the **spleen** on its left. Because it sits behind the peritoneum, it is considered a **retroperitoneal organ**.

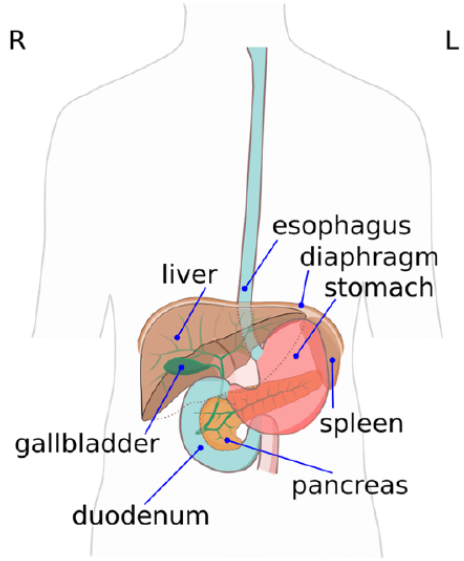


Figure 8.8.1: **Location of the Pancreas as Part of the Upper Abdominal Cavity.** The pancreas is situated posterior to the bottom half of the stomach.

Exocrine Function

Most of the pancreas functions as an **exocrine gland**. It is composed of acinar cells, which produce **digestive enzymes** that form **pancreatic juice**. These cells are arranged in small, pouch-like clusters that connect to the **pancreatic duct**, a central passageway that carries the digestive secretions into the **duodenum**, where they help break down food.

Endocrine Function

Scattered among the acinar tissue are about a **million small clusters of endocrine cells** known as **pancreatic islets** (*islets of Langerhans*). These islets function as tiny hormone factories, secreting several vital hormones, most notably:

- **Insulin**, which lowers blood glucose
- **Glucagon**, which raises blood glucose

Together, these hormones maintain **blood glucose homeostasis** and ensure the body has a stable energy supply.

Cells and Secretions of the Pancreatic Islets

For this course, we will focus on the **alpha** and **beta cells** of the pancreatic islets (Figure \PageIndex1{8{.}8{.}\eatSpaces{1} \endSpaces}\PageIndex1 and Figure \PageIndex2{8{.}8{.}\eatSpaces{2} \endSpaces}\PageIndex2). In addition, there are two other cell types whose secretions are distinct hormones that also enter the bloodstream and act on their specific target cells.

- The **alpha cell** produces the hormone glucagon and makes up approximately 20 percent of each islet. Glucagon plays an important role in blood glucose regulation; low blood glucose levels stimulate its release.
- The **beta cell** produces the hormone insulin and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin.

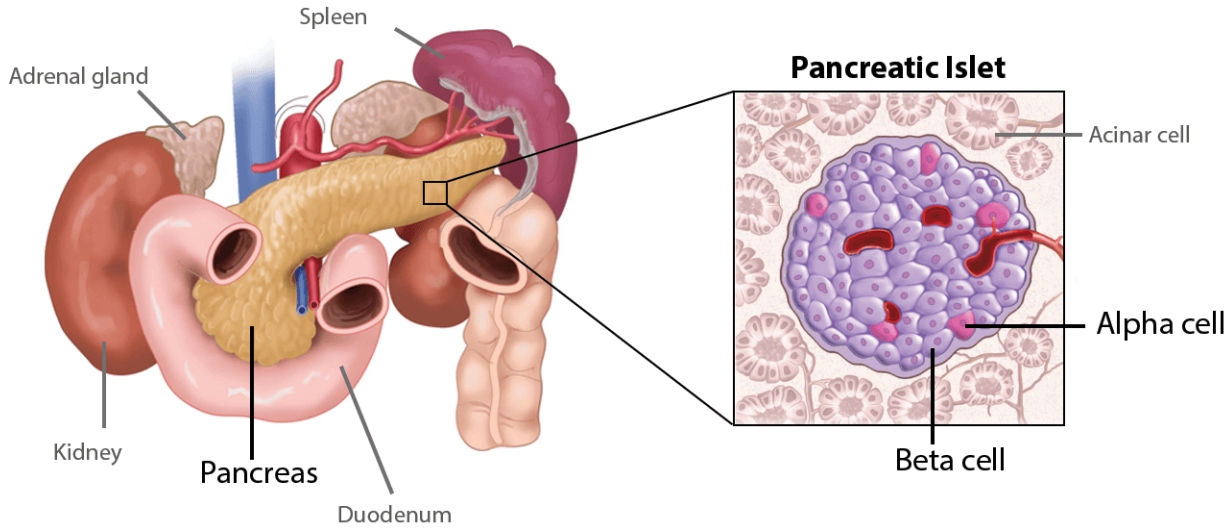


Figure 8.8.2: **The Pancreas.** The endocrine portion of the pancreas is small clusters of cells called pancreatic islets. Multiple hormones are secreted by the islets, with the two regulating blood glucose levels coming from the beta cells (insulin) and alpha cells (glucagon). *(Image credit: "Endocrine Pancreas" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, derivatives of original works "Leiden - Drawing pancreas and neighbouring organs - no labels" by Ron Slagter and "Endocrine Pancreas" by Cenveo.)*

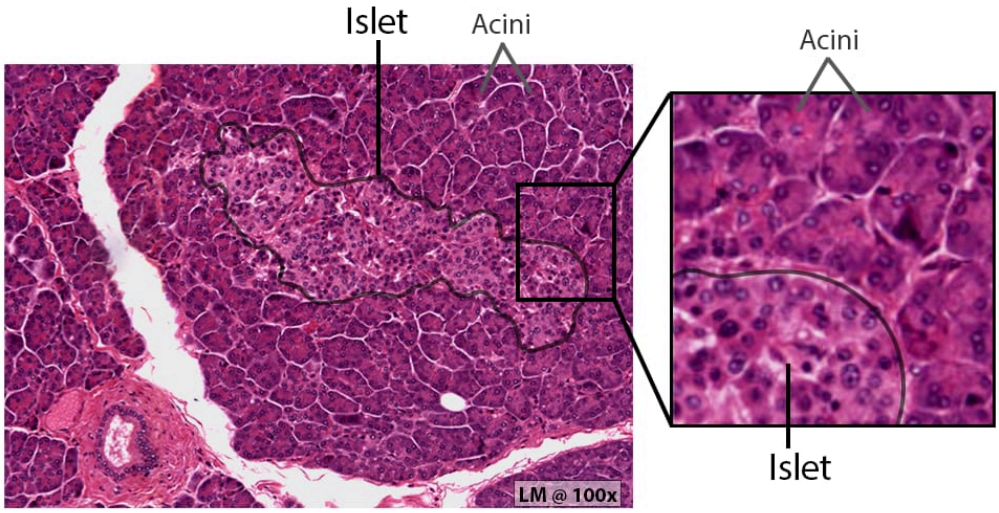


Figure 8.8.3: **Histology of the Pancreas.** On slides the pancreatic islets are seen as clusters of smaller, lighter staining cells that the surrounding blocks of acini (acinar cells). *(Image credit: "Histology of the Pancreas" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022.)*

Regulation of Blood Glucose Levels by Insulin and Glucagon

Glucose is the body's main energy source and the fuel most cells rely on for **cellular respiration**, the process that produces ATP. The body obtains glucose by digesting carbohydrate-rich foods and beverages, breaking down complex carbohydrates into simple sugars that are absorbed into the bloodstream. After eating, when blood glucose levels rise, cells can immediately use glucose for energy. Any extra glucose is stored in the **liver** and **skeletal muscles** as **glycogen** for short-term energy needs, or converted into **triglycerides** and stored in **adipose tissue** for long-term use.

The body keeps glucose levels within a narrow, healthy range through precise **hormonal regulation**. Specialized receptors in the **pancreas** constantly monitor blood glucose concentrations. When levels are high, the **pancreatic islets** release **insulin**, which promotes glucose uptake into cells and glycogen storage. When levels drop, the alpha cells of the pancreatic islets release **glucagon**, which triggers glycogen breakdown and glucose release into the blood. This ongoing balance ensures homeostasis, specifically a steady supply of energy for all the body's cells.

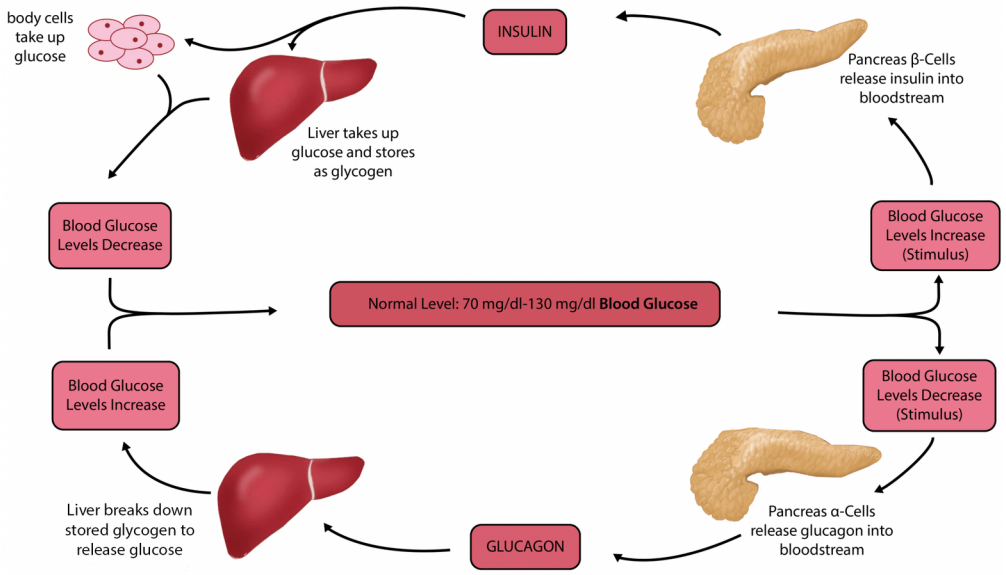
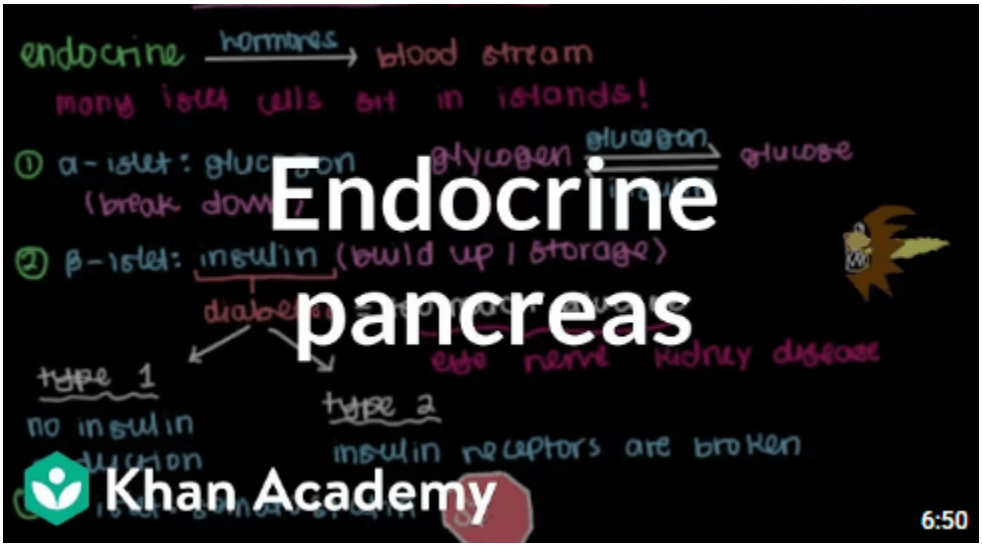


Figure 8.8.4: **Glucose Homeostasis.** Blood glucose levels are regulated by two pancreatic hormones that act antagonistically. *(Image credit: "Glucose Homeostasis" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0. Pancreas image by Ron Slagter; liver image by Ron Slagter.)*

Hormones of the Pancreas

Associated hormone (and the cells that secretes it)	Effect
Insulin (beta cells)	Reduces blood glucose levels
Glucagon (alpha cells)	Increases blood glucose levels

Interactive Element



Watch this Kahn Academy video up to time-point 5:39. (We are not covering the third hormone talked about).

DISORDERS OF THE...

Endocrine System: Diabetes Mellitus

When the body's finely tuned system for controlling blood glucose goes awry, the result can be a chronic disorder known as **diabetes mellitus**. This condition arises when the pancreas does not produce enough insulin, or when body cells stop responding properly to it. The outcome is the same either way — **too much glucose stays in the bloodstream**, and that creates serious health problems over time.

How Common Is It?

Diabetes mellitus is one of the most rapidly growing health concerns worldwide. In the United States alone, more than **18 million adults** and over **200,000 children** have been diagnosed, and an additional **7 million adults** may have it without knowing. Another **79 million people** are thought to have **pre-diabetes**, where blood glucose levels are elevated but not yet high enough to be classified as diabetes.

The Two Major Types

Type 1 Diabetes: When the Body Attacks Itself

Type 1 diabetes is an **autoimmune disease** — the immune system mistakenly targets and destroys the pancreas's **β (beta) cells**, which normally produce insulin. Without insulin, cells cannot absorb glucose for energy. People with this form of diabetes must rely on **synthetic insulin injections or pumps** to survive.
Type 1 diabetes accounts for **less than 5 percent** of all cases and often begins in childhood or adolescence. Certain genetic factors are known to increase susceptibility.

Type 2 Diabetes: When Cells Stop Listening

Far more common, **Type 2 diabetes** makes up about **95 percent** of all cases. Here, the pancreas still produces insulin, but **body cells become resistant** to its effects. In response, the pancreas works overtime to release even more insulin — until the β cells eventually burn out.
Lifestyle factors play a big role: **poor diet, inactivity, and excess body weight** all increase risk. In fact, 80–90 percent of people with type 2 diabetes are overweight or obese.
The good news? In many cases, **type 2 diabetes can be reversed** through moderate weight loss, regular physical activity, and a balanced diet. If these steps are not enough, medications — or eventually insulin — may be required to keep blood glucose within a healthy range.

Classic Signs and Symptoms

Two early warning signs are **excessive urination (polyuria)** and **excessive thirst (polydipsia)**.
When glucose levels rise too high, the kidneys can no longer reabsorb all the sugar. Glucose spills into the urine, dragging water with it by osmosis. The result is a large volume of **sweet-smelling urine**, dehydration, and an almost unquenchable thirst. Because the body's cells cannot use glucose properly, people with diabetes also often experience **constant hunger (polyphagia)** and fatigue.

Long-Term Complications

Uncontrolled high blood glucose (**hyperglycemia**) damages tissues throughout the body, particularly **blood vessels and nerves**. Over time, this can lead to:

- **Atherosclerosis**, increasing the risk of **heart attack and stroke**
- **Kidney failure**, from damage to the tiny filtration vessels
- **Retinopathy and blindness**, from injury to eye blood vessels
- **Poor circulation** and **neuropathy**, especially in the hands and feet
  These changes can result in **ulcers, infections, and even amputations** of toes, feet, or legs.

If the body cannot use glucose at all, it begins burning fat for energy instead. This process produces **ketone bodies**, which are acidic. When they accumulate, **ketoacidosis** develops—a dangerous condition that can lead to **diabetic coma** if untreated.
Altogether, diabetes remains one of the **leading causes of death** in the United States.

Diagnosis and Treatment

A diagnosis is made when **blood tests** show abnormally high glucose levels. Treatment depends on the **type and severity** of diabetes and the individual's ability to make **lifestyle changes**.
For many people with type 2 diabetes, **healthy eating, exercise, and modest weight loss** can significantly lower blood glucose. If that is not enough, doctors may prescribe **oral medications** that improve the pancreas's insulin response or increase insulin sensitivity. In advanced cases, **insulin therapy** becomes necessary.
Ongoing research continues to expand treatment options, offering hope that one day we can prevent or even cure this complex metabolic disease.

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8.9: Adrenal Glands

The adrenal glands sit atop the kidneys and function as powerful endocrine organs whose outer cortex produces steroid hormones regulating metabolism, fluid balance, and stress, while the inner medulla releases epinephrine to trigger the body's fight-or-flight response.

Master this section and you'll be able to

- Describe the location and structure of the adrenal glands
- Identify the hormones produced by the adrenal cortex and adrenal medulla, and summarize their target cells and effects
- Explain the role of the adrenal medulla in the fight-or-fight response.
- Recognize two disorders caused by cortisol hyper- and hyposecretion.

Anatomy of the Adrenal (Suprarenal) Glands

Perched like little caps on top of each kidney, the **adrenal glands** — also called suprarenal glands — are small but mighty powerhouses of the endocrine system *(See figure below)*. Each gland is wrapped in a tough fibrous capsule that anchors it to the kidney and protects its delicate inner tissues. Despite their size, the adrenal glands have an **exceptionally rich blood supply**, receiving one of the highest rates of blood flow in the entire body. This makes sense — when these glands release their hormones, they need them to reach target tissues **fast**.

Structurally, each adrenal gland has **two distinct regions** with very different jobs:

- The **outer adrenal cortex**, which produces vital steroid hormones that help regulate metabolism, salt balance, and stress responses.
- The **inner adrenal medulla**, which functions more like a **neuroendocrine organ**, releasing adrenaline and noradrenaline to kick the body into high gear during "fight-or-flight" situations.

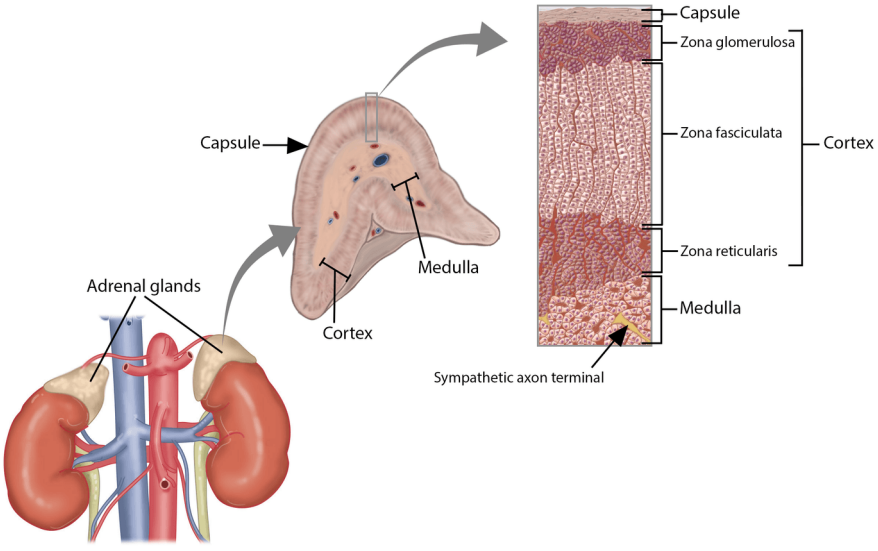


Figure 8.9.1: **The Adrenal Glands.** Both adrenal glands sit atop the kidneys and are composed of an outer cortex and an inner medulla, all surrounded by a connective tissue capsule. The cortex can be subdivided into additional zones. *(Image credit: "The Adrenal Glands" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; includes section of "Slagter - Drawing Anatomy of the kidney, adrenal glands and bladder - no labels" by Ron Slagter, license: CC BY-NC-SA.)*

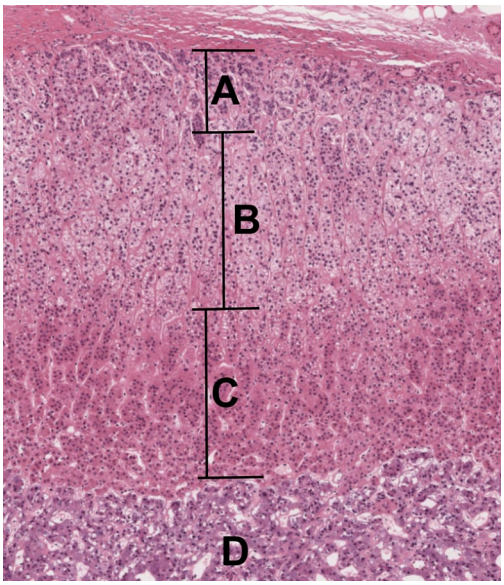


Figure 8.9.2: **Adrenal Gland Histology.** The adrenal gland is located on top of each kidney. The histology seen here shows the different parts of the gland that is responsible for the production of different types of hormones. A - Zona Glomerulosa, B - Zona Fasciculata, C - Zona Reticularis, and D - Medulla. (*Image credit: "Histology of Adrenal Gland" by Yancy Aquino is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022 under CC BY-NC-SA 3.0.*)

Stress!



Adrenal Glands and the Stress Response

One of the adrenal glands' most important jobs is to help the body **respond to stress** — whether that stress is **physical, psychological, or both**.

- **Physical stress** might come from an injury, exposure to cold weather without proper clothing, or malnutrition.
- **Psychological stress** can stem from arguments, looming deadlines, or simply having a rough day.

The body's overall reaction to stress follows a pattern called the **General Adaptation Syndrome (GAS)**, which occurs in **three stages**.

1. Alarm Reaction – The "Fight-or-Flight" Response

This is the body's **immediate reaction to short-term stress**. It's powered by the adrenal medulla, which releases the hormones **epinephrine (adrenaline)** and **norepinephrine (noradrenaline)**.
These hormones rapidly prepare the body for intense physical action by:

- Stimulating the **liver and muscles** to convert glycogen to glucose, raising blood sugar levels.
- Increasing **heart rate, pulse, and blood pressure**.
- Dilating the **airways** to boost oxygen intake.
- Directing blood flow toward vital organs like the **heart, lungs, brain, and skeletal muscles**, while reducing flow to the **digestive system, kidneys, and skin**.

Other typical signs include **dry mouth, dilated pupils, decreased appetite, and tunnel vision** — all part of a body ready for action.
Once the threat passes, the body quickly returns to normal conditions.

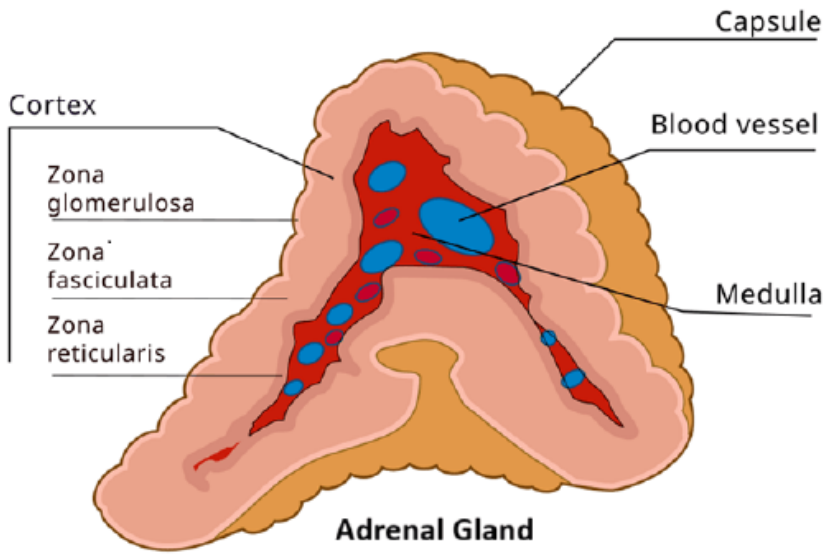
2. Resistance Stage – Adapting to Ongoing Stress

If the stressor persists, the body enters a phase of **adjustment and adaptation**. For example, someone who is starving might experience increased signals to the digestive system to **maximize nutrient absorption**. The goal is to maintain stability (homeostasis) while the stress continues.

3. Exhaustion Stage – The Consequences of Chronic Stress

Prolonged or repeated stress can eventually overwhelm the body's adaptive systems. This **final stage of GAS** is mediated by the **adrenal cortex**, particularly through the hormone **cortisol**.
Long-term elevation of cortisol can lead to:

- **Fatigue and depression**
- **Suppressed immunity**
- **Muscle wasting and weight changes**
- **Cardiovascular problems**, including increased risk of heart attack



The Adrenal Cortex

The **adrenal cortex** is the outer part of the adrenal gland, made up of layers of cells packed with lipids (fats) that give the tissue a yellowish color. It has **three distinct regions**, each responsible for producing different steroid hormones. These hormones help the body manage **long-term stress**, **blood pressure and volume**, **nutrient balance**, **fluid and electrolyte levels**, and **inflammation**.

The three regions are:

1. **Zona glomerulosa** – controls minerals and water balance
2. **Zona fasciculata** – manages metabolism and long-term stress
3. **Zona reticularis** – produces small amounts of sex hormones

1. Zona Glomerulosa – Regulating Minerals and Blood Pressure

The outermost layer, the **zona glomerulosa**, produces **mineralocorticoids**, hormones that regulate **sodium (Na⁺)** and **potassium (K⁺)** levels — key to maintaining fluid balance and healthy blood pressure.

The most important mineralocorticoid is **aldosterone**. It acts mainly on the **kidneys**, helping the body to:

- **Retain sodium (Na⁺)** and **excrete potassium (K⁺)**
- **Hold on to water**, which increases blood volume and blood pressure

Aldosterone secretion is triggered when blood pressure or sodium levels are low — or when potassium levels are high. It's also part of a hormone cascade called the **renin–angiotensin–aldosterone system (RAAS)**:

1. The kidneys release **renin** when blood pressure drops.
2. Renin activates a molecule that becomes **angiotensin II**.
3. Angiotensin II constricts blood vessels, signals the kidneys to retain water, and tells the adrenal cortex to release **aldosterone**.

For people with **high blood pressure**, medications called **ACE inhibitors** block the enzyme that produces angiotensin II, lowering blood pressure by interrupting this system.

2. Zona Fasciculata – Managing Long-Term Stress

The middle layer, the **zona fasciculata**, produces **glucocorticoids**, which help the body handle **long-term stress** and regulate **glucose metabolism**. The main hormone here is **cortisol** (some of which the liver converts to cortisone).

Cortisol is controlled by the **HPA axis** (Hypothalamus–Pituitary–Adrenal):

1. The **hypothalamus** releases CRH.
2. CRH triggers the **anterior pituitary** to release ACTH.
3. ACTH stimulates the **adrenal cortex** to produce cortisol.

When cortisol levels rise, the body shifts energy priorities:

- **Glycogen** is broken down to glucose for energy.
- **Fat stores** are converted into fatty acids.
- **Muscle proteins** are broken down into amino acids.

Cortisol ensures cells have enough fuel during ongoing stress, but **too much for too long** can harm the body—especially the **hippocampus**, the brain region critical for learning and memory, which is very sensitive to stress hormones.

You've probably seen cortisol's effects in medicine: **hydrocortisone creams** for rashes, **prednisone tablets** for inflammation, and **steroid inhalers** for asthma. These drugs work by **suppressing the immune and inflammatory responses**, mimicking cortisol's natural effects.

3. Zona Reticularis – Supplementary Sex Hormones

The innermost layer, the **zona reticularis**, produces small amounts of **androgens**, a class of sex hormones. Androgens are often called "male" sex hormones because they promote traits like facial hair, a deeper voice, and greater muscle mass, but **both males and females produce them** — in the testes for males and in the ovaries and adrenal cortex for both sexes. All steroid hormones share a **common origin from cholesterol** and can be **converted into one another** through enzymes. For example, androgens such as **testosterone** can be converted into estrogens (like **estradiol**) by the enzyme **aromatase** in tissues such as the ovaries, fat, and even the brain. After menopause, when ovarian hormone production declines, the adrenal cortex becomes an important source of **estrogens** for individuals with ovaries.

The adrenal androgens are often referred to as "weak androgens" and serve as precursors that the body converts into more potent androgens like testosterone and estrogen. So, while the gonads (ovaries and testes) are the main producers, these adrenal androgens provide a **backup supply**.

Table \(\PageIndex{1}\): Hormones of the Adrenal Glands

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

The Adrenal Medulla

The **adrenal medulla** is the **inner core** of the adrenal gland and is made up of **chromaffin cells** — specialized cells that are actually **modified postganglionic sympathetic neurons**. Like the rest of the sympathetic nervous system, these cells develop from neural crest tissue, the same embryonic origin as the sympathetic ganglia.

The adrenal medulla serves as a **bridge between the nervous and endocrine systems**. It functions like a neural structure because it is controlled by **direct sympathetic nerve stimulation**, yet it behaves like an endocrine gland because it releases its secretions — **epinephrine (adrenaline)** and **norepinephrine (noradrenaline)** — directly into the bloodstream. These hormones rapidly prepare the body for **"fight-or-flight"** situations by increasing heart rate, blood pressure, and energy availability.

Unlike most hormones, the effects of the adrenal medulla are **immediate but short-lived**, giving the body a quick burst of energy and alertness during sudden stress.

DISORDERS OF THE...

Endocrine System: Disorders Involving the Adrenal Glands

Hormones are secretive messengers that quietly work behind the scenes to keep the body in balance. Most of the time, their actions go unnoticed — until something disrupts that balance. The best way to understand what a hormone really does is to study what happens when there is either **hypersecretion** (too much hormone) or **hyposecretion** (too little hormone). These conditions reveal the hormone's true influence on the body and help explain how each contributes to maintaining homeostasis.

For example, hypersecretion of thyroid hormones can make a person feel restless and overheated, while hyposecretion slows metabolism and causes fatigue. Too much insulin can drop blood glucose dangerously low, whereas too little leads to diabetes. By examining these hormonal imbalances, we can see how hormones regulate energy, mood, growth, and nearly every physiological system in our body.

Several disorders result from **dysregulation** — either **hypersecretion** or **hyposecretion** — **of adrenal hormones.**

One well-known example is **Cushing's disease**, a condition caused by **hypersecretion of cortisol.** Cushing's disease is often triggered by a **pituitary tumor** that secretes excessive amounts of **ACTH**, which in turn overstimulates cortisol production. The excess cortisol leads to **elevated blood glucose levels** and the **accumulation of fat deposits** on the face and neck, resulting in the classic *"moon face"* and *"buffalo hump"* appearance. Other common symptoms include rapid weight gain, hair loss, and muscle weakness.

Because cortisol also affects metabolism and the immune system, **chronically high levels** can increase the risk of **type 2 diabetes**, impair immune defenses, and reduce resistance to infection. Long-term cortisol hypersecretion can also interfere with memory.

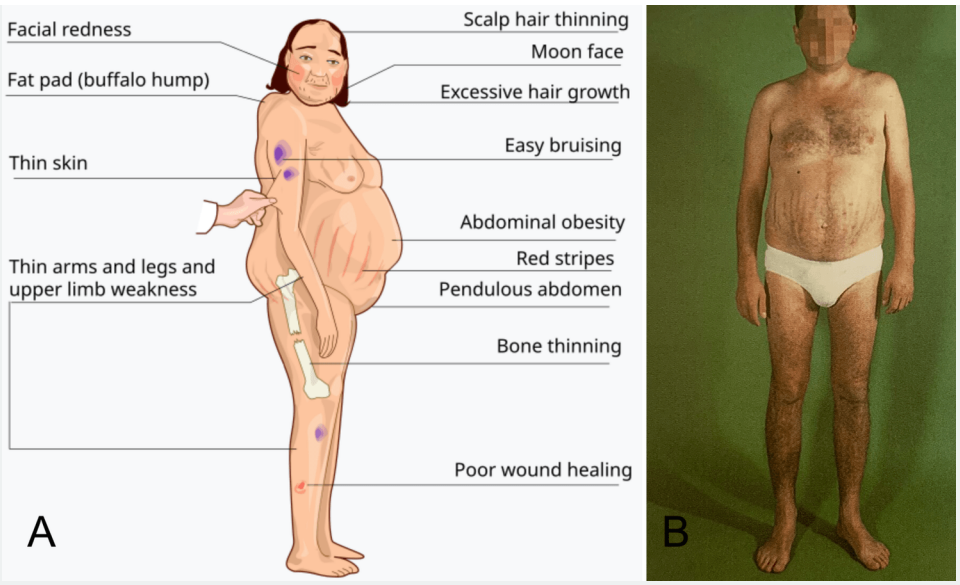


Figure 8.9.3: **Cushings Syndrome.** A. The different symptoms of a person with Cushing's syndrome. B. A picture of a person with Cushing's syndrome showing the prominent stretch marks on the abdomen. (Image credit: "A. Cushing Syndrome Symptoms" and "B. Cushign Syndrome" by Yancy Aquino is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)

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

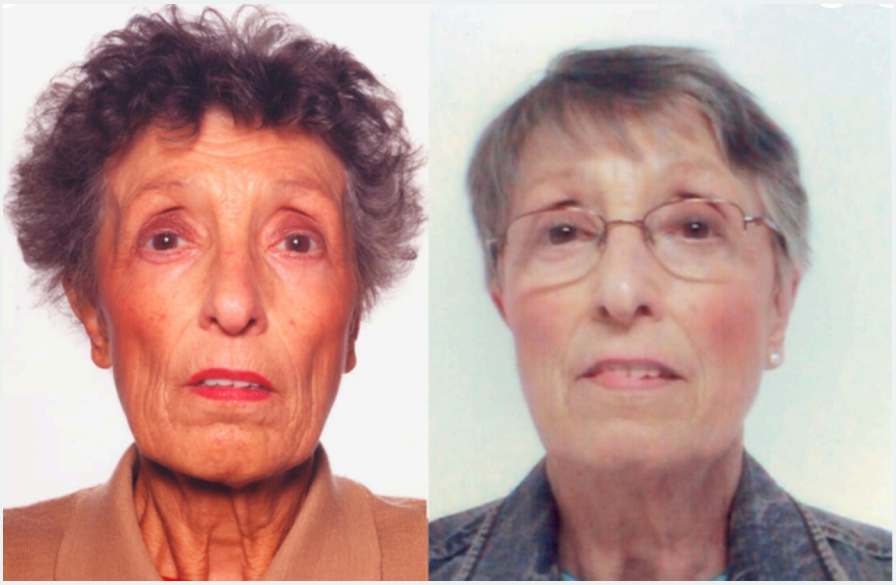


Figure 8.9.4: **Addison's Disease.** A 69-year-old female with tiredness and a persistent tan. Facial appearance at presentation (left), showing pigmentation, and after treatment (right). *(Image credit: "Addison's Disease" by Yancy Aquino is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*

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9: BLOOD, LYMPH, AND THE IMMUNE SYSTEM

9.1: The Fluid of Life- Introduction to Blood

9.2: Hematocrit

9.3: Blood Plasma

9.4: Cells and Platelets of the Blood

9.5: Erythrocytes — Tiny Oxygen Taxis

9.6: RBC Life Cycle

9.7: Aberrations from the Normal Blood Profile — Anemia vs. Polycythemia

9.8: Blood Doping

9.9: Hemostasis

9.10: Blood Clotting Disorders

9.11: Overview of the Lymphatic and Immune Systems

9.12: Barrier Defenses and the Innate Immune System

9.13: Key Concepts of Adaptive Immunity

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9.15: Cell-Mediated Immune Response

9.16: Immune Dysfunction and Clinical Connections

9.17: Blood Types and Transfusions

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9.1: The Fluid of Life- Introduction to Blood

Blood is a circulating connective tissue composed of plasma and three main types of formed elements — erythrocytes, leukocytes, and platelets.

Master this section and you'll be able to

- Describe the overall composition of blood.
- Explain the basic structure and function of erythrocytes, Leukocytes, and thrombocytes.
- Summarize the functions of the blood.

Characteristics of Blood

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

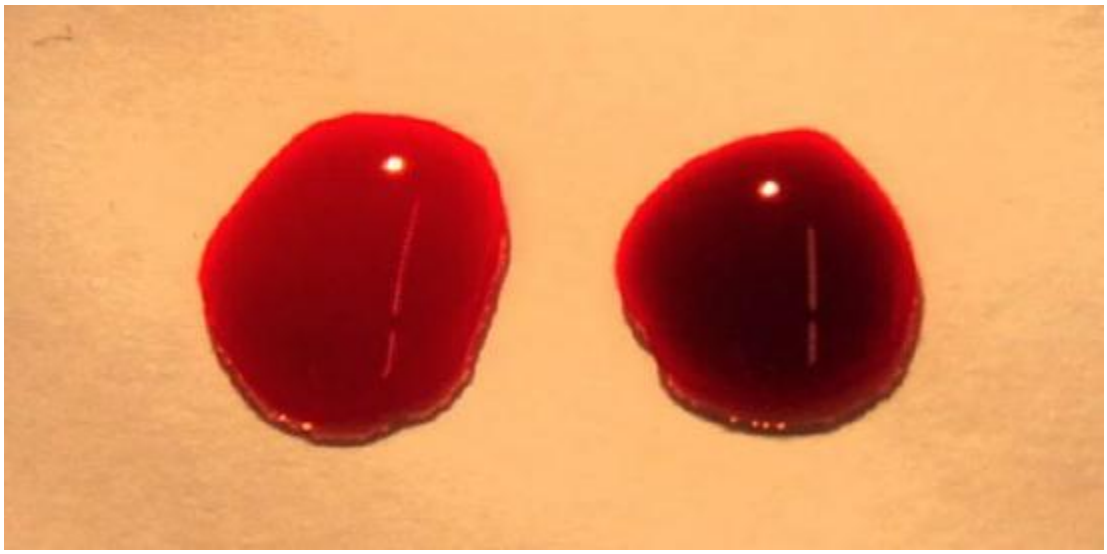


Figure 9.1.1: **Shades of Red Blood.** The bright red hue of oxygenated blood is shown on the left while the deeper red hue of deoxygenated blood is shown on the right. ("Drops of Blood Medium" by unknown author is licensed under CC BY 3.0)

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

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

The pH of blood averages about 7.4; it is maintained within an extremely tight range from 7.35 to 7.45 in a healthy person. At an average pH of 7.4, blood is somewhat more basic (alkaline) on a chemical scale than pure water, which has a pH of 7.0. Blood contains numerous buffers that contribute to the regulation of pH.

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

Composition of Blood

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



Figure 9.1.2: **Composition of Blood**: Two tubes of EDTA-anticoagulated blood. Left tube: after standing, the RBCs have settled at the bottom of the tube.

Blood is a specialized **circulating connective tissue** composed of a fluid component called **plasma** and several types of **formed elements** suspended within it. These cellular elements include **erythrocytes** (red blood cells, or RBCs), **leukocytes** (white blood cells, or WBCs), and **thrombocytes** (platelets).

By volume, erythrocytes make up about 45 percent of whole blood, forming what is known as the **hematocrit**. Plasma accounts for roughly 54 percent, and less than 1 percent consists of white blood cells and platelets, collectively known as the **buffy coat**.

Although blood might seem like a liquid rather than a tissue, it is classified as a connective tissue because it contains cells (the formed elements) embedded in a nonliving extracellular matrix (the plasma). The plasma serves as the transport medium for nutrients, hormones, waste products, and dissolved gases.

Functionally, blood acts as the body's transport highway — it carries oxygen from the lungs to tissues, removes carbon dioxide, distributes nutrients such as glucose and amino acids, and delivers hormones to target organs. It also plays a vital role in immune defense, pH and temperature regulation, and clotting to prevent blood loss after injury.

The three major cellular components each have specialized roles:

- **Erythrocytes** (RBCs) transport oxygen and carbon dioxide.
- **Leukocytes** (WBCs) defend the body against pathogens and remove debris.
- **Thrombocytes** (platelets) help prevent blood loss by initiating clot formation.

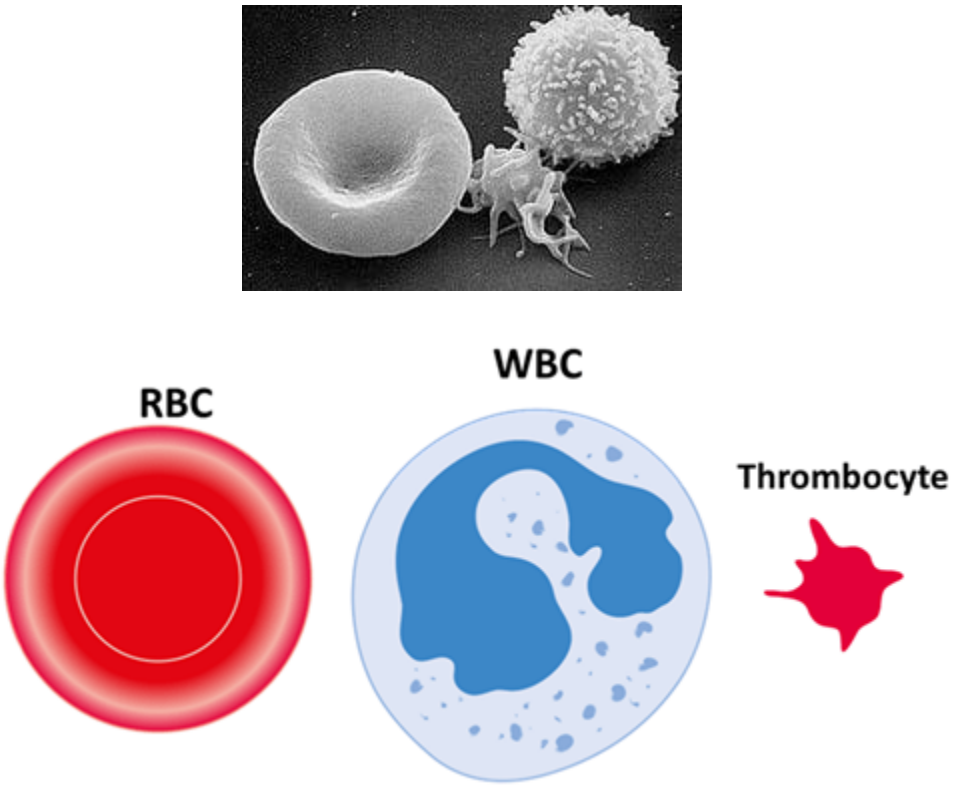


Figure 9.1.3: **Blood Cells.** *Left image:* From left to right, a diagram of an erythrocyte, thrombocyte, and leukocyte.

Erythrocytes (RBCs)

Erythrocytes, or red blood cells (RBCs), are the **most abundant** formed elements in the blood and are responsible for **transporting respiratory gases** between the lungs and the body's tissues. Each erythrocyte is a small, flexible **disc** about **seven to eight micrometers (µm)** in diameter. Its distinctive biconcave shape increases surface area relative to volume, which enhances the efficient exchange of oxygen and carbon dioxide across the cell membrane.

Mature red blood cells lack a nucleus and organelles, including mitochondria, and therefore cannot divide or repair themselves. Their energy is produced through anaerobic metabolism, allowing them to transport oxygen without consuming it. Packed within each cell are millions of molecules of **hemoglobin**, an iron-containing protein that binds oxygen in the lungs and releases it in tissues where oxygen concentration is lower. Hemoglobin also binds a portion of carbon dioxide for return transport to the lungs.

Red blood cells display glycoprotein markers on their surfaces that determine an individual's **blood type** (such as A, B, AB, or O). These surface antigens play an essential role in safe blood transfusions and immune compatibility. Stay tuned for more details.

The proportion of red blood cells relative to the total volume of blood is called the **hematocrit**, which averages about 45 percent in healthy adults. The efficiency of this system is remarkable — the combined surface area of all the red blood cells in one human body is estimated to be roughly two thousand times greater than the body's exterior surface area, providing an enormous interface for gas exchange and metabolic support.

Leukocytes (WBCs)

Leukocytes, or white blood cells (WBCs), are the body's **main line of defense against disease and infection**. They are generally **larger** than red blood cells, ranging from about 10 to 14 micrometers (µm) in diameter, and are far less numerous in circulation. Unlike red blood cells, leukocytes contain a nucleus and organelles, and they lack hemoglobin. Their cellular structure reflects their complex roles in identifying, attacking, and removing harmful or abnormal materials in the body.

White blood cells are the key functional components of the immune system. They defend the body by destroying and removing old, damaged, or aberrant cells and by recognizing and attacking invading pathogens such as bacteria, viruses, and parasites. They also clear away cellular debris and foreign substances.

There are several distinct types of white blood cells, each with specialized functions. These include the **granulocytes**—basophils, eosinophils, and neutrophils—as well as the **agranulocytes**, which include monocytes and lymphocytes. Lymphocytes can be further divided into B cells, T cells, and natural killer cells, while monocytes can mature into macrophages and dendritic cells once they leave the bloodstream and enter tissues.

Together, these diverse cells coordinate the body's immune responses. Neutrophils rapidly engulf and digest bacteria; eosinophils target parasites and modulate allergic reactions; basophils release histamine and other chemicals that promote inflammation; lymphocytes produce antibodies or destroy infected cells; and monocytes and macrophages clean up debris and alert other immune cells to potential threats.

Although they typically make up less than one percent of total blood volume, white blood cells are vital to maintaining health and protecting the body from infection and disease.

Thrombocytes (Platelets)

Thrombocytes, or platelets, are small, **membrane-bound cell fragments** that play a crucial role in **blood clotting and wound repair.** Measuring only 1- 2 µm in diameter, they are much smaller than red or white blood cells and lack nuclei. Platelets originate from the fragmentation of large precursor cells called **megakaryocytes**, which develop from stem cells in the bone marrow. This process is regulated by the hormone **thrombopoietin**, ensuring the continuous production of roughly 200 billion platelets per day. Platelets contain mitochondrial DNA but no nuclear DNA, reflecting their partial cellular origin.

The sticky surface of platelets allows them to rapidly adhere to sites of vascular injury. When a blood vessel is damaged, the exposed collagen fibers trigger platelet activation. The activated platelets change shape, become more adhesive, and release signaling molecules and clotting factors that initiate a complex cascade known as hemostasis—the process that stops bleeding.

During hemostasis, platelets secrete several important substances: thromboxane A, which promotes platelet aggregation; serotonin, which causes vasoconstriction to reduce blood flow; and thromboplastin and fibrinogen, which participate in the clotting cascade leading to fibrin formation. The resulting fibrin mesh stabilizes the platelet plug, effectively sealing the injured vessel.

Platelets are essential for wound healing because tissue repair cannot proceed until bleeding has stopped and a stable clot has formed. Once the vessel wall is repaired, enzymes gradually dissolve the clot, restoring normal circulation.

Functions of Blood

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

Transportation

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

Defense

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

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

Maintenance of Homeostasis

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

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

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9.2: Hematocrit

The hematocrit test measures the proportion of red blood cells in whole blood, providing important information about oxygen-carrying capacity and helping to identify conditions such as anemia, dehydration, or polycythemia.

Master this section and you'll be able to

- Identify the major components of blood and describe how centrifugation separates them.
- Describe how a hematocrit test is performed.
- Explain what a hematocrit test measures and interpret how changes in hematocrit values can indicate specific conditions.

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

During a routine doctor's visit, **blood testing** is often performed to evaluate overall health and detect potential problems early. One key part of this evaluation is the **hematocrit (Hct) test**, which **.** This value indicates how effectively the body can carry oxygen to tissues. The test is commonly ordered when patients experience symptoms such as fatigue, weakness, or shortness of breath, or to monitor conditions that affect blood volume or red blood cell production. Because abnormal hematocrit levels can **signal anemia, dehydration, or disorders such as polycythemia**, it provides important information about a person's blood health and oxygen-carrying capacity.

Seeing Blood in Layers: Testing for Hematocrit

A hematocrit test — also called **packed cell volume** — measures the **percentage of erythrocytes (RBCs)** in a blood sample. One common way to perform this test is by using a small capillary **hematocrit tube** and a centrifuge.

Erythrocytes are the specific cells that carry oxygen in the blood. The hematocrit test is performed by spinning the blood sample in a specialized centrifuge, a process that causes the heavier elements suspended within the blood sample to separate from the lightweight, liquid plasma. Because **the heaviest elements in blood are the iron-containing erythrocyte**s, these settle at the very bottom of the hematocrit tube. Located above the erythrocytes is a pale, thin layer composed of the remaining formed elements of blood: leukocytes and platelets. The layer containing the **leukocytes and platelets** is referred to as the **buffy coat** because of its color; it normally constitutes less than 1 percent of a blood sample. Above the buffy coat is the blood **plasma**, normally a pale, straw-colored fluid matrix, that constitutes the remainder of the sample.

Centrifugation

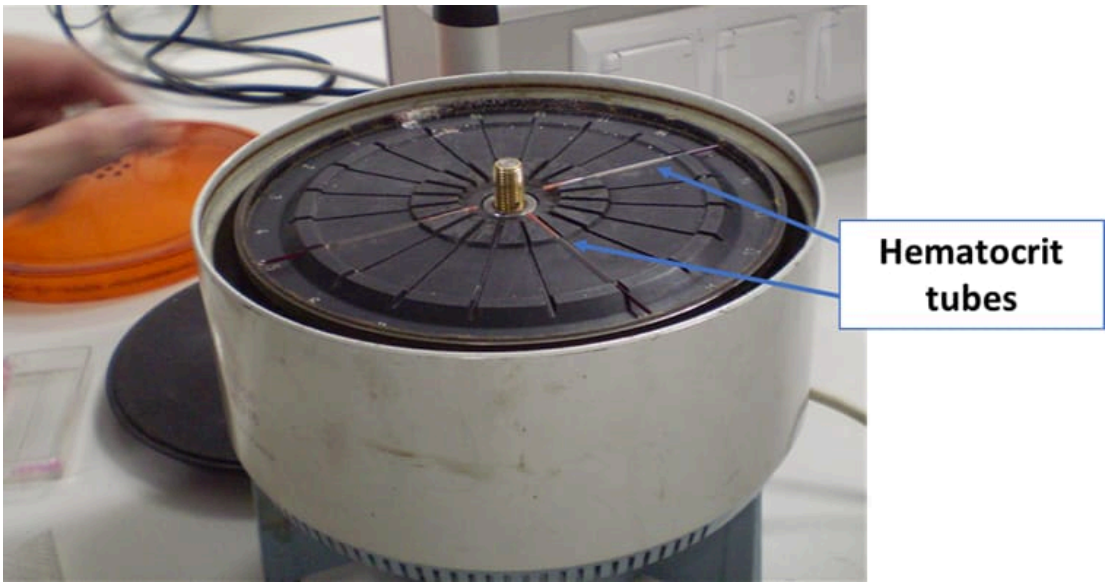


Figure 9.2.1: **Measuring Hematocrit Using a Centrifuge.** A microhematocrit centrifuge is shown with several capillary hematocrit tubes placed in the rotor slots. Each tube is partially filled with anticoagulated whole blood and sealed at one end. (Image credit: [insert your preferred source, e.g., Wikimedia Commons, CC BY-SA 3.0])

The centrifuge always needs to be **balanced** by placing tubes opposite each other. After securing the centrifuge lid tightly, the samples are spun for several minutes at a very high speed, typically around 10,000-12,000 revolutions per minute (RPM).

Results After Centrifugation

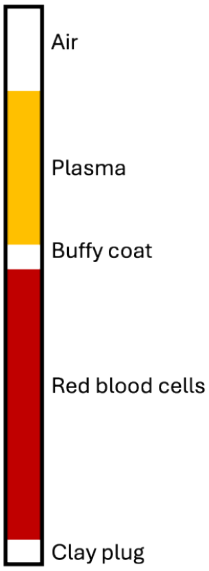


Figure 9.2.2: **Centrifuged capillary tube.** The three layers of blood can be seen after centrifugation. **Red cell layer:** dark red, at the bottom (clay-plug sealed end); **Buffy coat:** thin whitish line on top of the red layer (may be hard to see if very thin); **Plasma layer:** clear straw-yellow fluid at the top of the tube. *(Image by Harmony Folse is licensed under CC BY-SA 4.0)*

The key point of the hematocrit is that the test measures the **ratio of red blood cells to the total volume of blood**. It is expressed as a **percentage** or **volume fraction** and is sometimes called the ***packed cell volume (PCV)***.

After a capillary tube of blood is spun in a centrifuge, the contents separate into **three visible layers**:

- **Bottom red layer:** packed red blood cells (RBCs)
- **Middle thin layer:** the pale “buffy coat,” which contains white blood cells and platelets

- **Top layer:** clear, yellowish plasma

In a healthy sample, about **45%** of the blood volume consists of red blood cells, **1% or less** is the buffy coat, and the remaining **~54%** is plasma. These values can vary depending on age, sex, and health status.

To calculate the hematocrit, the **height of the red cell layer** is compared to the **total height** of all the blood in the tube. A special reading device or scale is often used for accuracy.

- If red cells fill about **half** the tube, the hematocrit is roughly **50%**.
- If they fill only about **one-quarter**, the hematocrit is around **25%**, which may suggest **anemia** (too few red blood cells).

Typical Normal Adult Hematocrit Values:

- **Males:** 42–52%
- **Females:** 37–47%

The exact proportions will vary depending on the patient's age, gender, and condition, but these numbers give an idea of typical healthy blood.

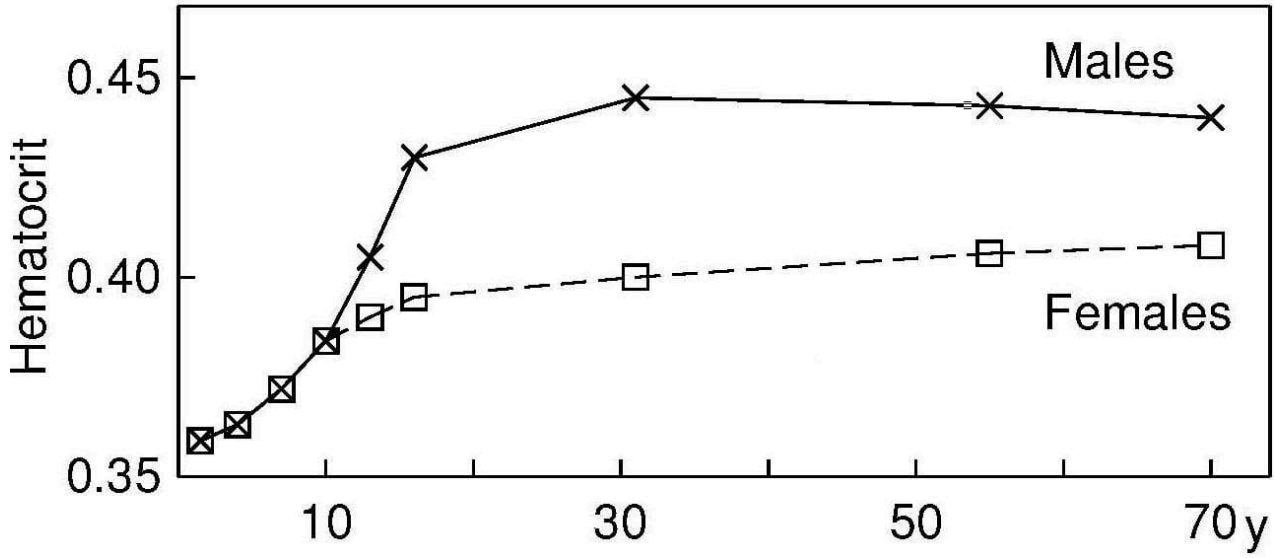


Figure 9.2.3: **Median values for hematocrit by age and sex.** Hematocrit values increase with age and are generally higher in males than in females, reflecting testosterone's role in stimulating red blood cell production. Redrawn from Yip et al. (1984).

Hematocrit Interpretation

The hematocrit test provides important clues about a person's overall blood health and oxygen-carrying capacity.

A **low hematocrit** means there are fewer red blood cells than normal, which can indicate **anemia**, **blood loss**, **nutrient deficiencies** (such as iron, vitamin B_{12}, or folate), or **overhydration** that dilutes the blood.

Hematocrit values also need to be observed during pregnancy as the levels gradually **decrease** because the **plasma volume expands more** than the red blood cell mass. This normal dilution effect reaches its **lowest point** around **28–36 weeks** in women who are not taking iron supplements. If **iron deficiency** develops, hematocrit levels may fall further once hemoglobin production is affected. In the **early stages** of iron deficiency, hemoglobin may drop slightly while the hematocrit still appears normal, but in **more severe cases**, both hemoglobin and hematocrit become noticeably reduced, indicating **iron-deficiency anemia** *(adapted from Graitcer et al., 1981)*.

A **high hematocrit** suggests an increased number of red blood cells or reduced plasma volume, as seen in **dehydration**, **living**

at high altitudes, or in conditions such as **polycythemia**.

Because red blood cells transport oxygen, abnormal hematocrit values can affect how efficiently tissues receive oxygen. For this reason, hematocrit testing is often used to help diagnose or monitor diseases that impact the lungs, heart, bone marrow, or hydration status.

CAREER CONNECTIONS

Phlebotomy and Medical Lab Technology

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

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

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

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9.3: Blood Plasma

Blood plasma is mostly water containing proteins that maintain fluid balance, transport materials, and aid in clotting.

Master this section and you'll be able to

- Identify the main components of blood plasma and describe the functions of albumin, globulins, and fibrinogen.
- Distinguish between plasma and serum and explain how their compositions differ.

Composition of Blood Plasma

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

Major Plasma Proteins

Plasma contains many dissolved proteins that help transport materials and maintain proper fluid balance in the body. About 7 percent of the volume of plasma — nearly all that is not water — is made of proteins. These include several plasma proteins (proteins that are unique to the plasma), plus a much smaller number of regulatory proteins, including enzymes and some hormones. The major components of plasma are summarized in Table 9.3.1.

The three major groups of plasma proteins are **albumin, globulins,** and **fibrinogen**.

1) Albumins

Albumin, **produced in the liver,** is the most abundant plasma protein, accounting for about **50–60%** of the total plasma proteins. Albumins help maintain the osmotic balance between blood and tissue fluids by exerting a force that draws water toward them, known as *oncotic* or *osmotic pressure*. By retaining water within the bloodstream, albumins play a crucial role in maintaining **normal blood volume and pressure**.

During **inflammation**, albumin molecules can leak through the vascular endothelium and enter surrounding tissues. Plasma pulled into the tissues by albumin-driven oncotic pressure becomes interstitial fluid, which eventually drains into the lymphatic system and is recirculated back into the plasma. This movement of fluid contributes to *exudate edema* — the swelling commonly associated with inflammation.

In addition, albumins serve as **carriers** for various substances, including vitamins and drugs (for example, penicillin). They also transport lipids and other lipophilic compounds — such as bilirubin, fatty acids, and steroid hormones — that are not soluble in water.

2) Globulins

Globulins make up about **38%** of plasma proteins. They are a diverse group of proteins designated into **three groups:** alpha, and beta, and gamma, based on how far they move during electrophoresis tests. Their main function is to **transport various substances** in the blood.

- **Alpha** and **beta** globulins: transport **iron, lipids,** and **fat-soluble vitamins** (A, D, E, and K). Also, **alpha** globulins are notable for inhibiting certain proteases, and **beta** globulins often function as enzymes in the body.
- **Gamma** globulins are also called **antibodies (**or **immunoglobulins).** They are part of the immune system and are made by **plasma cells**, a type of white blood cell.

3) Fibrinogen and Other Clotting Factors

Clotting proteins are mainly produced in the **liver**. Twelve proteins known as “clotting factors” participate in the cascade clotting process during endothelial injury when blood vessels are damaged. The most abundant factor is **fibrinogen** (making up about 7% of the total plasma proteins). Fibrinogen generates **fibrin** when activated by the coagulant thrombin, which forms a mesh that clots blood with the assistance of a platelet plug. Normally, anticoagulants and fibrinolytics in the plasma, such as plasmin and heparin, break up fibrin clots and inactivate thrombin. However, during endothelial injury, damaged cells will release tissue factor, another type of clotting factor that causes a cascade of thrombin production that will overpower the anticoagulants and cause a clotting response.

Serum: What’s Left After the Clot

When blood is allowed to clot in a test tube, the clot removes cells and clotting proteins (like fibrinogen) from the mixture. What is left is a clear, yellowish fluid called **serum**. Serum still contains many of the same components as plasma — such as water, electrolytes, nutrients, hormones, and waste products, as well as albumin and globulins, — but it **lacks the clotting factors** that were used up during clot formation.

In clinical testing, serum is often used to measure things like hormones, glucose, electrolytes, and antibodies because it provides a clean sample without the interference of clotting proteins.

In short:

- **Plasma** = blood fluid ***with*** clotting factors (collected from blood that did not clot).
- **Serum** = blood fluid ***without*** clotting factors (collected after blood has clotted).

Other Plasma Solutes

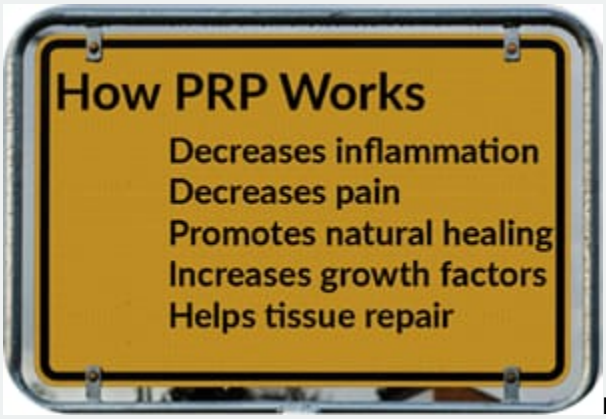
In addition to proteins and clotting factors, plasma contains a wide variety of other substances. These include various electrolytes, such as sodium, potassium, and calcium ions; dissolved gases, such as oxygen, carbon dioxide, and nitrogen; various organic nutrients, such as vitamins, lipids, glucose,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

Summary of Major Blood Components

Category and % of blood	Sub-component (% of Category)	Type and % (where appropriate)	Site of production	Major function(s)
Plasma 46-63%	**Water** ~92%	Fluid	Absorbed by intestinal tract or produced by metabolism	Transport medium
	Plasma proteins ~7%	**Albumin** ~54-60% of plasma proteins	Liver	Maintain osmotic concentration, transport lipid molecules
		Globulins 35-38% of plasma proteins	Alpha globulins Liver	Transport, maintain osmotic concentration
			Beta globulins Liver	Transport, maintain osmotic concentration

Category and % of blood	Sub-component (% of Category)	Type and % (where appropriate)	Site of production	Major function(s)
			Gamma globulins (immunoglobulins) Plasma Cells	Antibody immune responses
		Fibrinogen 4-7% of plasma proteins	Liver	Blood clotting in hemostasis
	Regulatory proteins <1%	Hormones and enzymes	Various sources	Regulate various body functions
	Other solutes ~1%	Nutrients, gases, and wastes	Absorbed by intestinal tract, exchanged in respiratory system, or produced by cells	Numerous and varied
Formed Elements 37-54%	**Erythrocytes** ~99%	**Erythrocytes**	Red bone marrow	Transports gases, primarily oxygen and some carbon dioxide
	Leukocytes <1%	**Granular leukocytes:** neutrophils, eosinophils, basophils	Red bone marrow	Nonspecific immune responses
		Agranular leukocytes: lymphocytes, monocytes	**Lymphocytes**: red bone marrow and lymphatic tissues	Specific immune responses
			Monocytes: red bone marrow	Nonspecific immune responses
	Platelets <1%	**Platelets**	Megakaryocytes: red bone marrow	Hemostasis

Medical Breakthrough



Platelet-Rich Plasma (PRP) Therapy: Heal Yourself — with Your Own Blood!

While the **idea of concentrating platelets** dates back over 50 years, modern PRP therapy as a regenerative treatment really took off in the early 2000s.

You have just learned that **plasma**, the liquid part of blood, does **not** normally contain platelets. So how is it that people talk about "platelet-rich plasma" therapy? Is that a contradiction? Not at all! It is actually a clever medical technique that depends on **how the blood is centrifuged**.

You have learned that when whole blood is spun in a centrifuge, it separates into three main layers:

1. **RBCs** at the **bottom** — the heaviest layer.
2. The **buffy coat** in the **middle** — a thin whitish layer containing WBCs and platelets.
3. **Plasma** at the **top** — the lightest layer, mostly water and dissolved substances.

When using standard laboratory centrifuge technique to make regular plasma, most platelets end up **in or just above the buffy coat** but are usually removed with the cells or lost when the plasma is drawn off the top.



In **platelet-rich plasma (PRP) preparation**, however, the technician uses a **two-step centrifugation method**:

- The **first, gentle spin** separates the blood into layers but keeps many platelets suspended just above the buffy coat, in the lower part of the plasma.
- The technician then collects that **platelet-rich lower plasma fraction** (including the layer immediately above the buffy coat) and **spins it again** at higher speed to further concentrate the platelets.

The result is a small volume of plasma that is **3–5 times richer in platelets** than normal blood.

This specially prepared PRP is then **injected back into an injured joint, tendon, or surgical site**. The concentrated platelets release **growth factors** that stimulate tissue repair, reduce inflammation, and speed up healing.

So, while ordinary plasma has almost no platelets, **PRP is plasma that has been engineered to keep and concentrate them—turning the body's own blood into a powerful healing booster.**



Figure 9.3.1: **Process of Injecting a Knee with PRP:** Blood is drawn from a vein, spun using a special technique to concentrate the platelets, and the enriched plasma is then injected into the knee joint.

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9.4: Cells and Platelets of the Blood

The formed elements of blood include RBCs, WBCs, and platelets — each with distinct structures, essential for their function in transporting gases, defending against disease, and preventing blood loss.

Master this section and you'll be able to

- Identify all the formed elements of blood and describe their origins.
- Compare the structure and function of these formed elements.
- Explain what a CBC is and relate it to health or disease.

Formed Elements

Blood cells and cell fragments are collectively known as **formed elements**. This group includes **erythrocytes** (red blood cells, or RBCs), **leukocytes** (white blood cells, or WBCs), and **thrombocytes** (platelets). All of them are produced primarily in the red bone marrow rather than within the bloodstream itself. Because platelets are actually fragments of much larger cells called **megakaryocytes**, it is technically incorrect to refer to all formed elements as “cells.” For this reason, the term *cellular components* is not used to describe them.

Erythrocytes function to carry oxygen through the bloodstream so it may be delivered throughout the body.

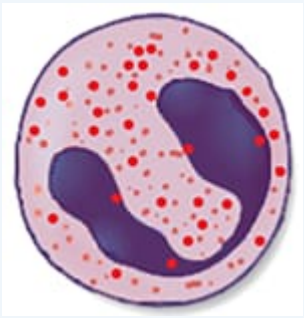
There are several different types of leukocytes that have unique functions contributing to the body's housekeeping and sickness fighting efforts.

Platelets, finally, function in helping to maintain blood volume (a process called hemostasis) by forming blood clots to prevent blood loss.

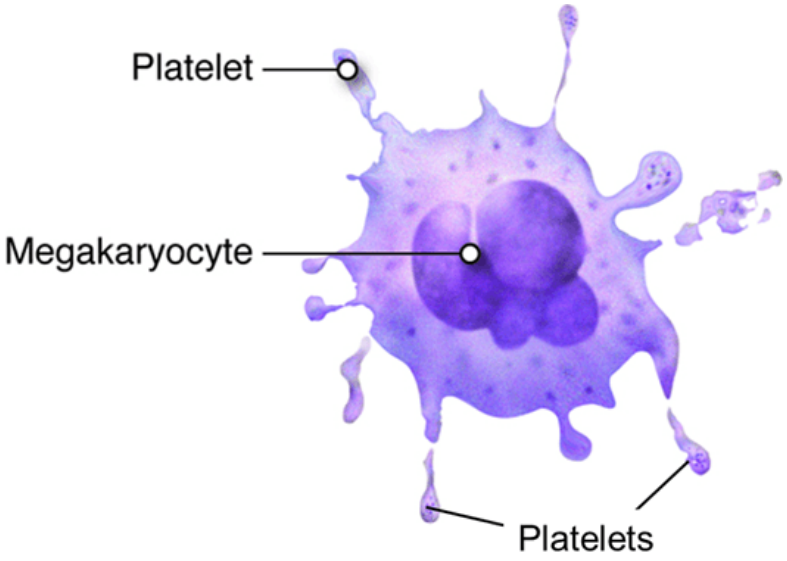
The formed elements are summarized in the table below. Each category of formed element is covered in more detail in a dedicated section below.

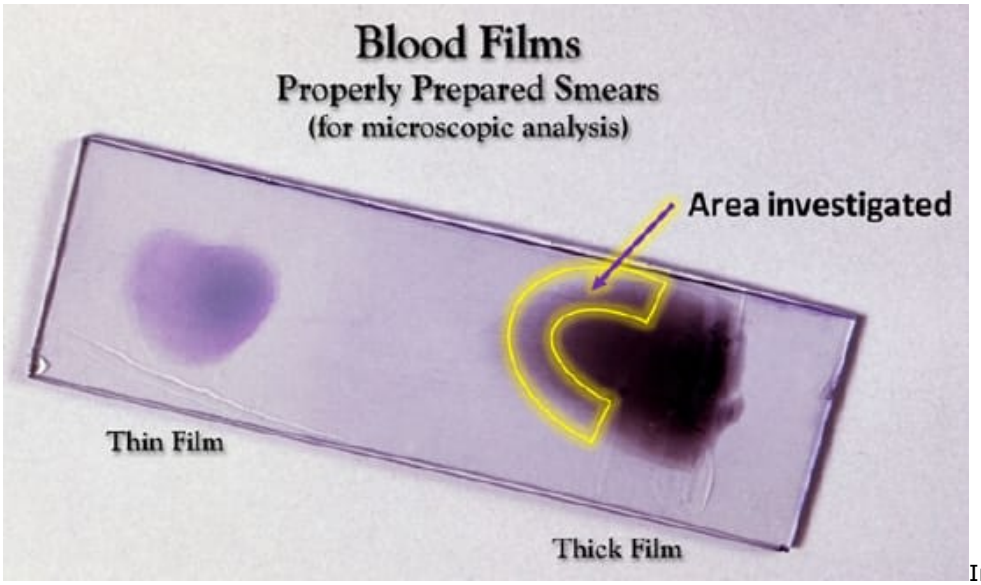
Summary of Formed Elements in Blood

Formed Element	Major Subtypes	Numbers Present per Microliter (µL); Mean (Range)	Appearance in a Standard Blood Smear	S F
Erythrocytes (red blood cells)		5.2 million (4.4-6.0 million)	Flattened biconcave disc; no nucleus; pale red color	T o s d b ti lu

Formed Element	Major Subtypes	Numbers Present per Microliter (µL); Mean (Range)	Appearance in a Standard Blood Smear	S F
Leukocytes (white blood cells)	Granulocytes (neutrophils, eosinophils, and basophils)	7000 (5000-10,000)	Obvious dark-staining nucleus	A b
	Neutrophils 	4150 (1800-7300)	Nuclear lobes increase with age; pale lilac granules	P p e a b R c c fr
	Eosinophils 	165 (0-700)	Nucleus generally two-lobed; bright red-orange granules	P c w a c re a ir a p ir
	Basophils 	44 (0-150)	Nucleus generally two-lobed but difficult to see due to presence of heavy, dense, dark purple granules	P ir

Formed Element	Major Subtypes	Numbers Present per Microliter (µL); Mean (Range)	Appearance in a Standard Blood Smear	S F
	Agranulocytes (lymphocytes and monocytes)	2640 (1700-4950)	Lack abundant granules in cytoplasm; have a simple-shaped nucleus that may be indented	B
	Lymphocytes 	2185 (1500-4000)	Spherical cells with a single often large nucleus occupying much of the cell's volume; stains purple; seen in large (natural killer cells) and small (B and T cells) variants	P sp (a ir c a c re a n c c n
	Monocytes 	455 (200-950)	Largest leukocyte with an indented or horseshoe-shaped nucleus	V p c p w a a p c fc c th sy

Formed Element	Major Subtypes	Numbers Present per Microliter (µL); Mean (Range)	Appearance in a Standard Blood Smear	S F
Platelets		350,000 (150,000-500,000)	Cellular fragments surrounded by a plasma membrane and containing granules; purple stain	H p g fo h ti



In addition to measuring hematocrit, another very common blood test is the **complete blood count (CBC) with differential**. In this test, a small sample of blood is placed on a microscope slide, spread into a thin film (see image on the right), and stained so that the different formed elements — RBCs, WBCs, and platelets —can be clearly distinguished. A trained laboratory technician then examines the sample under a microscope to count and identify each type of cell or cell fragment.

The **differential** portion of the CBC focuses on determining the numbers and percentages of each type of leukocyte, while the rest of the test provides detailed information about the sizes, shapes, and overall appearance of all the formed elements. In some cases, a slide imprinted with a fine grid is used to make it easier to calculate cell concentrations per unit volume of blood. These values are then compared with standard reference ranges (such as those shown in the table above) to help identify possible abnormalities.

Elevated or decreased numbers of specific cell types can give important clues about a person's health. For example, unusually high **neutrophil** counts — called **neutrophilia**— might suggest a bacterial infection. If, on the other hand, the neutrophil count is low, a condition known as **neutropenia**, it may indicate that the body's ability to fight bacterial infections is reduced. Neutropenia can occur with certain viral infections, bone marrow disorders, autoimmune diseases, or as a side effect of chemotherapy.

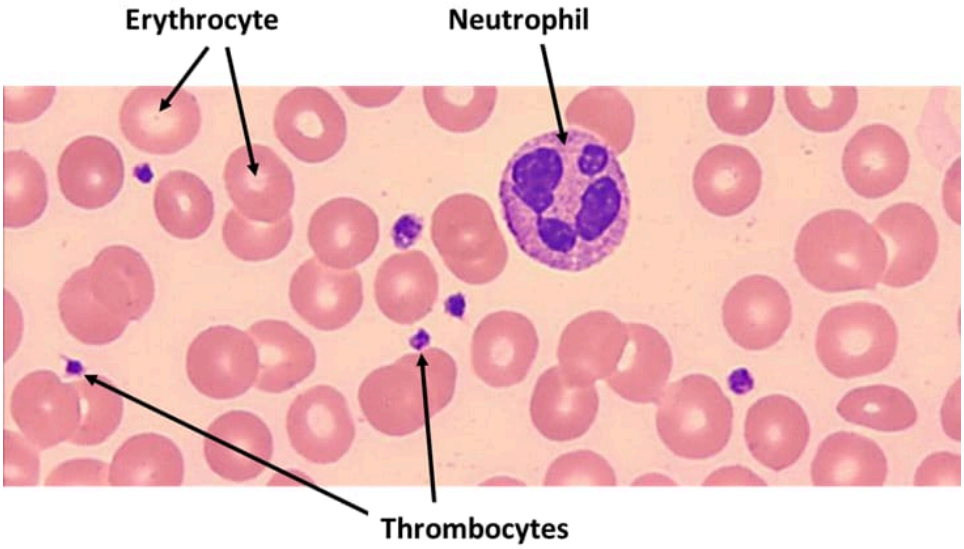


Figure 9.4.1: **RBCs, Neutrophil and Thrombocytes in a Peripheral Blood Smear.** In a typical sample, there are about 600 - 700 times more RBCs than WBCs. Most of the pink, non-nucleated cells seen here are **erythrocytes**, which transport oxygen and carbon dioxide. The large cell with a **multilobed purple nucleus** is a **neutrophil**, the most common type of WBC and an important defender against bacterial infection through **phagocytosis**. The tiny, irregular purple-stained fragments are **thrombocytes (platelets)**, which aid in **hemostasis** by forming temporary plugs and releasing clot-promoting factors. *Image credit: OpenStax, CC BY 4.0.*

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9.5: Erythrocytes — Tiny Oxygen Taxis

Red blood cells are the most numerous formed elements in blood and play a vital role in gas transport and oxygen regulation.

Master this section and you'll be able to

- Describe the structure and function of erythrocytes.
- Discuss the various steps in the lifecycle of an erythrocyte
- Explain how hemoglobin transports oxygen and carbon dioxide.
- Outline how erythropoietin regulates red blood cell production

Red Blood Cells

The **erythrocyte**, commonly known as a red blood cell (or RBC), is by far the most common formed element. A single drop of blood contains millions of erythrocytes and just thousands of leukocytes. Males typically have about 5.4 million red blood cells per microliter (µL) of blood, and females about 4.8 million per µL. In fact, erythrocytes are estimated to make up about 25 percent of the total cells in the body. Erythrocytes are also smaller than leukocytes and most other body cells — only about 7–8 micrometers (µm) wide, much smaller than most white blood cells.

The main job of red blood cells is to **carry oxygen and carbon dioxide**, since these molecules cannot be efficiently transported dissolved in plasma. RBCs pick up oxygen in the lungs and deliver it to tissues throughout the body, then carry part of the carbon dioxide waste back to the lungs to be exhaled.

Unlike white blood cells, which leave the bloodstream to fight infection, RBCs stay within the vessels — if they escape, something is wrong.

Red blood cells are made in the **red bone marrow** at an incredible rate — more than 2 million cells per second. Their production depends on nutrients such as glucose, amino acids, and lipids, as well as trace elements like iron, copper, zinc, folate, and vitamin B_{12}. Each red blood cell circulates for about **120 days** before being broken down by macrophages in the bone marrow, liver, and spleen. The useful parts, including iron and amino acids, are recycled to make new cells.

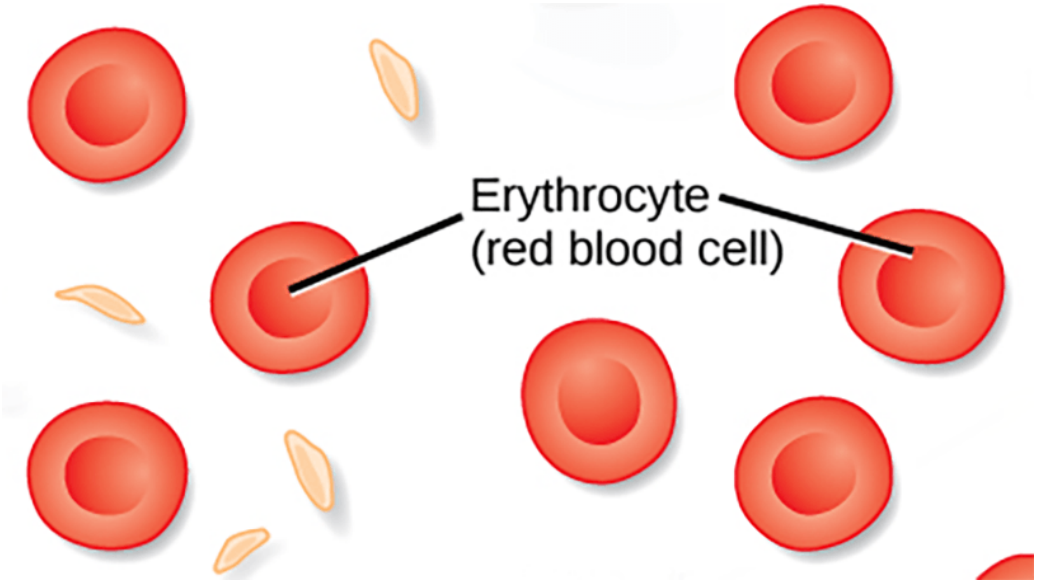


Figure 9.5.1: **Erythrocytes.** Erythrocytes are most numerous blood cells. They are red in color and biconcave in shape. *(Image credit: "Erythrocytes" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*Shape and Structure of Erythrocytes

As red blood cells (erythrocytes) develop and mature in the red bone marrow, they gradually extrude (push out) most of their internal structures (organelles) and aslo the nucleus. In their final stage before full maturity, they are called **reticulocytes**. These young cells still contain a few bits of cellular machinery that finish making **hemoglobin**, the protein that carries oxygen. Within a day or two in the bloodstream, reticulocytes lose their remaining organelles and become mature erythrocytes — essentially flexible sacs packed with about **300 million hemoglobin molecules**. Because they have no mitochondria, they rely on **anaerobic respiration**, so they do not use any of the oxygen they carry, leaving all of it available for delivery to tissues. Normally, reticulocytes make up about **1–2%** of the circulating red blood cells, and their numbers give doctors a rough idea of how quickly new red blood cells are being made. Too few may mean underproduction, while too many may signal overproduction.

Mature erythrocytes have a distinctive **biconcave disc shape** — thicker around the edges and thinner in the center. This shape increases their surface area for gas exchange and, since they got rid of their nucleus and most of their organelles, there is more room inside for hemoglobin, the oxygen carrier protein. As they travel through the narrow capillaries, oxygen diffuses out of the red blood cells into body tissues, while carbon dioxide moves in to be carried away. The smallest capillaries are so narrow that erythrocytes must bend or fold to pass through, but flexible structural proteins like **spectrin** allow them to stretch and spring back into shape. In wider vessels, they often stack together like a roll of coins, a formation called a **rouleaux** (from the French word for “roll”).

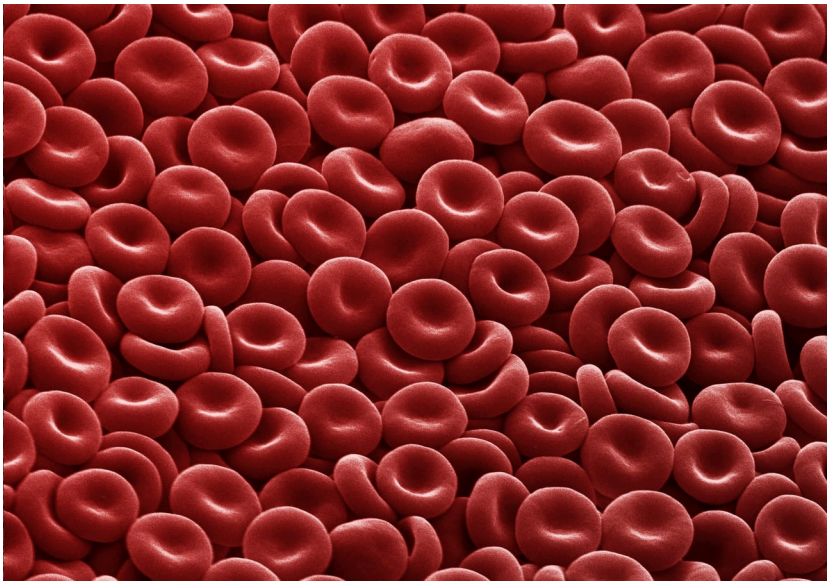


Figure 9.5.2: **Shape of Erythrocytes.** Erythrocytes are biconcave discs with very shallow centers. This shape optimizes the ratio of surface area to volume, facilitating gas exchange. It also enables them to fold up as they move through narrow blood vessels. (Image credit: "Jn7ws94a-2" by Annie Cavanagh is licensed under CC BY-SA 4.0)

Hemoglobin

Hemoglobin is a **large, iron-containing protein** that gives red blood cells their color and oxygen-carrying ability. Each hemoglobin molecule is made up of four folded chains of a protein called globin—two alpha chains and two beta chains. Each globin chain is bound to a red **pigment molecule** called **heme**, which contains an **iron** ion (Fe^{2+}) at its center *(see Figure below)*. Each iron ion can bind to one oxygen molecule, so one hemoglobin molecule can carry up to four oxygen molecules. Because a single erythrocyte contains about 300 million hemoglobin molecules, each red blood cell can transport roughly 1.2 billion oxygen molecules through the bloodstream.

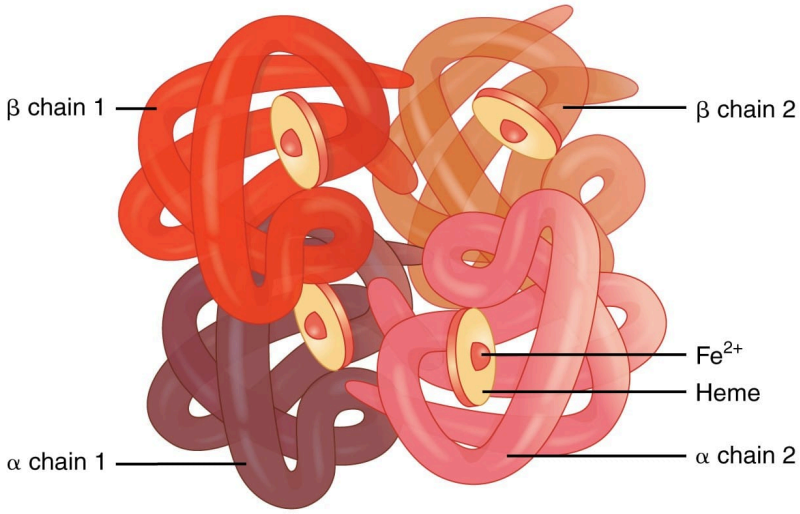


Figure 9.5.3: **Hemoglobin.** A molecule of hemoglobin contains four globin protein subunits, each of which is bound to one molecule of the iron-containing red pigmented heme. A single erythrocyte can contain 300 million hemoglobin molecules, and thus more than 1 billion oxygen molecules. (Image credit: "Hemoglobin" by OpenStax is licensed under CC BY 3.0)

Hemoglobin and Oxygen Transport

In the lungs, hemoglobin binds oxygen molecules to the iron ions within its heme groups, forming **oxyhemoglobin**. This bright red, oxygen-rich form of hemoglobin circulates through the bloodstream to deliver oxygen to body tissues. As it releases oxygen to the tissues, hemoglobin becomes darker red **deoxyhemoglobin**, sometimes called *reduced hemoglobin*. Oxygen release depends on the oxygen demand of the surrounding tissues, so hemoglobin almost never unloads all of its oxygen.

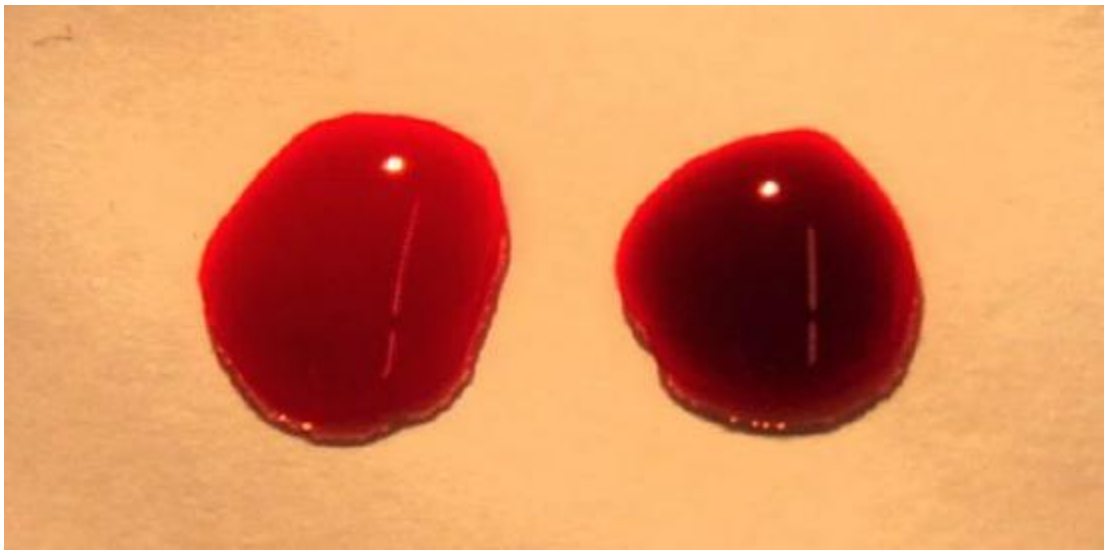


Figure 9.5.4: **Shades of Red Blood.** The bright red hue of oxygenated blood is shown on the left while the deeper red hue of deoxygenated blood is shown on the right. (*"Drops of Blood Medium" by unknown author is licensed under CC BY 3.0.*)

Carbon Dioxide Transport

When blood reaches the capillaries, carbon dioxide from the tissues enters the bloodstream. About **76%** of this carbon dioxide dissolves in the plasma — some remaining as dissolved CO_2 and the rest is converted into **bicarbonate ions (HCO_3^-)**. Another **23–24%** binds to the amino acids of hemoglobin to form **carbaminohemoglobin**. Hemoglobin then transports this carbon dioxide back to the lungs, where it is released in exchange for fresh oxygen.



Measuring Oxygen Saturation

In healthcare, a key measure of tissue oxygenation is **percent saturation**, which reflects the percentage of hemoglobin binding sites occupied by oxygen. It is commonly measured using a **pulse oximeter** *(see image on the right)*, a device clipped onto a thin part of the body — usually the fingertip. The oximeter sends red and infrared light through the tissue and measures how much light is absorbed. Because oxygenated and deoxygenated hemoglobin absorb light differently, the device can calculate the percentage of oxygen saturation.
Normal readings range from **95 to 100%**. Lower values indicate **hypoxemia**, meaning low blood oxygen. The broader term **hypoxia** refers to generally low oxygen levels within tissues.

Erythropoietin and the Feedback Loop

The total blood volume circulating in your body is about **5 liters** (a little over 10 pints). At any given moment, your **kidneys receive about 20% of your resting cardiac output**, meaning **about one-fifth of all the blood that the heart pumps with each beat** goes to the kidneys to be filtered. Over the course of a whole day, that adds up to a huge total volume: the kidneys **filter about 180 liters (around 380 pints)** of blood **per day**!

Therefore, the kidneys are well-positioned to monitor oxygen levels. When oxygen saturation falls (**hypoxemia**) the kidneys sense it and in response, interstitial fibroblasts in the kidney release the hormone **erythropoietin (EPO)**, which stimulates red blood cell production in the bone marrow.

As oxygen levels rise again, EPO secretion declines — a classic **negative-feedback loop** that maintains oxygen homeostasis.

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9.6: RBC Life Cycle

Red blood cells are continuously produced and broken down in a balanced cycle that maintains healthy oxygen transport and blood composition.

Master this section and you'll be able to

- Outline the life cycle of erythrocytes.
- Describe how erythropoietin regulates red blood cell production.
- Explain how old red blood cells are removed and their components recycled.

Erythropoiesis

In the adult human erythrocytes are made in the red bone marrow by a process called **erythropoiesis**. During early development, the fetal liver is the major site of erythropoiesis; production shifts to the bone marrow before birth and continues there throughout life.

Multipotent hematopoietic stem cells commit to the erythroid lineage under the influence of **erythropoietin** (EPO), a hormone from the kidneys that is released when blood O_2 levels are low (see previous page). Unlike mature RBCs, bone marrow cells contain a nucleus and other organelles.

Developing erythrocytes progress through several defined stages. Near the end of maturation, the cell ejects its nucleus and most organelles, becoming a **reticulocyte** that enters the bloodstream and completes maturation within 1–2 days. The time from lineage commitment to release is about seven days. To maintain a stable count, adults produce roughly 2–3 million new erythrocytes per second! These cells circulate in the blood for about **100 to 120 days**, performing their normal function of oxyen (and carbon dioxide) transport. At the end of their lifespan, they degrade and are removed from circulation.

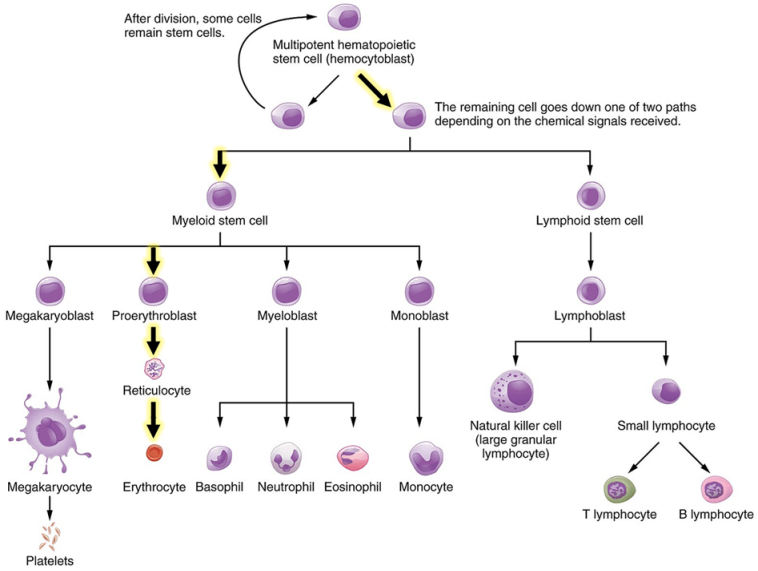


Figure 9.6.1: **Pathways of Blood Cell Formation (Hematopoiesis).** All formed elements of the blood originate from multipotent hematopoietic stem cells in the red bone marrow. Depending on the chemical signals they receive, these stem cells differentiate along one of two main lines: the **myeloid line** or the **lymphoid line**. Follow the arrows highlighted in yellow to trace the steps of erythropoiesis — the formation of red blood cells.

Eryptosis: The End of the RBC Life Cycle

After about 100-120 days, RBCs are removed from circulation through the processes of **eryptosis followed by phagocytosis**. Eryptosis is a form of **apoptosis** (cell suicide, a natural, programmed process of cell death in which senescent (old), damaged, or unnecessary cells break down in an orderly way without causing inflammation, allowing the body to remove and replace them efficiently.

As RBCs age, their plasma membranes undergo structural changes that **make them recognizable to macrophages, which then engulf and digest them,** primarily in the spleen, liver, and bone marrow. This process continuously **clears old or damaged cells from the circulation, helping to maintain healthy blood composition.** Under normal conditions, eryptosis occurs at the same rate as erythropoiesis, keeping the total number of circulating RBCs in balance.

Certain conditions — such as hemolytic anemia, sepsis, malaria, or nutritional deficiencies — as well as cellular stressors like oxidative damage, can accelerate eryptosis. In contrast, the hormone erythropoietin and the vasodilator nitric oxide both inhibit eryptosis, prolonging RBC lifespan.

Following the death of the RBC, the liver breaks down old hemoglobin into the green pigment **biliverdin** and into **iron**. The iron is taken back to the bone marrow for reuse by **transferrins** (iron carrying proteins), while biliverdin is broken down into **bilirubin**, a yellow pigment that circulates to the liver bound to albumin. The liver secretes bilirubin into bile, which is stored in the gallbladder and later excreted through the digestive system.

Key Terms

- **Erythropoietin**: A hormone produced by the kidneys in response to hypoxia, which stimulates erythropoiesis.
- **Bilirubin**: A bile pigment that arises when biliverdin is separated from the iron of old hemoglobin molecules in the liver. Bilirubin becomes part of bile salts in the digestive system (to be discussed in the digestive system module) and is excreted, while the iron content is reused.

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9.7: Aberrations from the Normal Blood Profile — Anemia vs. Polycythemia

Blood disorders such as anemia and polycythemia disrupt the balance of red blood cell production and function, leading to changes in oxygen transport, blood viscosity, and overall tissue health.

Master this section and you'll be able to

- Explain how anemia and polycythemia affect blood oxygen delivery and viscosity.
- Differentiate the main classes of anemia and their common causes.
- Distinguish key symptoms, complications, and basic diagnostic approaches for these blood disorder

At the start of the 20th century, hookworm infection was a widespread and debilitating problem across the southern United States. These tiny parasitic worms mature in the small intestine, where they latch onto intestinal villi and drink blood — often leading to severe anemia. Infected individuals were frequently tired, unfocused, and sluggish, which sadly fueled unfair stereotypes about Southerners being “lazy” or “unintelligent.” When the Rockefeller Foundation funded large-scale treatment programs and helped build outhouses to prevent reinfection, the transformation was dramatic — people regained their energy, alertness, and productivity almost overnight.

Anemia — the most common blood disorder — is the condition caused by a **reduced number of red blood cells or a lower-than-normal amount of hemoglobin.** Anemia limits the blood’s ability to carry oxygen. Because the hemoglobin within RBCs delivers oxygen from the lungs to tissues, anemia leads to **tissue hypoxia** — a shortage of oxygen that can affect every organ. Since all body cells rely on oxygen to function, even mild anemia can cause fatigue and poor concentration, while severe anemia can have far more serious consequences.

Three Main Classes of Anemia

The three main classes of anemia are based on the cause or mechanism of the condition:

1. **Anemia caused by blood loss: hemorrhagic anemia.**

   Chronic hemorrhagic anemia develops slowly over weeks or months as small amounts of blood are lost continuously, such as from bleeding stomach ulcers, colon polyps, or heavy menstrual periods. Because the loss is gradual, the body can initially compensate by producing more red blood cells, but over time iron stores become depleted, leading to anemia characterized by fatigue, pallor, and weakness.

   In contrast, **acute hemorrhagic anemia** occurs suddenly, often within hours, as a result of trauma, surgery, or a ruptured blood vessel that causes rapid and severe blood loss. The body cannot replace the lost blood quickly enough, leading to low blood pressure, dizziness, and possible circulatory shock, therefore presenting as a medical emergency.

1. **Anemia caused by decreased or faulty red blood cell production: hypoproliferative anemia,** also called **aplastic or deficiency anemia.**

   Hypoproliferative anemias occur when the bone marrow fails to produce enough healthy RBCs to meet the body’s needs. This group includes several distinct types. **Iron-deficiency anemia** results when dietary iron intake is inadequate or chronic blood loss depletes iron stores *(see hemorrhagic anemia above)*, limiting hemoglobin synthesis. **Megaloblastic anemia** develops from deficiencies in **vitamin B_{12}** or **folate**, both of which are required for normal DNA synthesis; without them, developing red blood cells become unusually large and fragile. **Aplastic anemia**, on the other hand, arises when the **bone marrow itself is damaged** — for example, by certain drugs, radiation, or autoimmune attack — leading to a severe decrease in all types of blood cells. Although their causes differ, all hypoproliferative anemias share the common feature of insufficient red blood cell production.

1. **Anemia caused by increased red blood cell destruction: hemolytic anemia.**

Hemolytic anemias occur when red blood cells are destroyed faster than the bone marrow can replace them. The destruction, known as **hemolysis**, can happen inside blood vessels or in the spleen and liver. Causes may be **intrinsic**, such as inherited defects in the red blood cell's structure or enzymes — as in **sickle cell disease,** or **extrinsic**, such as autoimmune attacks, certain infections, or mechanical damage from artificial heart valves. Because red blood cells are broken down prematurely, hemolytic anemias often lead to **jaundice** and **an enlarged spleen** due to the buildup of hemoglobin breakdown products like bilirubin.

Signs and Symptoms of Anemia

Anemia often goes undiagnosed because its symptoms can be mild, gradual, or nonspecific. The signs may stem from the anemia itself or from its underlying cause. Many people experience **fatigue, weakness, general malaise**, and sometimes **poor concentration**. **Shortness of breath** during exertion, such as climbing stairs or performing light exercise, and heart enlargement are also common.

In cases of **severe anemia**, the body attempts to compensate for the reduced oxygen-carrying capacity of the blood by **increasing cardiac output**. This extra workload on the heart can lead to **palpitations**, **chest pain (angina)** in those with heart disease, **leg pain from poor circulation (intermittent claudication)**, or even **symptoms of heart failure** if the strain becomes too great.

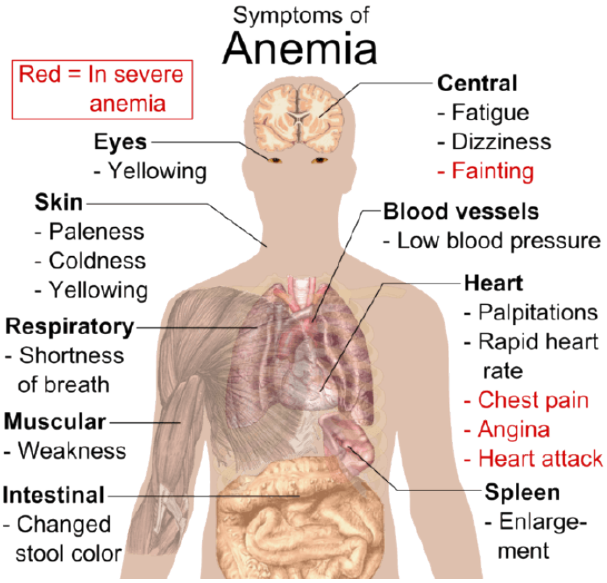


Figure 9.7.1: **Symptoms of Anemia.** Displayed are the common symptoms of anemia.

Diagnosis

Anemia is most often diagnosed with a **complete blood count (CBC)**, which provides information about the **number of RBCs**, **hemoglobin levels**, and **RBC size**. The latter is measured by **flow cytometry**, a valuable tool for distinguishing between different causes of anemia. In addition, examining a **stained blood smear** under a microscope can reveal important details about cell shape and size, and remains essential in areas where automated testing is limited.

Modern laboratory instruments can also measure **reticulocyte counts**, which indicate how actively the bone marrow is producing new red blood cells. This "**kinetic approach**" helps determine whether anemia results from decreased production or increased loss of red cells. The **reticulocyte production index (RPI)** compares the severity of anemia to the bone marrow's response—so even a normal reticulocyte count may actually represent an **inadequate response** in the setting of significant anemia.

In the **morphological approach**, anemia is classified based on red blood cell size, described by the **mean corpuscular volume (MCV)**. This classification can quickly suggest likely causes; for example, **microcytic anemia** (small RBCs) commonly indicates **iron deficiency**. In clinical practice, MCV is one of the first available results, so even when physicians favor the kinetic approach, **morphology remains a key part of diagnosis and classification**.

Examples

1) Iron Deficiency Anemia

Iron-deficiency anemia is the most common type of anemia worldwide and can **arise from many causes.** Iron is an essential component of hemoglobin, and when iron levels are low, the body cannot produce enough hemoglobin for healthy red blood cell formation. This deficiency may result from **insufficient dietary intake**, **poor absorption**, or **increased demand**, as seen in **infants, children, and pregnant women**. It can also develop when iron loss exceeds intake, such as with **heavy menstrual bleeding**, **frequent blood donations**, or **chronic bleeding from the digestive tract**.

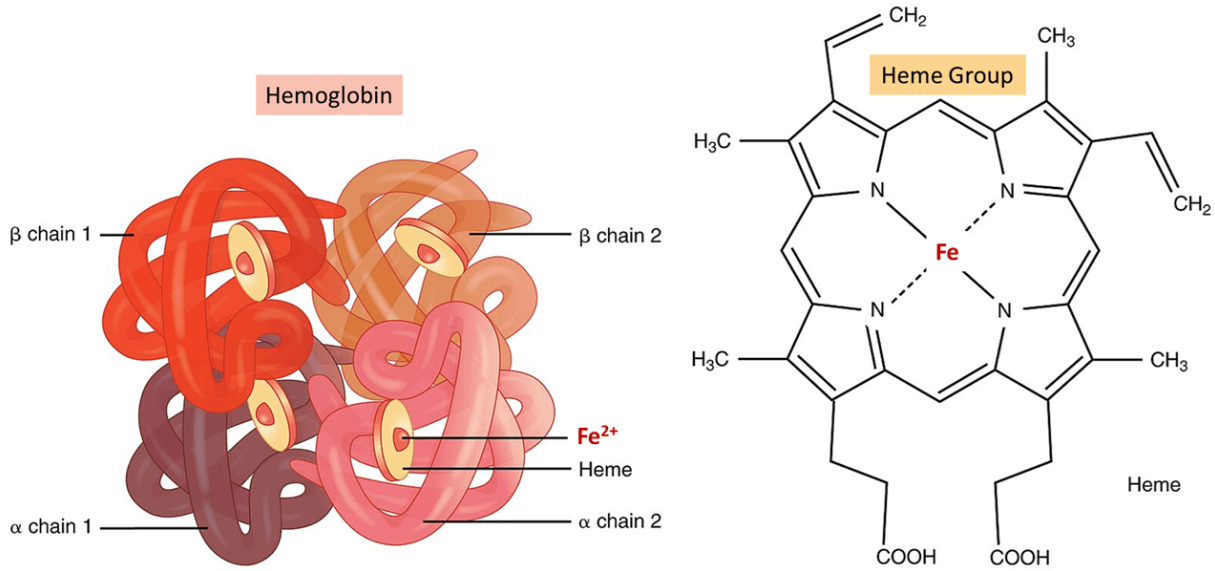


Figure 9.7.2: **Hemoglobin, Heme Group, and Iron.**

In the **United States**, the leading cause of iron-deficiency anemia is **occult gastrointestinal bleeding**, often from ulcers, polyps, or cancers. Especially in older men and women, the chances are higher that bleeding from the gastrointestinal tract could be due to colon polyp or colorectal cancer. Diagnostic evaluation may include **fecal occult blood testing**, **upper endoscopy**, or **colonoscopy** to locate the source of bleeding.

In contrast, in many **developing countries**, the predominant cause is **parasitic infection** — most commonly **hookworm** — which can cause slow, chronic blood loss and iron depletion.

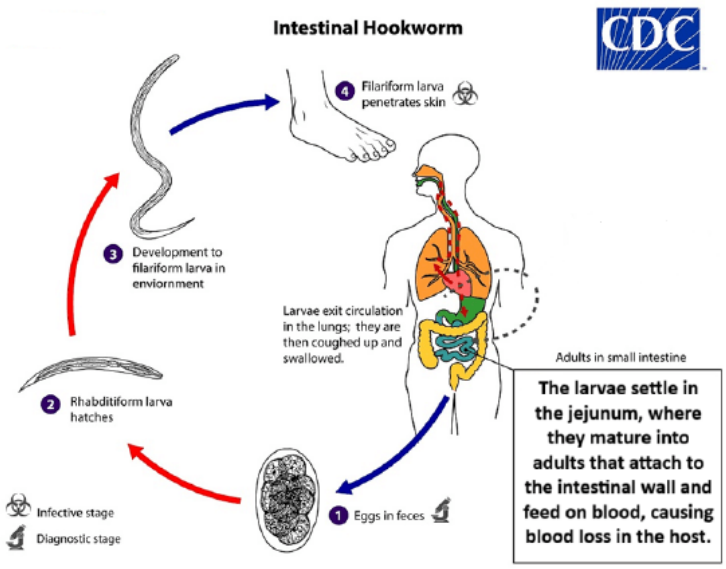


Figure 9.7.3: **Hookworm Life Cycle.** Hookworm eggs are passed in human feces and hatch into larvae within a couple of days in warm, moist soil. Over 5–10 days, these larvae mature into the **infective stage** and can survive for several weeks in the environment. When they come into contact with human skin — often bare feet — they **penetrate the skin** and travel through the bloodstream to the **lungs**, then move up the airway, are **swallowed**, and reach the **small intestine**. There they **mature into adult worms** that attach to the intestinal wall and **feed on blood**, leading to chronic blood loss and iron-deficiency anemia. Adult worms usually live for 1–2 years, though some can survive for several years.

2) Sickle Cell Anemia

Also known as **sickle cell disease,** this is an inherited disorder that affects hemoglobin — the oxygen-carrying protein in red blood cells. A single mutation in the gene for hemoglobin causes the body to produce an abnormal form called **hemoglobin S**. When oxygen levels in the blood drop, hemoglobin S molecules tend to **stick together, distorting the normally round, flexible red blood cells into rigid, crescent-shaped, or "sickle-shaped" cells.** These misshapen cells do not move smoothly through blood vessels and often clump together, blocking blood flow and reducing oxygen delivery to tissues.

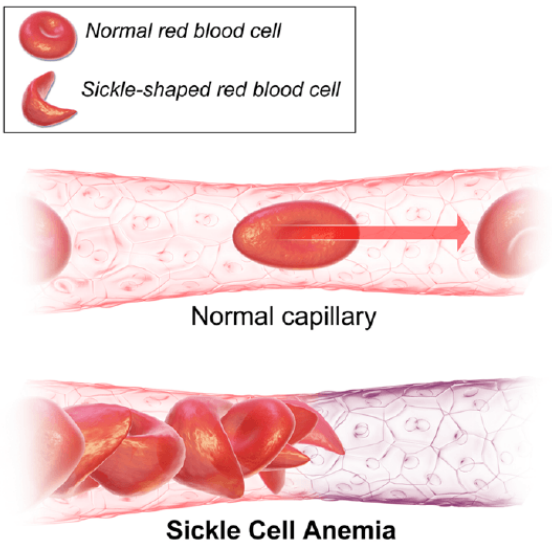


Figure 9.7.4: **Capillaries with Normal RBCs and in Sickle Cell Disease.** The image compares normal RBCs (top) with those affected by sickle cell anemia (bottom). Normal erythrocytes are round, flexible, and travel smoothly through capillaries, allowing efficient oxygen transport. In contrast, sickle cells become **rigid and crescent-shaped** due to abnormal hemoglobin (**HbS**). These distorted cells **clump together**, blocking blood flow and reducing oxygen delivery to tissues. The resulting poor circulation causes episodes of pain and tissue damage characteristic of sickle cell disease.

Because sickled cells are fragile, they break apart more easily than normal red blood cells, leading to **chronic anemia and episodes of severe pain called vaso-occlusive crises.** Repeated blockages can also damage organs such as the spleen, kidneys, and brain. Symptoms may include fatigue, shortness of breath, delayed growth, and increased susceptibility to infection. The disease is most common among people whose ancestry traces to regions where malaria is or was widespread — carrying one copy of the sickle-cell gene (the “trait”) offers some protection against malaria, while having two copies causes the disease. Treatments focus on preventing complications and improving oxygen delivery; these may include medications such as hydroxyurea, blood transfusions, and, in some cases, bone marrow transplantation.

Polycythemia



Polycythemia: Elevated hematocrit %

Polycythemia is a condition in which the body produces too many red blood cells (RBCs). This makes the blood thicker (more viscous) and slows blood flow, which increases the risk of forming blood clots, stroke, or heart attack.

There are two main types: **primary** and **secondary** polycythemia. **Primary polycythemia**, also called *polycythemia vera*, happens

when a genetic mutation in the bone marrow causes RBCs to be made without normal control. In this case, RBC production increases even when the body does not need more oxygen.

Secondary polycythemia develops when the kidneys release too much of the hormone erythropoietin (EPO), which normally stimulates RBC production in response to low oxygen. This can happen in people who live at high altitudes, smoke, or have chronic lung or heart disease. Some kidney tumors can also cause this by releasing excess EPO.

Both types lead to thickened blood and poor circulation. Treatment often includes removing blood (phlebotomy) to reduce RBC numbers, medications to control symptoms, and treating the underlying cause. Managing polycythemia carefully helps prevent serious complications such as blood clots or stroke.

Signs and Symptoms of Polycythemia

The symptoms of polycythemia can vary widely from person to person. Many people experience general symptoms such as fatigue, headache, or dizziness. These occur because thickened blood flows less easily through the vessels.

If clumps of blood cells block a large vessel, the symptoms depend on where the blockage happens. For example, if a clot forms in a coronary artery (which supplies the heart), a person may feel chest pain, shortness of breath, tiredness, or nausea — signs of a possible heart attack. If a clot forms in an artery leading to the brain, it can cause stroke-like symptoms such as weakness on one side of the body, vision problems, or trouble speaking.

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9.8: Blood Doping

Blood doping boosts oxygen delivery by raising RBCs or altering oxygen transport, which can improve endurance, but most methods are unsafe and prohibited in sport.

Master this section and you'll be able to

- Describe how blood doping increases oxygen delivery and endurance.
- Compare the main methods used to increase oxygen-carrying capacity.
- Identify major health risks, ethical issues, and detection strategies related to blood doping.

What Is Blood Doping?



Blood doping is the non-medical enhancement of the blood's ability to carry oxygen in order to improve athletic performance. As you have learned, hemoglobin inside RBCs binds oxygen in the lungs and releases it to body tissues. Increasing the number of circulating RBCs or the amount of hemoglobin per unit of blood raises the total oxygen-carrying capacity, allowing more oxygen to reach working muscles and delaying fatigue during endurance exercise.

Blood doping is widely considered unethical because it violates the rules of sport, undermines fair play, and erodes trust in competition. It also exposes athletes to preventable medical risks, which conflicts with the health professional duty to do no harm; clinicians who facilitate non-medical doping act outside professional ethics. The practice can create coercive pressure on teammates and rivals to take similar risks just to remain competitive.

Altitude training (see section SG9.6) is generally viewed as acceptable because it relies on natural adaptation rather than prohibited artificial manipulation.

The practice of increasing the amount of red blood cells (RBCs) and hemoglobin in the bloodstream so more oxygen can be carried to working muscles emerged in the late 1960s and was banned by the IOC in 1985, with multiple high-profile cases in endurance sports since then.

How Do People Do It?

1) Blood Transfusions

- **Autologous blood transfusions:** Your own blood is drawn, stored, then reinfused later.
- **Allogeneic** (or **homologous**) **blood transfusions (donor):** Someone else's blood is transfused.
  Effect: Fast increase in hematocrit and total hemoglobin.

2) Drugs That Make More RBCs

- **Erythropoietin (EPO)** and other **erythropoiesis-stimulating agents (ESAs)**. In fact, in addition to EPO itself, several **erythropoiesis-stimulating agents (ESAs)** have been developed — mostly for legitimate medical use in treating anemia caused by kidney disease, chemotherapy, or certain chronic illnesses. However, these same drugs can be misused in blood doping because they all stimulate red blood cell production in the bone marrow.

- **HIF stabilizers** and **cobalt salts,** both mimicking low-oxygen signals and therefore inducing EPO release.

  HIF stands for **hypoxia-inducible factor**, a protein that helps the body sense and respond to low oxygen levels. Under normal oxygen conditions, HIF is broken down quickly, but when oxygen is scarce — such as at high altitude — HIF becomes stable and signals the kidneys to release EPO, which then stimulates red blood cell production.

  HIF stabilizers are drugs that trick the body into thinking it is at low oxygen. They prevent HIF from being broken down, so EPO continues to be produced even when oxygen levels are normal. This leads to an increase in red blood cell count and hemoglobin. Medically, these drugs are used to treat anemia in chronic kidney disease. When used improperly by athletes, however, they are considered **blood-doping agents** because they artificially boost oxygen-carrying capacity.

  Cobalt salts (for example, **cobalt chloride**) act in a similar way. Cobalt ions stabilize HIF inside cells, again promoting EPO release and extra red blood cell formation. Although cobalt is an essential trace mineral, high doses are toxic and can cause heart damage, thyroid problems, and other serious health problems.

  Effect: Gradual rise in RBC production over days to weeks.

- **Oxygen Carriers and experimental agents.** Some experimental or synthetic substances have been engineered to transport oxygen in place of, or in addition to, red blood cells. These are known as **oxygen carriers** and include **hemoglobin-based oxygen carriers (HBOCs)**, **perfluorocarbons (PFCs)**, and newer compounds like **ITPP (myo-inositol trispyrophosphate)**.

  Hemoglobin-based oxygen carriers (HBOCs) are engineered molecules that contain purified or modified hemoglobin (from humans, cows, or other sources) suspended in solution. Because they lack the red blood cell membrane, they can circulate directly in plasma and deliver oxygen to tissues. However, without the normal protective environment of the cell, the hemoglobin tends to bind oxygen too tightly, causing poor oxygen release and leading to harmful side effects such as **high blood pressure, inflammation, and oxidative stress**. While these have potential medical uses — for example, in trauma care when stored blood is unavailable — they have also attracted interest for blood doping, even though they are **not approved** for performance enhancement and can be dangerous.

  In human trials, HBOCs increased the risk of **heart attack and death**, and are therefore **not approved for clinical or athletic use**.

What Are The Risks Of Blood Doping?

Blood doping can temporarily boost athletic performance because more red blood cells (a higher hematocrit) mean more hemoglobin to carry oxygen to muscles. With better oxygen delivery, athletes can work harder before fatigue sets in and produce less lactic acid at a given effort level. In other words, the muscles can keep burning fuel efficiently for longer periods of time.

However, this “supercharged” blood comes at a price. As the hematocrit rises, **blood thickens** and **flows more sluggishly** through vessels, **forcing the heart to pump harder**. This extra workload **increases blood pressure** and raises the risk of circulation problems — especially when dehydration makes the blood even thicker.

The same changes that promise improved endurance can quickly become dangerous. Overly **viscous blood can form clots, leading to deep vein thrombosis, pulmonary embolism, heart attack, or stroke**.

The induced **polycythemia**, can also cause headaches, dizziness, itching, and vision disturbances. Contaminated or poorly stored blood carries infection risks, and transfusing blood from another person can trigger immune reactions. Repeated transfusions may cause **iron overload**, damaging organs like the liver and heart. Misusing **EPO or similar drugs** can send hematocrit levels soaring, leading to hypertension, flu-like symptoms, or even sudden cardiac events. So, while blood doping may look like a shortcut to better endurance, it’s a high-risk gamble that can push the cardiovascular system past its limits.

How Is Doping Detected In Sport?

In competitive sports, blood doping is monitored through several detection methods:

- The **athlete biological passport:** it tracks changes in hemoglobin, hematocrit, and reticulocyte counts over time to identify unusual patterns that suggest manipulation.
- **Direct laboratory tests:** These tests can distinguish synthetic EPO forms or uncover small differences in blood cell antigens that reveal transfusions from another person (allogenic transfusions).

However, techniques like micro-dosing or carefully timed use of these substances can make detection challenging, which is why education about the health risks and ethical consequences remains a crucial part of prevention.

Comparison of Blood Doping Methods and Their Associated Risks

Method	*How It Increases Oxygen Delivery*	*Onset of Effect*
Autologous transfusion	*Reinfuses stored RBCs from the same person, increasing hematocrit and total hemoglobin*	*Hours after transfu*
Allogeneic (homologous) transfusion	*Adds donor RBCs from another person to boost oxygen-carrying capacity*	*Hours after transfu*
Erythropoietin (EPO)	*Hormone that stimulates bone marrow to produce more RBCs*	*Days to weeks*
Other ESAs (e.g., darbepoetin, methoxy-PEG-EPO)	*Longer-acting forms of EPO that increase RBC production*	*Days to weeks*
HIF stabilizers (e.g., roxadustat, daprodustat)	*Mimic low-oxygen conditions, causing the kidneys to release more EPO naturally*	*Days to weeks*
Cobalt salts (e.g., cobalt chloride)	*Chemically stabilize HIF proteins to increase natural EPO release*	*Days*
Hemoglobin-based oxygen carriers (HBOCs)	*Contain free or modified hemoglobin to transport oxygen directly in plasma*	*Immediate*
Perfluorocarbons (PFCs)	*Synthetic fluids that dissolve and carry oxygen*	*Immediate (only w inspired oxygen)*
ITPP (myo-inositol trispyrophosphate)	*Alters hemoglobin to release more oxygen to tissues*	*Experimental*
Altitude training (legal)	*Natural EPO release due to low oxygen exposure*	*Weeks*

Mini case study: A 24-year-old marathoner collapses after a hard training run on a warm day. She is pale, tachycardic, hypertensive, and complains of

sharp pleuritic chest pain and shortness of breath. She reports a recent "high-altitude block" and denies taking any medications. What do you think is happening to her?

Answer available at the end of this section.

Answers

Check Your Understanding 9.8.1

This scenario suggests that the athlete is experiencing a **pulmonary embolism (PE)** — a blood clot that has traveled to the lungs. Her symptoms of **sudden chest pain, shortness of breath, rapid heart rate (tachycardia), and high blood pressure** fit this diagnosis. The fact that she recently engaged in a "high-altitude block" and denies medication use raises suspicion for **blood doping**, particularly an **autologous blood transfusion** or **EPO use** to boost red blood cell count and oxygen-carrying capacity.

If she had artificially increased her hematocrit, her blood would be thicker and flow more slowly, especially in a dehydrated state after a long, hot run. This hyperviscosity makes clot formation more likely, and a clot can easily dislodge and lodge in a pulmonary artery, causing the sharp pleuritic pain and difficulty breathing. In the field, this is a **medical emergency** — she should receive oxygen, be monitored for signs of shock or cardiac arrest, and transported rapidly for diagnostic imaging and anticoagulant treatment.

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9.9: Hemostasis

Hemostasis is the body's process for stopping bleeding, involving a rapid vascular spasm, formation of a temporary platelet plug, and a cascade of clotting reactions that produce a stable fibrin clot to seal the wound.

Master this section and you'll be able to

- Identify the three main steps of hemostasis and describe their roles in stopping blood loss.
- Explain how clots are stabilized and later removed to restore normal blood flow.

Platelets are the body's rapid-response team for bleeding. When a small vessel is injured, they rush in and help shut the leak long before a scab forms. **Hemostasis** is the three-step process that does this job. It handles everyday nicks and cuts well, although large vessel injuries still need medical care.

1. **Vascular spasm:** the damaged vessel squeezes down to reduce blood flow, buying time.
2. **Platelet plug:** platelets stick to the exposed vessel wall and to each other, forming a quick, temporary patch.
3. **Coagulation:** a cascade of clotting factors turns soluble fibrinogen into sticky fibrin strands that weave through the plug and lock it in place.

If any step is missing or weak, bleeding (also called **hemorrhaging)** continues.

Steps of Hemostasis: From Vascular Spasm to Clot Formation

1) Vascular Spasm — The Body's First Line of Defense

When a blood vessel is cut or damaged, the very first response is **vascular spasm** — a rapid contraction of the smooth muscle in the vessel wall that helps reduce blood loss.

The walls of blood vessels contain **circular layers** of smooth muscle that tighten to constrict the vessel's opening, slowing or even stopping blood flow. In larger vessels, **longitudinal muscle layers** also contract, pulling the ends of the vessel back into the surrounding tissue. (Fun fact: this makes it surprisingly tricky for surgeons to locate and clamp a bleeding vessel!)

The spasm is triggered by chemicals called **endothelins**, released by damaged endothelial cells and pain receptors at the injury site. This powerful but temporary response can last from a few minutes up to about **30 minutes** — sometimes even longer — while the next stages of hemostasis get underway.

Platelet Plug Formation — The Temporary "Patch Job"

Next, **platelets** rush to the scene of injury. Normally, these small, small cell fragments drift freely through the bloodstream, minding their own business. But when a blood vessel is torn, the **underlying collagen fibers** become exposed — an irresistible signal for the platelets to take action.

They quickly become **spiky and sticky**, clumping together and attaching to the damaged area. A plasma protein called von Willebrand factor (vWF) acts like biological glue, helping **platelets stick firmly to both the collagen and to each other**, stabilizing the growing plug.

As platelets pile up, they release powerful chemical signals that intensify the response — drawing in and activating more platelets to expand the plug. Other substances keep the vessel constricted to limit blood flow and help launch the next phase: **blood**

clotting.

Coagulation: Building the Reinforced Clot

The final and most durable step is **coagulation**, also known as **blood clotting**. This process strengthens the platelet plug with a **mesh of fibrin**, an insoluble protein that forms when **fibrinogen** (a plasma protein) is converted into long, thread-like strands.

Coagulation happens through a **cascade** —a chain reaction in which each activated clotting factor triggers the next, like a series of falling dominoes or a multi-level waterfall. The end result is a **gel-like clot** that traps red blood cells, white blood cells, and platelets within the fibrin mesh, forming a stable barrier that seals the wound until tissue repair is complete.

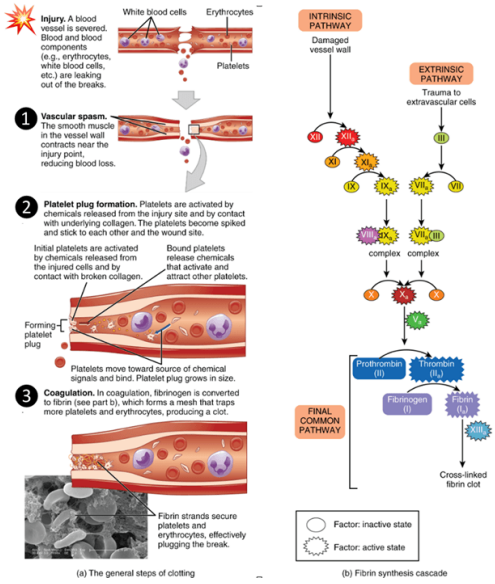


Figure 9.9.1: **Hemostasis. (a)** An injury to a blood vessel initiates the process of hemostasis. Blood clotting involves three steps. First, vascular spasm constricts the flow of blood. Next, a platelet plug forms to temporarily seal small openings in the vessel. Coagulation then enables the repair of the vessel wall once the leakage of blood has stopped. **(b)** The synthesis of fibrin in blood clots involves either an intrinsic pathway or an extrinsic pathway, both of which lead to a common pathway. (credit a: Kevin MacKenzie)

Clotting Pathways Made Simple

Extrinsic Pathway (Tissue Factor Pathway)

This is the **fast and direct route** that begins when blood escapes into damaged tissues outside the vessel, such as from a cut. The injured cells release a chemical called tissue factor (factor III). Tissue factor combines with calcium (Ca^{2+}) and factor VII to form an enzyme complex. This complex activates factor X, which kicks off the **common pathway** that produces the actual clot.

The timeframe is just a few seconds!

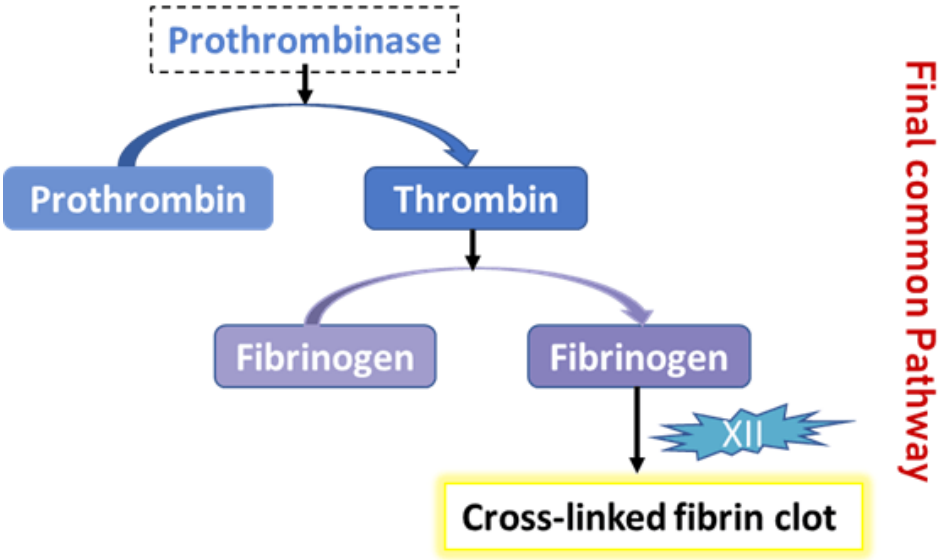
Intrinsic Pathway (Contact Activation Pathway)

This pathway takes a **few minutes** and **uses clotting factors already present in the blood.** It can be triggered by internal vessel damage, such as roughened vessel walls, or when blood comes into contact with a foreign surface like a glass tube.

The process begins when factor XII is activated. It then activates factor XI, which activates factor IX. Platelet chemicals help

speed up the sequence. Factor VIII from platelets joins factor IX to form another enzyme complex that also activates factor X, again leading into the **common pathway.**

Think of this as the slower, built-in backup system that works entirely within the blood.



Common Pathway

Once **factor X** is active, both pathways merge here.

1. **Prothrombin** is converted into **thrombin** by the enzyme **prothrombinase**.
2. **Thrombin** then converts **fibrinogen** into **fibrin**, which forms sticky protein threads that weave through the platelet plug.
3. **Factor XIII** strengthens and stabilizes the fibrin clot.
   Now the wound is sealed!

Fibrinolysis (Clot Breakdown)

When the vessel heals, the clot must be removed. Platelets contract like tiny muscles, pulling the edges of the wound together and squeezing out a yellowish fluid called **serum** (plasma without clotting proteins).
Later, the clot is dissolved in a process called **fibrinolysis**. The inactive enzyme **plasminogen** is converted to **plasmin**, which digests the fibrin threads. At the same time, **bradykinin** is released to relax the vessel walls and restore normal blood flow.

Plasma Anticoagulants (Clot Control)

An **anticoagulant** is any substance that opposes coagulation. Several circulating plasma anticoagulants play a role in limiting the coagulation process to the region of injury and restoring a normal, clot-free condition of blood. Two examples are:

- **Antithrombin** inactivates factor X and prevents prothrombin from becoming thrombin.
- **Heparin**, released by basophils and the endothelial cells lining the blood vessels, quickly reduces clotting. A pharmaceutical form of heparin is often administered therapeutically, for example, in surgical patients at risk for blood clots.

Interactive Link

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Coagulation pathway. View these animations to explore the intrinsic, extrinsic, and common pathways that are involved the process of coagulation. For this course, you do not need to know all the coagulation factors. Just focus on the last few steps of the common pathway.

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9.10: Blood Clotting Disorders

By the end of this section, you should be able to explain what happens when the blood's clotting system becomes unbalanced, leading to either too much bleeding or too much clotting.

Master this section and you'll be able to

- Explain how imbalances in platelet number or clotting factor function can lead to either excessive bleeding or abnormal clot formation.
- Discuss how liver disease or vitamin K deficiency interfere with normal clotting.
- Outline the pattern of inheritance of hemophilia.

Too Much or Too Little: When Clotting Goes Wrong

Understanding what causes clotting problems helps doctors diagnose and treat bleeding and clotting disorders correctly. Too much or too little clotting can both be dangerous.

The Trouble with Too Little Clotting

Vascular abnormalities are an uncommon cause of excessive bleeding compared with platelet or coagulation factor disorders. In this course, we will therefore focus on clotting problems that result from platelet disorders or coagulation disorders.

Thrombocytopenia: Low Platelet Count

When the body does not produce enough platelets — a condition called **thrombocytopenia** — the blood cannot form clots effectively. Thrombocytopenia can also occur when platelets are present but do not function properly. Diseases that affect the bone marrow, such as cancers or tumors, may disrupt normal platelet production. As a result, even minor cuts or bruises can lead to excessive bleeding because the normal "plug-the-leak" process fails. Thrombocytopenia is relatively uncommon, affecting about three out of every 100,000 people in the United States each year (NORD, 2022).

Platelet production begins in the **bone marrow** under the control of **thrombopoietin**, a hormone produced by the liver. Thrombocytopenia may arise from several mechanisms:

- **Decreased production** in bone marrow diseases such as leukemia or myelodysplastic syndromes.
- **Increased destruction** by the immune system, as seen in immune thrombocytopenic purpura (ITP).
- **Drug-related effects**, especially from medications like aspirin or heparin.
- **Infections** or **hereditary disorders** that shorten platelet lifespan.
- **Liver disease or heavy alcohol use**, which lower thrombopoietin levels and reduce platelet output.

The disorder results from a disruption in the normal balance between platelet production, circulation, and removal. Normal platelet counts range from **150,000 to 400,000 per microliter (μL) of blood** (NORD, 2022). Symptoms may include small pinpoint skin spots (**petechiae**), bruising, or more serious internal bleeding. Quick recognition and appropriate treatment help prevent severe complications (Nicolas et al., 2023).

Clotting Factor Shortage or Malfunction

Another cause of poor clotting is a **shortage of clotting factors**, the proteins needed to make a stable clot. This happens in **hemophilia**, a group of inherited bleeding disorders. The most common type, is

- **Hemophilia A**, resulting from a lack of **factor VIII**, while
- **Hemophilia B** involves **factor IX**.

Both are linked to the **X chromosome**, so males are more likely to have the disease, while females can be carriers. When a genetic disease is said to be "X-linked," it means that the defective gene is found on the X chromosome. Humans have two sex chromosomes: **females have two X chromosomes (XX), and males have one X and one Y (XY).** Because males have only one X chromosome, if that X carries a defective gene, they will have the disease. Females, on the other hand, have two X chromosomes, so even if one X has the defective gene, the other normal X can often compensate. These females do not usually show symptoms, but they can "carry" the gene and pass it on to their children.

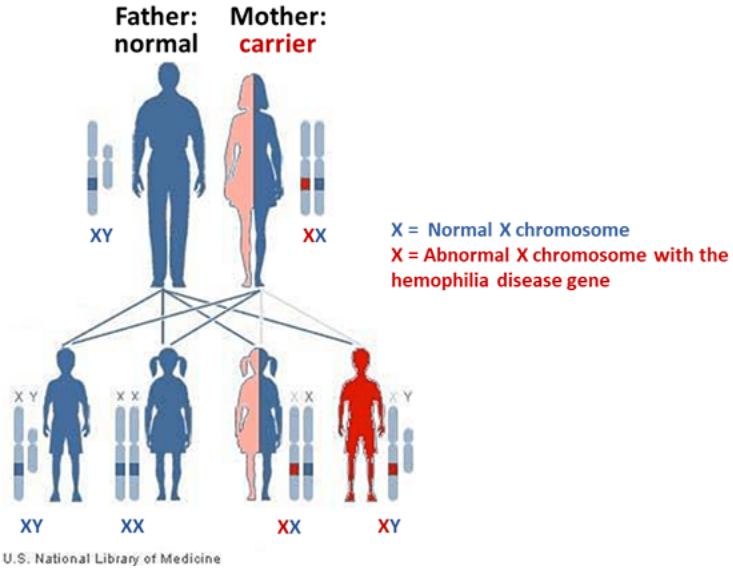


Figure 9.10.1: **Hemophilia Pedigree.** In the diagram, the mother is a carrier for this X-linked disorder and the father is normal. In X-linked inheritance, the gene causing the disorder is located on the **X chromosome**. A **carrier female** has one normal X chromosome and one X chromosome with the defective gene. A **normal male** has a normal X and a Y chromosome.

When they have children:

- Each **son** receives his X chromosome from his **mother** and his Y chromosome from his **father**.
    - If the son inherits the **defective X**, he will **have the disease**, because he does not have another X chromosome to compensate.
    - If he inherits the **normal X**, he will be **healthy**.
- Each **daughter** receives one X from each parent.
    - If she inherits the **defective X**, she becomes a **carrier** like her mother.
    - If she inherits two normal X chromosomes, she is **not a carrier** and **not affected**.

People with hemophilia may bleed too much from minor injuries or experience internal bleeding, especially into joints or urine. Treatment usually involves infusions of the missing clotting factors. Researchers are also exploring **gene therapy** as a possible long-term solution.

The Trouble with Too Much Clotting

Thrombocytosis: Too Many Platelets

Having too few platelets can cause too much bleeding — but having **too many platelets** can cause the opposite problem. This condition is called **thrombocytosis**, and it increases the risk of forming **abnormal blood clots**, known as **thrombosis.**

A **thrombus** (**plural: thrombi**) is a solid clump made of platelets, red blood cells, and fibrin that forms **inside a blood vessel**. Normal clots form only to seal a wound, but a thrombus can appear even when a vessel is not injured, blocking blood flow. Large thrombi may stick to the vessel wall (mural thrombi), while small ones can completely block a small vessel (occlusive thrombi).

If part of a clot breaks free and travels through the bloodstream, it becomes an **embolus (plural: emboli)**. When an embolus gets stuck in a smaller vessel, it causes an **embolism**. Depending on where it lands, it can block blood flow to the **heart (heart attack)**, **brain (stroke)**, or **lungs (pulmonary embolism** — *see image below).* All of these are medical emergencies.

True thrombocytosis — where platelet counts are abnormally high — is not very common and usually occurs secondary to another condition, such as **infection**, **chronic inflammation**, **iron deficiency**, or a **bone marrow disorder** (for example, *essential thrombocythemia*).

Thrombophilia: A Hypercoagulable State Caused by Overactive Clotting Factors

Although both platelets and clotting factors can trigger abnormal clots, **problems with clotting factors are more common** than true thrombocytosis.

Many people experience temporary or acquired hypercoagulable states when clotting factors become overactive. This can occur during **pregnancy**, **cancer**, **infection**, **inflammation**, or **periods of prolonged immobility** — such as long airplane flights or extended bed rest — when blood sits still for too long and clots may form in deep veins, a condition known as **deep vein thrombosis** (DVT).

Certain medications, like **oral contraceptives** or **hormone therapy**, can also raise clotting factor levels.

Some people have a higher tendency to form clots. This condition can be inherited or develop as a result of other factors such as lupus, pregnancy, obesity, polycythemia vera, or sickle cell disease.



Figure 9.10.2: **Deep Vein Thrombosis.** With deep vein thrombosis, a blood clot forms within a deep vein, most commonly in the leg or pelvis. (credit: "Behçet's Syndrome and Thrombosis" by E. Seyahi & S. Yurdakul/National Library of Medicine, CC BY 2.0)

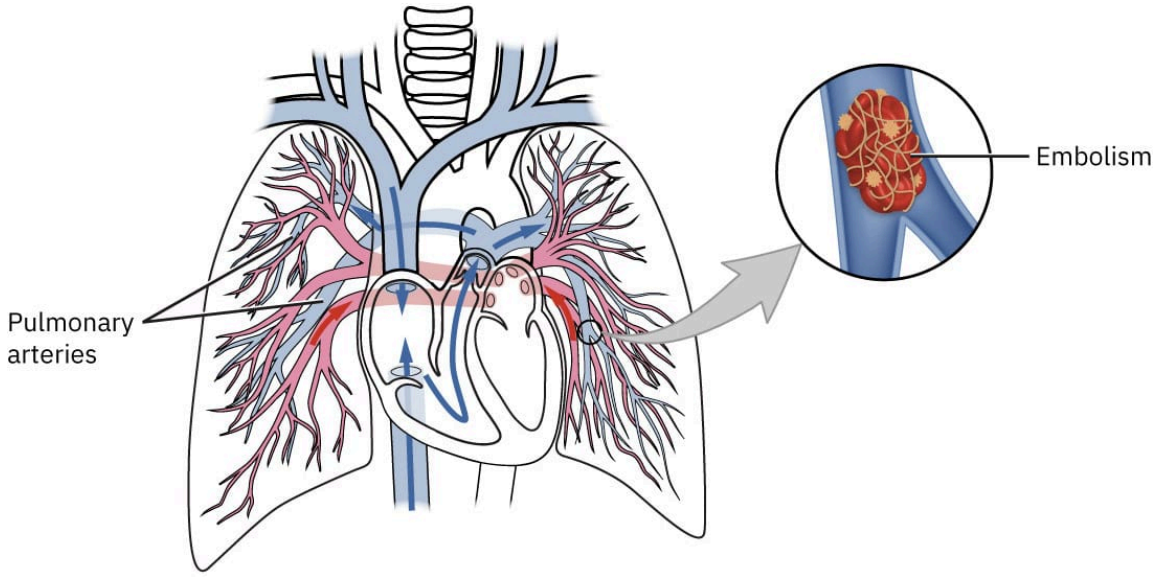


Figure 9.10.3: **Pulmonary Emboli.** With a pulmonary embolism, a blood clot breaks free and travels through the circulatory system to the lungs, where it lodges in a pulmonary artery. (attribution: modification of work *from Anatomy and Physiology*, OpenStax, under CC BY 4.0 license)

Several medications can be used to reduce the risk of abnormal clotting. **Aspirin** can prevent platelets from sticking together and is often given during or after a heart attack or stroke. However, it can also increase the risk of bleeding, so it should only be used under medical guidance.

If a clot has already formed, **clot-dissolving drugs** (called **thrombolytics**) can help. One example is **tPA**, a natural enzyme that breaks down fibrin and helps clear the blockage. When given quickly after a stroke, tPA can greatly improve recovery. Interestingly, scientists are also studying **snake venoms** — especially from **vipers and cobras** — for new clot-dissolving medicines.

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9.11: Overview of the Lymphatic and Immune Systems

The lymphatic and immune systems work together to maintain fluid balance, transport immune cells, filter pathogens, and coordinate the body's layered defenses — from physical barriers to highly specialized immune responses that protect against disease.

Master this section and you'll be able to

- Describe the major structures of the lymphatic system and their roles in fluid balance, immune defense, and lipid transport.
- Explain how white blood cells and lymphoid organs detect and respond to pathogens.
- Distinguish between barrier defenses, innate immunity, and adaptive immunity.

The Lymphatic System

The lymphatic vessels begin as a blind ending, or closed at one end, capillaries, which feed into larger and larger lymphatic vessels, and eventually empty into the bloodstream by a series of ducts. Along the way, the lymph travels through the lymph nodes, which are commonly found near the groin, armpits, neck, chest, and abdomen. Humans have about 500–600 lymph nodes throughout the body

Lymphatic Capillaries

Lymphatic capillaries are microscopic, thin-walled vessels found throughout the body's tissues. Unlike blood capillaries, they are closed at one end and have loosely overlapping endothelial cells that act like one-way flaps, allowing excess tissue fluid — called interstitial fluid — to enter but not escape back out. Once inside, this fluid is referred to as **lymph**. Without these tiny vessels constantly collecting fluid, tissues would swell with the excess — a condition known as **edema**.

Lymphatic (Lymph) Vessels

Once lymph is collected by the capillaries, it moves into larger lymphatic vessels that resemble veins in structure, complete with valves to prevent backflow. These vessels form a one-way network that carries lymph up through the body toward the chest, where it ultimately drains back into the bloodstream through two large ducts — the thoracic duct and the right lymphatic duct. Because the lymphatic system has no pump like the heart, lymph is moved along by the squeezing action of surrounding skeletal muscles and breathing movements.

Lymph Nodes

Scattered along the lymphatic vessels are small, bean-shaped structures called lymph nodes. They act as biological checkpoints, filtering the lymph as it passes through and monitoring it for foreign invaders such as bacteria, viruses, and abnormal cells. Inside each node, immune cells called **lymphocytes** and **macrophages** are ready to mount a defense if a threat is detected. This is why lymph nodes in the neck, armpits, and groin often become swollen and tender when the body is fighting an infection.

Tonsils

The tonsils are small masses of lymphatic tissue located in the throat region. They serve as one of the body's first lines of defense against inhaled or ingested pathogens. There are three pairs of tonsils: the **palatine tonsils** (the ones visible at the back of the throat), the **pharyngeal tonsil** (also called the adenoid, located at the back of the nasal cavity), and the **lingual tonsils** (found at the base of the tongue). Together, they form a ring of lymphatic tissue around the entrance to the throat. They trap and responds to pathogens before they can travel deeper into the body. Like lymph nodes, tonsils contain lymphocytes that identify and attack foreign invaders, though their open, exposed position means they themselves are prone to infection, which is the cause of the common condition known as tonsillitis.

Spleen

The spleen is the largest lymphatic organ in the body, located in the upper left region of the abdomen. Rather than filtering lymph, the spleen filters the blood directly, removing old or damaged red blood cells, platelets, and any blood-borne pathogens it detects. It also serves as a reservoir for blood and houses lymphocytes that can respond to infections in the bloodstream. Though a person can survive without their spleen, its removal does increase susceptibility to certain bacterial infections.

Thymus

The thymus is a small, two-lobed gland located in the chest, just behind the sternum. It plays a critical role in immunity by serving as the maturation site for T lymphocytes (T cells) — the immune cells responsible for recognizing and attacking specific pathogens. Immature T cells travel from the bone marrow to the thymus, where they are "educated" to distinguish the body's own cells from foreign threats. The thymus is most active during childhood and gradually shrinks with age, but the long-lived T cells it produces continue to protect the body throughout a person's life.

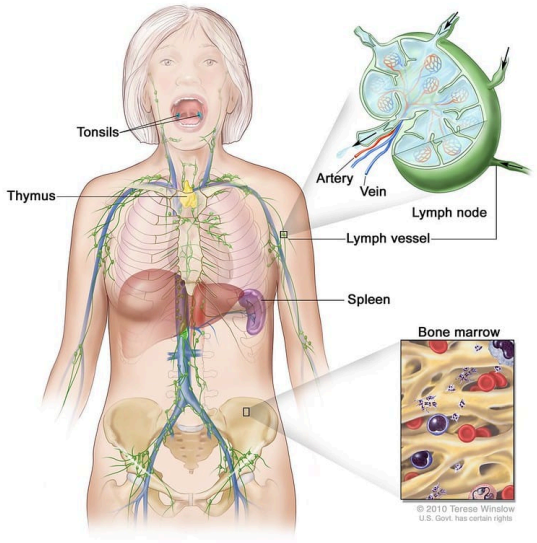


Figure 9.11.1**: Major Components of the Lymphatic System.** Major lymphoid organs and tissues, including the **tonsils**, **thymus**, **spleen**, **lymph nodes**, **lymph vessels**, and **bone marrow** are shown. Insets highlight the internal structure of a **lymph node**, showing the entry of lymph through vessels and the network of arteries and veins, and the **bone marrow**, depicting the production of blood cells including red blood cells, white blood cells, and platelets. These components work together to support immune surveillance, filter pathogens, and generate immune cells. (Image credit: "Lymphatic System" by Terese Winslow, commissioned by NIH National Cancer Institute, is licensed under CC-BY-NC 2.0.)

Structures of the Lymphatic System

Structure	Examples	Functions
Lymphatic Vessels	Lymphatic capillaries, vessels, trunks, and ducts containing lymph	• Return excess fluid from tissues to the bloodstream • Distribute lymphocytes and other leukocytes throughout the body • Transport lipid products of digestion to the bloodstream
Lymphoid Tissues	Tonsils, Mucosa-Associated Lymphoid Tissue (MALT)	• Support lymphocyte production, storage, and distribution

Structure	Examples	Functions
Lymphoid Organs	Lymph Nodes, Thymus, Red Bone Marrow, Spleen	• Support lymphocyte production, storage, and distribution • Filter blood and lymph of debris, abnormal cells, and pathogens

The lymphatic system is a central site for many immune system functions. It is a distinct system where many immune functions are concentrated, but it is important to understand that immune responses can occur throughout the body, not just in lymphoid tissues. Besides its intimate connection with the immune functions, the lymphatic system also has several roles of its own. For example, it **removes and filters interstitial fluid** from tissues, **absorbs and transports fatty acids and fats** from the digestive system as chyle, and **transports immune cells** via lymph throughout the body.

Removal of Fluid

Interstitial fluid collects in tissues mainly due to pressure from capillaries (see next chapter) or from protein leakage, which can occur during inflammation. The lymphatic system drains this excess fluid to prevent swelling, called **edema**. While edema can be part of normal inflammation, it can be dangerous in certain areas, such as the brain or lungs.

The lymphatic system is a **one-way flow system**. Tissue fluid, cells, and large molecules (collectively called **lymph**) enter **lymphatic capillaries** in the tissues. From there, lymph moves into larger **collecting lymphatic vessels**, which pass through **lymph nodes** that filter out pathogens and debris. Eventually, lymph is returned to the **bloodstream via the left and right subclavian veins** and into the **vena cava**. Lymph drains into veins because venous pressure is low, minimizing effects on overall blood pressure.

A diagram of the lymphatic system shows arteries (high-pressure oxygenated blood), capillaries, veins (low-pressure deoxygenated blood), large lymph vessels with valves, lymph nodes, lymph, lymph capillaries, and immune cells. It illustrates how tissue fluid delivers oxygen and nutrients to cells, collects waste products, and is either returned to capillaries or drained into lymph vessels.

Fatty Acid Absorption and Transport

The lymphatic system also helps absorb fats from digestion. Fatty acids are digested and converted into **chylomicrons** within intestinal cells. Lymphatic vessels in the small intestine, called **lacteals**, absorb chylomicrons into lymph. From there, they are transported into the bloodstream, where they interact with HDL cholesterol and are eventually processed by the liver.

Immune Cell Transport

The lymphatic system is a key pathway for immune cells. **Lymphocytes** and **antigen-presenting cells** travel via lymph to regional lymph nodes, where they encounter pathogens and other immune triggers. This is where much of the **adaptive immune response**, mediated by dendritic cells, occurs. Lymphatic vessels can take up antigens from tissues, and **chemokines and cytokines** released during inflammation help direct these antigens to lymph nodes, where dendritic cells present them to lymphocytes to initiate an immune response.

While this transport is essential for immunity, it can also provide a route for disease. Lymph circulation can carry cancer cells, allowing tumors to spread to other parts of the body.

The Immune System

Cells and Proteins

The immune system is made up of a collection of barriers, cells, and soluble proteins that interact and communicate with each

other in extraordinarily complex ways. The modern model of immune function is organized into three phases based on the timing of their effects.

The Three Temporal Phases

1. **Barrier defenses** such as the skin and mucous membranes, which act instantaneously to prevent pathogenic invasion into the body tissues.

2. **The innate immune response.** This rapid but nonspecific immune response consists of a variety of specialized cells and soluble factors.

3. **Adaptive immune response**. This is a slower but highly effective immune response that involves many cell types and soluble factors, but is primarily controlled by white blood cells (leukocytes) known as **lymphocytes**, which help control immune responses

Leukocytes

The **immune system is largely carried out by white blood cells (WBCs), also called leukocytes**. These cells are the primary cellular components responsible for detecting, attacking, and eliminating pathogens such as bacteria, viruses, fungi, and parasites. While organs such as the **bone marrow, thymus, spleen, and lymph nodes** provide the locations where immune cells are produced, mature, and interact, it is the white blood cells themselves that perform most immune system functions.

WBCs are produced in the **red bone marrow** and circulate through both the **bloodstream and the lymphatic system**, allowing them to move throughout the body and respond wherever infection or injury occurs. When pathogens enter the body, WBCs can leave the bloodstream and migrate into tissues, where they recognize and destroy harmful organisms.

Different types of white blood cells carry out specialized immune functions:

- **Phagocytic cells**, such as **neutrophils** and **macrophages**, engulf and digest pathogens through a process called **phagocytosis**.
- **Lymphocytes**, including **B cells and T cells**, are responsible for the highly specific responses of the adaptive immune system. B cells produce **antibodies** that bind to pathogens, while T cells help coordinate immune responses or destroy infected cells.
- Other leukocytes help regulate inflammation, release signaling molecules, and coordinate communication between different parts of the immune system.

In summary, **white blood cells are the main functional cells of the immune system**. Together, these cells allow the immune system to **recognize foreign invaders, destroy them, and remember them for faster responses in the future**. In this way, white blood cells are the **key functional components that allow the immune system to protect the body from disease.**

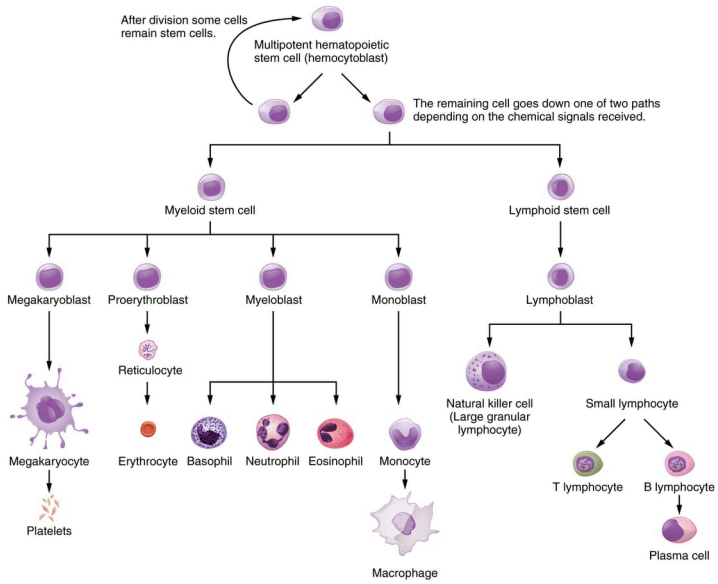


Figure 9.11.2: Hematopoietic System of the Bone Marrow. All the cells of the immune response as well as of the blood arise by differentiation from hematopoietic stem cells. Platelets are cell fragments involved in the clotting of blood.

The Functions of the Immune System: Immune Responses

The **human immune system** is a coordinated network that defends the body against disease-causing organisms such as viruses, bacteria, fungi, and parasites. At the same time, it must be able to distinguish these foreign threats from the body's own healthy tissues.

To protect the body effectively, the immune system relies on **multiple layers of defense**. These defenses work together to detect pathogens, limit their spread, and eliminate them from the body.

Innate and Adaptive Immunity

The immune system functions through two major types of defenses: **innate immunity** and **adaptive immunity**.

1. **Innate immunity** provides the body's first line of defense. It responds rapidly but **non-specifically** to invading pathogens. Physical barriers such as the **skin and mucous membranes** help prevent microbes from entering the body. If pathogens bypass these barriers, innate responses—including **inflammation, phagocytosis by immune cells, antimicrobial proteins, and the complement system**—help slow the infection and signal other immune cells to respond.

2. If pathogens persist, the **adaptive immune system** is activated. Adaptive immunity is **highly specific** and involves specialized lymphocytes called **B cells and T cells**. These cells recognize particular molecules (antigens) on pathogens and generate targeted immune responses.

One of the most important features of adaptive immunity is the development of **immunological memory**. After the body encounters a pathogen for the first time, some lymphocytes remain in the body as **memory cells**. If the same pathogen enters the body again, these memory cells allow the immune system to respond **more quickly and more effectively**. This ability to form immune memory is the basis of **vaccination**.

Both innate and adaptive immunity depend on the immune system's ability to distinguish **"self" from "non-self."** *Self* molecules belong to the body's own tissues, while *non-self* molecules originate from pathogens or other foreign substances.

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9.12: Barrier Defenses and the Innate Immune System

The body's innate immune defenses include physical and chemical barrier protections, phagocytic immune cells, and the inflammatory response that helps detect, attack, and remove pathogens or damaged tissue.

Master this section and you'll be able to

- Identify the major physical and chemical barrier defenses that prevent pathogens from entering the body.
- Describe the roles of neutrophils and macrophages as key innate immune cells.
- Explain the major steps and purpose of the inflammatory response.

The immune system can be divided into two overlapping mechanisms to destroy pathogens:

- **the innate immune response**, which is relatively **rapid** but nonspecific and thus not always effective, and
- **the adaptive immune response**, which is **slower** in its development during an initial infection with a pathogen, but is **highly specific** and effective at attacking a wide variety of pathogens.

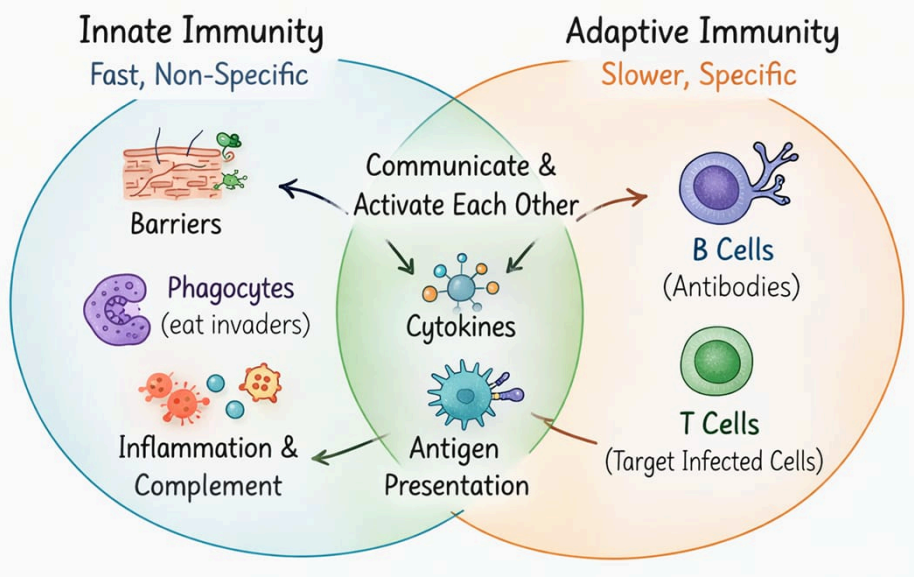


Figure 9.12.1: **Innate and Adaptive Immunity.** The innate immune system provides rapid, non-specific defenses such as physical barriers, phagocytic cells, and inflammation. The adaptive immune system responds more slowly but with high specificity through the actions of B cells (which produce antibodies) and T cells (which target infected cells). The overlapping region illustrates how these systems communicate through cytokines and antigen presentation, allowing innate responses to activate and guide adaptive immune responses.

Physical and Chemical Barriers

Any discussion of the innate immune response usually begins with the **barrier defenses** that prevent pathogens from entering the body or remove them before they can establish an infection. These defenses represent the body's most basic level of protection. Unlike many other immune responses, barrier defenses are not activated only after infection occurs; instead, they operate continuously to protect the body against a wide variety of potential pathogens.

Barrier defenses are located primarily at the body's external surfaces, where microorganisms are most likely to attempt entry. The most important physical barrier is the **skin**. The outer layer of the skin consists of dead, keratinized epithelial cells that form a tough, dry surface that is difficult for most microbes to penetrate or grow on. These surface cells are constantly shed, a process that helps remove attached microbes from the body. In addition, sweat and other skin secretions contribute to protection by

lowering surface pH, containing antimicrobial substances such as toxic lipids, and physically washing microbes away.

Another important barrier is **saliva**, a chemical barrier rich in lysozyme — an enzyme that helps destroy bacterial cell walls. The **acidic environment of the stomach** also serves as a powerful chemical barrier, killing many pathogens that enter with food or swallowed mucus. In addition, **mucus** lines the gastrointestinal, respiratory, reproductive, and urinary tracts, as well as the eyes, ears, and nose. This sticky layer traps microbes and debris, helping prevent them from reaching deeper tissues.

Table 1: Barrier Defenses

Site	Specific area defended	Protective aspect
Skin	Epidermal surface	Keratinized cells of surface and antigen presenting cells
Skin (sweat/secretions)	Sweat glands, sebaceous glands	Low pH and washing action
Oral cavity	Salivary glands	Lysozyme (enzyme that breaks down bacterial cell walls)
Stomach	Gastrointestinal tract	Low pH of stomach acid
Mucosal surfaces	Mucosal epithelium	Non-keratinized epithelial cells
Normal flora (nonpathogenic bacteria)	Mucosal tissues	Prevent pathogens from growing on mucosal surfaces

In the **upper respiratory tract**, ciliated epithelial cells continually move mucus upward toward the throat, where it is swallowed and carried into the digestive tract, eventually reaching the highly acidic environment of the stomach. Given how frequently we breathe compared with other exposures to pathogens, it is not surprising that multiple barrier mechanisms have evolved to work together to protect the respiratory system.

Cells of the Innate Immune Response

A **phagocyte** is a cell capable of surrounding and engulfing particles or other cells in a process called **phagocytosis**. In the immune system, phagocytes ingest bacteria, dead cells, and other debris, helping to clean damaged tissues and eliminate invading pathogens. Because they respond rapidly to microbes that have bypassed the body's barrier defenses, phagocytes serve as an important early component of the innate immune system's second line of defense.

Phagocytes: Macrophages and Neutrophils

Many immune cells have the ability to perform phagocytosis at some point during their life cycles. Phagocytosis is an important and effective mechanism for destroying pathogens during the innate immune response. During this process, the phagocyte engulfs a microorganism into a membrane-bound vesicle called a **phagosome**. The phagosome then fuses with a **lysosome**, whose digestive enzymes break down and destroy the pathogen. However, some microbes — such as *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis — can resist these enzymes, making them much more difficult for the immune system to eliminate. The major phagocytic cells of the immune system are macrophages, neutrophils, and dendritic cells.



Macrophage

A **macrophage** is a large, irregularly shaped phagocyte that moves through tissues in an amoeboid fashion using extensions called pseudopodia. Macrophages can migrate through capillary walls and patrol tissues, where they engulf pathogens and cellular debris. In addition to their role in innate immunity, macrophages also interact with lymphocytes and help activate the adaptive immune response. They are found in many tissues throughout the body, either freely moving through connective tissue or attached to supporting fibers in organs such as lymph nodes. Macrophages are somethimes known by different names depending on their location: for example, **Kupffer cells** in the liver and **alveolar macrophages** in the lungs.



Neutrophil

A **neutrophil** is another important phagocytic cell. Neutrophils circulate in the bloodstream and are rapidly recruited to sites of infection through **chemotaxis**, the movement of cells in response to chemical signals released during inflammation. These spherical cells belong to a WBC group called **granulocytes**, which contain cytoplasmic granules filled with antimicrobial substances and inflammatory mediators. In contrast, macrophages are **agranulocytes**, meaning they have few visible cytoplasmic granules. While macrophages act as resident sentinels in tissues, neutrophils function more like reinforcements, arriving quickly at sites of infection to help destroy invading pathogens. Although traditionally viewed as key cells of the innate immune response, research suggests that neutrophils may also influence adaptive immune responses.



A **monocyte** is a circulating white blood cell that serves as a **precursor to macrophages and dendritic cells.** When inflammation occurs, monocytes leave the bloodstream and migrate into tissues, where they differentiate into these specialized immune cells and contribute to pathogen defense.

Table 2: Phagocytic Cells of the Innate Immune System

Cell	Cell type	Primary location	Function in the innate immune response
Macrophage	Agranulocyte	Body tissues and organs	Phagocytosis; also helps activate adaptive immunity
Neutrophil	Granulocyte	Blood	Rapid phagocytosis of pathogens at infection sites
Monocyte	Agranulocyte	Blood	Precursor of macrophages and dendritic cells
Dendritic cell	Agranulocyte	Tissues (especially skin and mucosal surfaces)	Phagocytosis and antigen presentation to activate adaptive immunity

Recognition of Pathogens

Cells of the innate immune system, including the **phagocytic cells** introduced above, can detect patterns on pathogens, such as bacterial cell walls or flagella. They do this using **pattern recognition receptors (PRRs)**. A PRR is a receptor on the cell surface that can recognize parts of pathogens or signals from stressed or damaged cells.

PRRs are always present on the cell surface. Unlike the adaptive immune system, which makes many different receptors for specific pathogens, the innate immune system has **only a limited number of receptor types**. This is because each receptor needs its own gene, and the cell membrane can only hold so many receptors. The innate immune system uses this smaller set of receptors to fight many different pathogens.

When an innate immune cell detects a pathogen it recognizes, it can **bind to it and destroy it**. Phagocytic cells do this by **engulfing the pathogen.** Different innate immune cells have slightly different receptors, but they usually recognize common bacterial components and molecules.

Soluble Mediators of the Innate Immune Response

Cells communicate mostly via chemical signals. Chemical signals are molecules released from one cell that affect other cells. In immunity, many of these signal molecules are cytokines and chemokines, which tell immune cells to change how they work. These signals are released during innate immune responses and later during adaptive immune responses.

Cytokines and Chemokines

- A **cytokine** is a chemical messenger that helps nearby cells communicate by telling the receiving cell to change how it behaves.
- A **chemokine** is a type of cytokine whose main job is to attract immune cells from farther away, guiding them to the site of infection.

Inflammatory Response

The key feature of the **innate immune response** is **inflammation** — something everyone has experienced! The main function of inflammation is to trigger an immune response in an area of the body that needs it to fight off pathogens that may cause an infection or to help heal an injury.

Think about stubbing your toe, cutting your finger, or hitting your thumb with a hammer. The area becomes **red, warm, swollen, and painful**, and sometimes it can even lose a little function for a while.

Inflammation is not only caused by germs, it can happen from **any tissue injury**. When cells are damaged, they release signals that act like a **“help wanted” alert**. Immune cells rush in like a **cleanup crew at a construction site**, removing dead cells and debris and getting the area ready for repair. So the next time you stub your toe, imagine your body’s little cleanup team running to fix the mess — it’s your innate immune system in action!

Step 1: Vasodilation and Increased Vascular Permeability



Inflammation begins when innate immune cells release chemical signals called i**nflammatory mediators**. The most common short-term mediators are released by **mast cells** and include **histamine** and serotonin, though other chemicals like **bradykinin** and certain interleukins can also trigger inflammation. Mast cells are tissue-resident cells with specialized receptors for pathogens and signals from damaged cells. When triggered, they release their mediators to initiate the inflammatory process.

Imagine your blood vessels are highways. They can narrow to slow traffic — a process called **vasoconstriction** — or widen to open extra lanes, allowing immune cells to rush to the site of injury; this is called **vasodilation**. Histamine causes vasodilation, but also **increases vascular permeability**, making it easier for fluid and immune cells to leave the bloodstream and enter the surrounding tissue. Bradykinin also causes vasodilation and **sensitizes nerve endings,** which helps explain the **pain** associated with inflammation.

Together, vasodilation, increased vascular permeability, and increased sensitivity of nerve endings account for the four classic signs of inflammation: redness, warmth, swelling, and pain.

Step 2: Neutrophil Migration to the Injured Tissues

The next step of the acute inflammatory response is the movement of neutrophils to the injured area. This process is called **chemotaxis** and occurs when neutrophils follow chemical signals released at the site of inflammation. Cytokines help recruit neutrophils from the bloodstream. Other inflammatory mediators, such as TNF-alpha and IL-1, cause endothelial cells lining the blood vessels to produce adhesion molecules that help neutrophils stick to the vessel wall.

This causes the neutrophils to slow down and roll along the vessel wall, a process called **rolling**. Next, stronger attachments form allowing the neutrophils to bind firmly to adhesion molecules on the endothelial cells. This step is called **adhesion**. Together, rolling and adhesion are called **margination**, which means white blood cells are collecting along the vessel wall.

After this, neutrophils squeeze through small gaps between the endothelial cells and leave the bloodstream. Once in the tissue, neutrophils follow the chemical signals via **chemotaxis** to the exact site of infection or injury. There, they release antimicrobial substances (degranulation) and engulf pathogens by phagocytosis. Later, macrophages arrive and help clean up dead neutrophils and cellular debris.

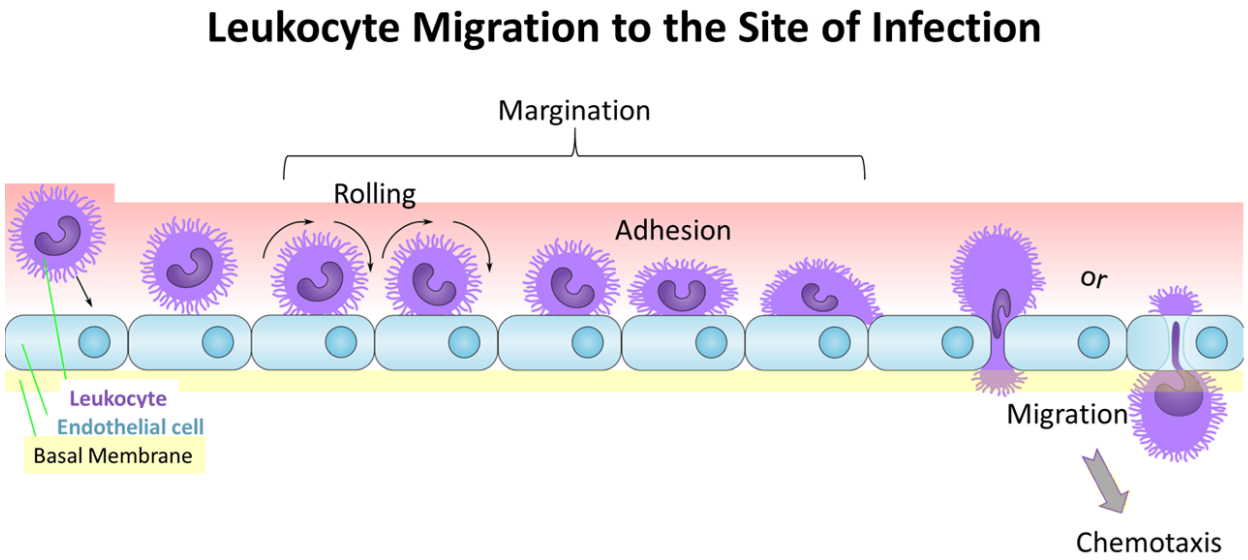


Figure 9.12.2: **Leukocyte Migration.** During inflammation, circulating leukocytes move from the bloodstream into the affected tissue through several coordinated steps. First, leukocytes slow down and roll along the endothelial cells lining the blood vessel through weak interactions. Next, stronger binding occurs through integrins, causing firm adhesion to the endothelium. The leukocytes then migrate between endothelial cells and across the basal membrane in a process called extravasation (or diapedesis), allowing them to enter the surrounding tissue and move toward the site of infection or injury.

Outcomes of Acute Inflammation

When acute inflammation ends, the body releases anti-inflammatory signals (such as IL-10) or stops producing inflammatory mediators. If the problem that caused the inflammation has been fixed, the body moves into a stage called **resolution**. During resolution, healing processes begin, such as **wound repair**.

If the problem is not solved, inflammation may occur again. Repeated episodes of acute inflammation can lead to **chronic inflammation**. In chronic inflammation, the types of immune cells at the site begin to change, and the tissue may be damaged while the body is also trying to repair it. Over time, this can lead to **fibrosis (scar tissue) and tissue necrosis (cell death).**

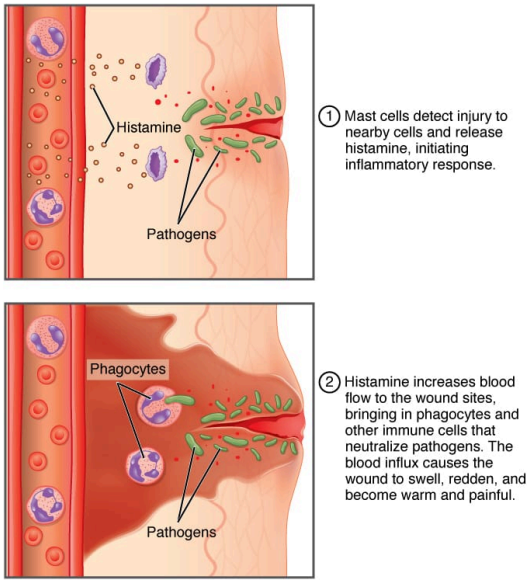


Figure 9.12.3: Early Events of the Inflammatory Response. When tissue injury occurs, mast cells in the damaged area detect signals from injured cells or invading pathogens and release histamine. Histamine acts on nearby blood vessels, causing vasodilation and increased blood flow to the affected area. This increased blood flow allows neutrophils and macrophages to leave the bloodstream and move into the tissue where they can attack pathogens. The increased blood flow and fluid in the

tissue lead to the characteristic signs of inflammation: redness, heat, swelling, and pain.

Summary of Inflammation

1. **Tissue injury:** When cells are damaged, they release signals (like histamine) that start inflammation. These signals come from mast cells and other nearby cells and act as alarms to the immune system.

2. **Vasodilation** (vessels widen): Local blood vessels get wider, so more blood flows to the area. This extra blood flow makes the area look red and feel warm.

3. **Increased permeability** (leakier vessels): Blood vessels become “leaky,” so fluid, proteins, and immune cells can leave the blood and enter the tissue. This leakage causes swelling.

4. **Recruitment of phagocytes:** Neutrophils and then macrophages are attracted to the area. They move out of the blood, eat (phagocytose) germs and debris, and many die there, forming pus in bad infections.

Together, these steps explain the four classic signs of inflammation: redness, heat, swelling, and pain.

Overall, inflammation is valuable for many reasons. Not only are the pathogens killed and debris removed, but the increase in vascular permeability encourages the entry of clotting factors, the first step towards wound repair. Inflammation also facilitates the development of the adaptive immune response.

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9.13: Key Concepts of Adaptive Immunity

Adaptive immunity is a highly specific defense system that uses B cells, T cells, and antibodies to recognize pathogens, eliminate infected cells, and create immunological memory for faster protection during future infections.

Master this section and you'll be able to

- Explain how the adaptive immune system responds to pathogens and how it differs from innate immunity.
- Describe the roles of B cells, T cells, and antigen-presenting cells in the adaptive immune response.
- Describe the structure and function of antibodies and identify the major antibody classes.
- Explain immunological memory and distinguish between active and passive immunity.

What is Adaptive or Specific Immunity?

The adaptive immune system relies on white blood cells called T and B lymphocytes. T cells produce a cell-mediated immune response, and B cells produce the humoral immune response (as seen in Figure 6.3). These immune responses will be discussed in more detail in the subsequent sections.

Adaptive immunity is activated when a pathogen is able ot overcome the initial first and second lines of defense of the innate immune system, and they are not able to completely stop an infection. The adaptive immune system kicks in when enough of a **foreign molecule**, called an **antigen**, is present and it is necessary to trigger a **stronger and more specific immune response.**

An antigen is any molecule, most often a protein, that can trigger an immune response. Examples include toxins released by bacteria or molecules found on the surface of a pathogen's cell membrane. Each pathogen carries its own unique antigens, which allows the immune system to specifically recognize and target it.

If a pathogen passes the body's first line of defense, the second line of defense responds quickly. Phagocytes and other innate immune cells attempt to destroy the invader right away. In contrast, the adaptive immune system takes several days to fully activate, but once it does, it produces a much more specific and coordinated response against the pathogen.

The main functions of the adaptive immune system include:

• Recognizing **specific foreign molecules** (**antigens**) while ignoring the body's own cells.
• Producing **targeted responses** that destroy particular pathogens or infected cells.
• Creating **immunological memory** so the body can respond much faster if the same pathogen enters again.

Formation of Adaptive Immunity

A typical adaptive immune response involves several steps:

1. An **antigen** from the pathogen is **engulfed by an antigen-presenting cell (APC)**, such as a dendritic cell or macrophage, through phagocytosis.

2. The APC travels to a lymph node or another lymphatic organ that contains immature **B and T lymphocytes,** often just called B and T cell .

3. Inside the APC, the antigen is processed and displayed on the cell surface attached to MHC class I or MHC class II molecules.

4. The presented antigen binds to T-cell receptors on immature T cells. Antigens presented on MHC II activate helper T cells,

while antigens presented on MHC I activate cytotoxic T cells.

5. The activated T cells multiply and differentiate. **Helper T cells** stimulate B cells to divide and produce **antibodies** specific to the antigen, while **cytotoxic T cells** destroy infected cells that display that antigen.

6. After the infection is cleared, some B cells and T cells remain in the body as **memory cells**, allowing the immune system to respond faster if the same pathogen appears again.

B and T Lymphocytes

B and T lymphocytes are the main cells of the adaptive (specific) immune system and allow the body to recognize and respond to specific pathogens.

B cells are responsible for **humoral immunity**. When activated, they develop into **plasma cells** that produce **antibodies** that circulate in the blood and lymph and bind to specific antigens.

T cells are responsible for **cell-mediated immunity. Helper T cells** coordinate and strengthen the immune response by activating other immune cells, while **cytotoxic T cells** destroy infected or abnormal body cells.

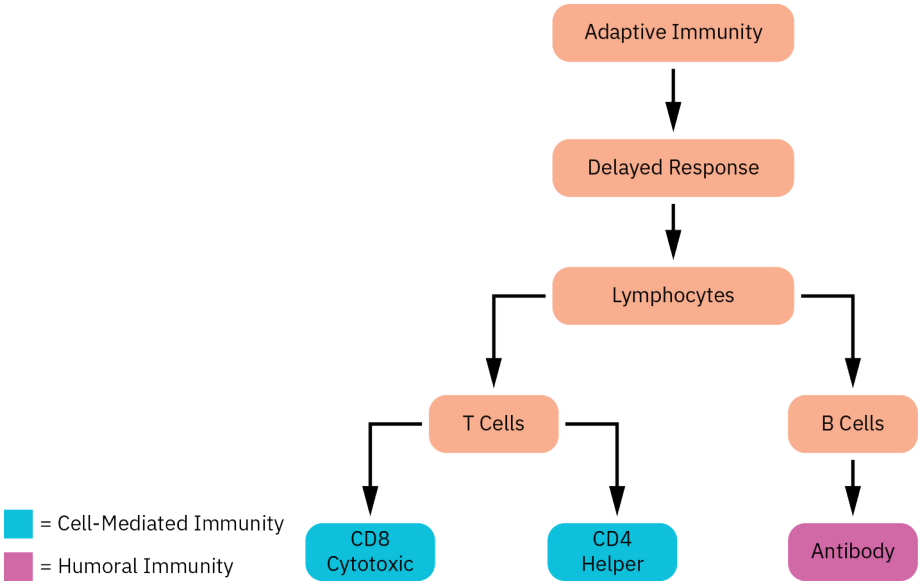


Figure 9.13.1: **Overview of the adaptive immune response.** Adaptive immunity develops more slowly than innate immunity and is carried out by **lymphocytes**, primarily **T cells** and **B cells**. **T cells** include **CD4 helper T cells**, which coordinate immune responses, and **CD8 cytotoxic T cells**, which destroy infected cells. **B cells** produce **antibodies** that bind to specific antigens on pathogens.

Some B and T cells also become **memory cells**, which help the body respond much faster if the same pathogen enters the body again.

Antigen Presentation

Antigen presentation is necessary because most T cells cannot recognize whole pathogens directly. Instead, antigen-presenting cells (such as dendritic cells, macrophages, or B cells) must first capture a pathogen, break it into smaller fragments, and display these fragments (antigens) on their surface using molecules called major histocompatibility complex (MHC) proteins.

T cells then examine these displayed antigens with their T-cell receptors. Helper T cells recognize antigens presented on MHC II molecules and become activated, allowing them to coordinate the immune response and help activate B cells. Cytotoxic T cells recognize antigens presented on MHC I molecules and can then destroy infected body cells. B cells, in contrast, can recognize intact antigens directly, but they usually still require signals from activated helper T cells to fully respond and produce large

amounts of antibodies.

In this way, antigen presentation serves as the critical communication step that allows T cells and B cells to identify specific pathogens and mount a targeted adaptive immune response.

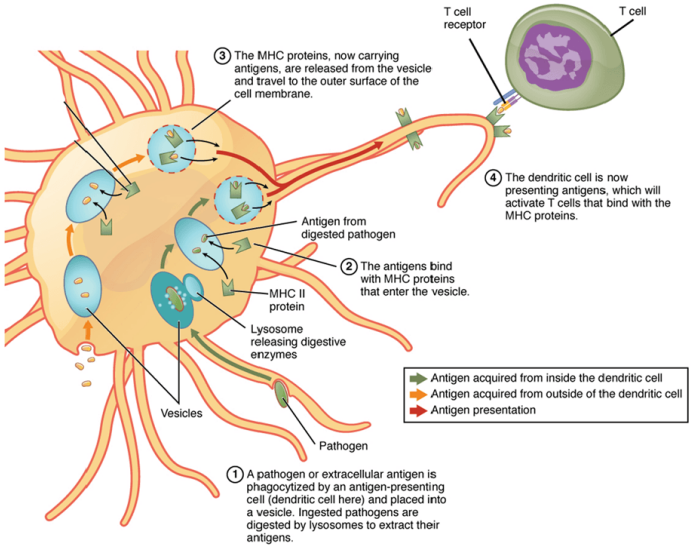


Figure 9.13.2: **Antigen Processing and Presentation by a Dendritic Cell.** A dendritic cell engulfs a pathogen through phagocytosis and digests it in lysosomes, producing antigen fragments. These antigen fragments bind to MHC II proteins inside vesicles and are transported to the cell surface. The MHC II–antigen complex is then displayed on the plasma membrane, where it can be recognized by T cell receptors on T lymphocytes, initiating activation of the adaptive immune response.

Antibodies

Antibodies were one of the first parts of the adaptive immune system discovered by scientists. Early researchers noticed that people who recovered from a bacterial infection usually did not get sick again from the same pathogen.

To investigate this, scientists mixed blood serum from an immune person with bacteria of the same type. Under the microscope, the bacteria clumped together in a process called **agglutination**. When the serum was mixed with a different type of bacteria, this clumping did not occur. This showed that something in the blood could **specifically recognize and bind to certain bacteria**.

Today we know that these molecules are **antibodies** (also called **immunoglobulins**). Antibodies are proteins produced by **B lymphocytes (B cells)** that bind to specific antigens on pathogens.

B cells first display these antibody molecules on their surface as **B cell receptors**. When a B cell recognizes its specific antigen, it becomes activated and differentiates into a **plasma cell**, which releases large numbers of the same antibody into the bloodstream. These antibodies have the **same antigen specificity** as the original B cell receptor.

Humans produce **five main classes of antibodies,** and each class has different roles in the immune response.

Unlike T cells, **B cells can recognize antigens directly**. They do not need antigens to be presented by antigen-presenting cells. Instead, B cells can bind directly to free floating antigens or intact antigens on the surface of pathogens.

Antibody Structure

Antibodies are Y-shaped proteins produced by plasma cells (activated B cells). Each antibody is made of four protein chains: two identical heavy chains and two identical light chains. These chains join together to form the Y-shaped structure.

An antibody molecule has two main regions:

- **Constant region** (the same within a class of antibodies) at the bottom portion of the antibody, called the Fc region, interacts with other parts of the immune system and helps immune cells recognize antibody-coated pathogens.
- **Variable region**, the antigen-binding site (different from antibody to antibody). The variable regions at the tips of the "Y" are what recognize and bind to specific epitopes on antigens, which is why one antibody might bind a flu virus epitope while another binds a pollen epitope.

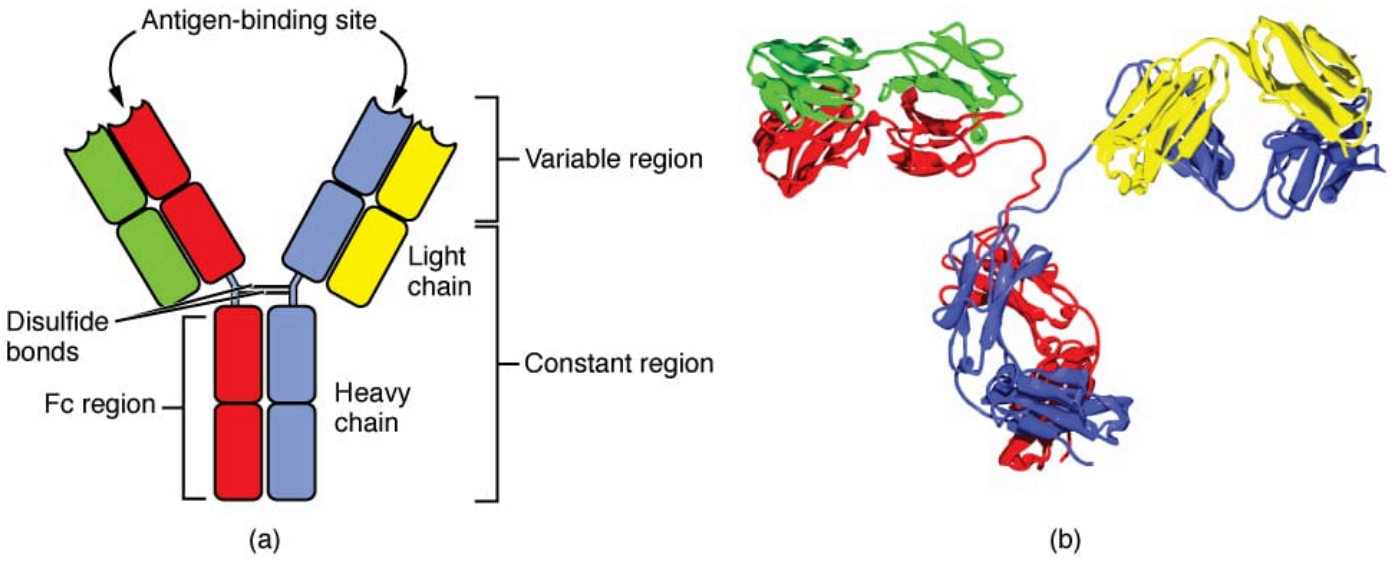
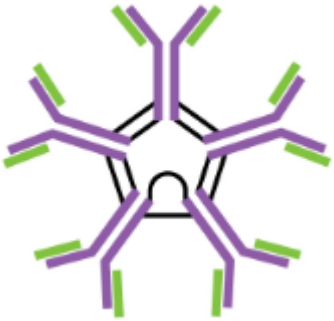
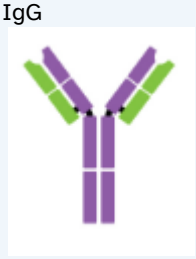
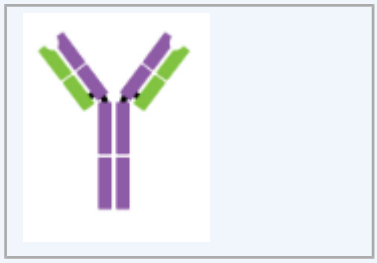


Figure 9.13.3: **Structure of an Antibody (Immunoglobulin).** (a) Diagram of the basic antibody structure showing two **heavy chains** and two **light chains** connected by **disulfide bonds**. The tips of the Y-shaped molecule form the **antigen-binding sites**, which contain variable regions that recognize specific antigens. The lower portion, called the **Fc region**, is the constant region of the antibody and helps interact with other components of the immune system. (b) Three-dimensional model of an antibody protein illustrating the folded structure of its chains and the two antigen-binding arms.

Classes of Antibodies

There are **five main classes** of antibodies, also called immunoglobulins. Each class has a slightly different role in protecting the body.

Antibody Class	Binding sites and Main Location	Main Function
IgM 	It is a pentamer with 10 binding sites Mostly in blood	First antibody produced during an infection; very effective for agglutination.

Antibody Class	Binding sites and Main Location	Main Function
IgG 	Monomer with 2 binding sites Blood and body fluids	Main blood antibody of secondary responses. Excellent at neutralization of toxins and opsonization. It can cross the placenta to protect the fetus.
 IgA	Dimer with 4 binding sites Mucus, saliva, tears, breast milk	Protects body surfaces such as the respiratory and digestive tracts from pathogens.
IgE 	Monomer with 2 binding sites Bound to mast cells	Involved in allergic reactions and defense against certain parasites.
IgD 	Monomer with 2 binding sites Surface of naïve B cells	Functions mainly as B cell receptor.

Together, these antibody classes help the immune system recognize pathogens, neutralize toxins and viruses, and mark harmful invaders so other immune cells can destroy them.

Immunological Memory

When **B cells and T cells become activated**, some of them develop into **memory cells**. These memory cells remain in the body for many years and allow the immune system to remember pathogens it has encountered before.

If the same pathogen enters the body again, the memory cells quickly recognize its **antigens** and activate a faster and stronger immune response. Because of this rapid response, the pathogen is often eliminated **before noticeable symptoms develop**. This ability to improve future responses is why the system is called **adaptive immunity**.

Immunological memory can develop in two ways:

Passive immunity
occurs when antibodies are transferred from another individual. For example, **maternal antibodies** passed from mother to baby before birth provide temporary protection to newborns. Passive immunity provides **short-term protection**, usually lasting from a few weeks to several months.

Active immunity
develops when the immune system is exposed to an antigen and produces its own memory B cells and T cells. This can occur after **natural infection** or after **vaccination (immunization)**. Active immunity provides **long-term protection**.

Although immunological memory is very effective, it is not perfect. Some pathogens **mutate and change their antigens**, allowing new strains to avoid recognition by existing memory cells. In addition, memory responses can sometimes contribute to **hypersensitivity reactions**, such as allergies or autoimmune diseases. In these cases, the immune system mistakenly attacks harmless substances or the body's own tissues, causing inflammation and tissue damage.

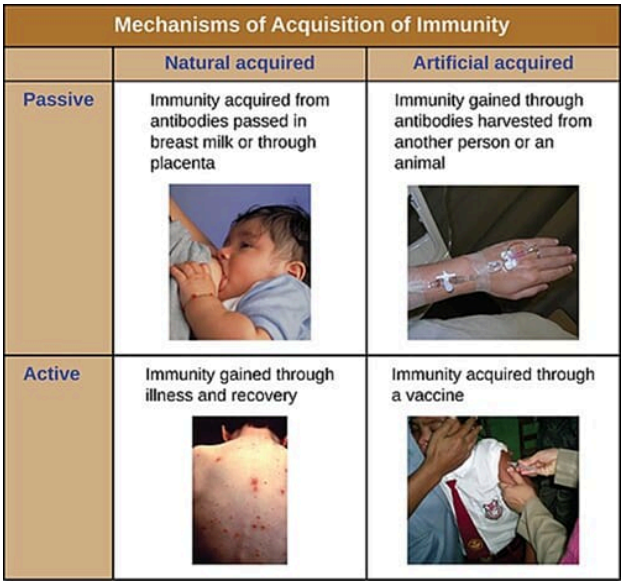


Figure 9.13.4: **Ways the body acquires immunity.** Immunity can be **passive** (receiving antibodies from another source) or **active** (producing antibodies after infection or vaccination). These forms can occur **naturally** (such as maternal antibodies or recovery from illness) or **artificially** through medical treatments like antibody



Vaccines work by exposing the immune system to a harmless form or component of a pathogen, allowing the body to produce **memory B and T cells** that can respond quickly and eliminate the pathogen if it is encountered later. That is exactly why they are so important to protect people from serious infectious diseases without requiring them to first become sick.

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9.14: Humoral Immune Response

Humoral immunity uses B cells and antibodies to recognize extracellular pathogens, eliminate them, and create immune memory for faster responses to future infections.

Master this section and you'll be able to

- Describe the role of B cells in humoral (antibody-mediated) immunity.
- Explain how B cells become activated and differentiate into plasma cells and memory B cells.
- Describe how antibodies help defend the body, including neutralization, opsonization, and agglutination.
- Compare primary and secondary immune responses and explain the role of memory B cells in faster future responses.

If the innate immune system cannot stop a pathogen, the **adaptive immune system** produces a stronger and more specific response. The adaptive immune system has two main parts: **cell-mediated immunity** and **humoral immunity**.

Humoral immunity involves **B cells and antibodies** that circulate in body fluids such as blood and lymph. The word “humoral” comes from the historical term *humors*, which referred to body fluids. In this type of immunity, **B cells produce antibodies that travel through the bloodstream and help identify and eliminate pathogens**.

Most B cells require help from **helper T cells (Th cells)** to become fully activated. Helper T cells interact with B cells and stimulate them to divide and produce many identical cells (clonal expansion). Some of these cells become **plasma cells**, which release large numbers of antibodies into the bloodstream.

Antibodies help protect the body in several ways. They can bind to pathogens and mark them for destruction by phagocytic cells (a process called **opsonization**). Antibodies can also **neutralize toxins** produced by microbes and **activate the complement system**, a group of proteins that can damage or destroy pathogen cell membranes.

B Cell Activation

B cell activation is the process by which the immune system turns a small number of specific B cells into a strong defense against a pathogen. Each B cell has receptors on its surface that recognize one specific antigen. When a B cell encounters the antigen that matches its receptor — like a key fitting into a lock — the B cell is selected for activation. This process is called **clonal selection**.

Once activated, the B cell rapidly divides to produce many identical copies of itself. This process is called **clonal expansion**. Many of these cells become **plasma cells**, which produce large amounts of antibodies. Antibodies are free-floating versions of the original B cell receptors and can bind to the same antigen to help eliminate the pathogen.

However, recognizing an antigen is usually not enough to fully activate a B cell. Most **naïve B cells** (B cells that have not yet encountered their antigen) require additional signals. These signals usually come from **helper T cells**, which assist in activating the B cell.

There are two main ways B cells can be activated:

1. **T cell–dependent activation**
   This is the most common form of B cell activation. It occurs in lymph nodes or other lymphatic tissues and requires help from helper T cells. This type of activation produces a stronger immune response and leads to the formation of **memory B cells**, which allow the immune system to respond faster if the same pathogen is encountered again.

2. **T cell–independent activation**
   In rare cases, certain antigens can activate B cells without help from helper T cells. These antigens bind directly to B cell receptors, often by **cross-linking multiple receptors** or by interacting with other receptors such as toll-like receptors. This

type of activation usually produces a weaker immune response and **does not generate memory B cells**.

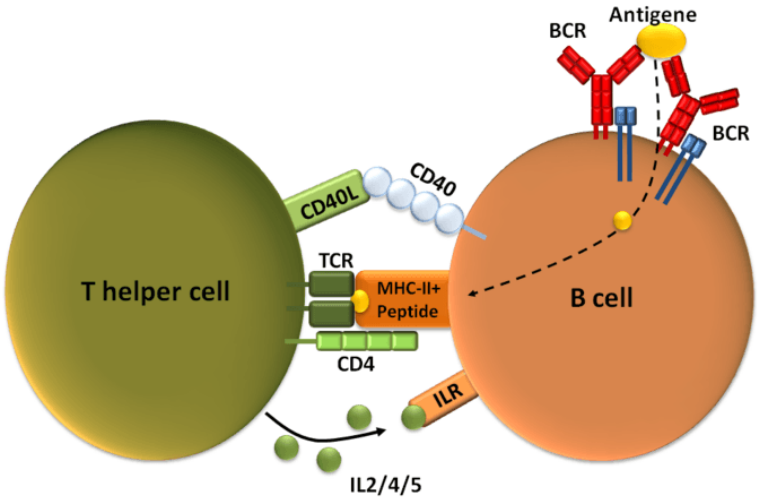


Figure 9.14.1: **T-dependent B cell activation**. T cell-dependent B cell activation, showing a T-helper cell (left), B cell (right), and several necessary interaction molecules.

Antigen-Antibody Interactions or What Antibodies Do

Different types of antibodies help protect us in several main ways. You can think of them as “tags” and “blockers” that help other parts of the immune system work better.

Neutralization

Antibodies can stick to viruses, bacteria, or toxins and block them from attaching to our cells. When they cannot attach, they cannot get in or do damage.

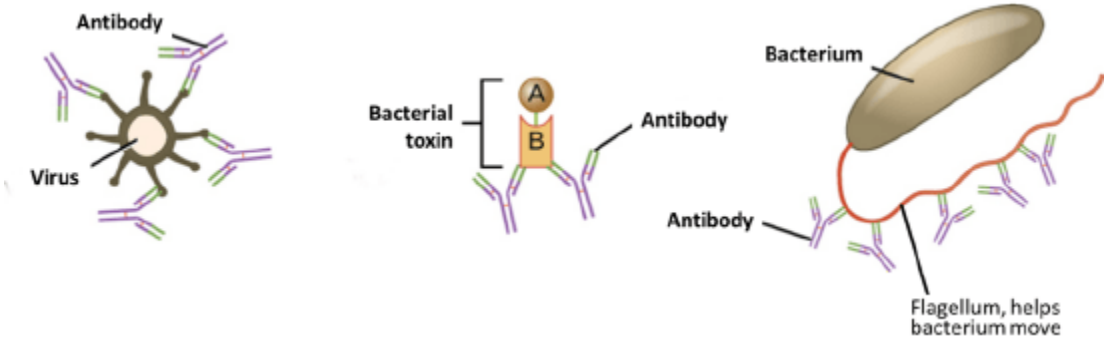


Figure 9.14.2: Neutralization involves the binding of specific antibodies to antigens found on bacteria, viruses, and toxins, preventing them from attaching to target cells.

Opsonization — Tagging for Eating

Some antibodies (especially IgG) coat or “tag” pathogens. This makes it easier for phagocytes (like macrophages and neutrophils)

to grab them and swallow them.

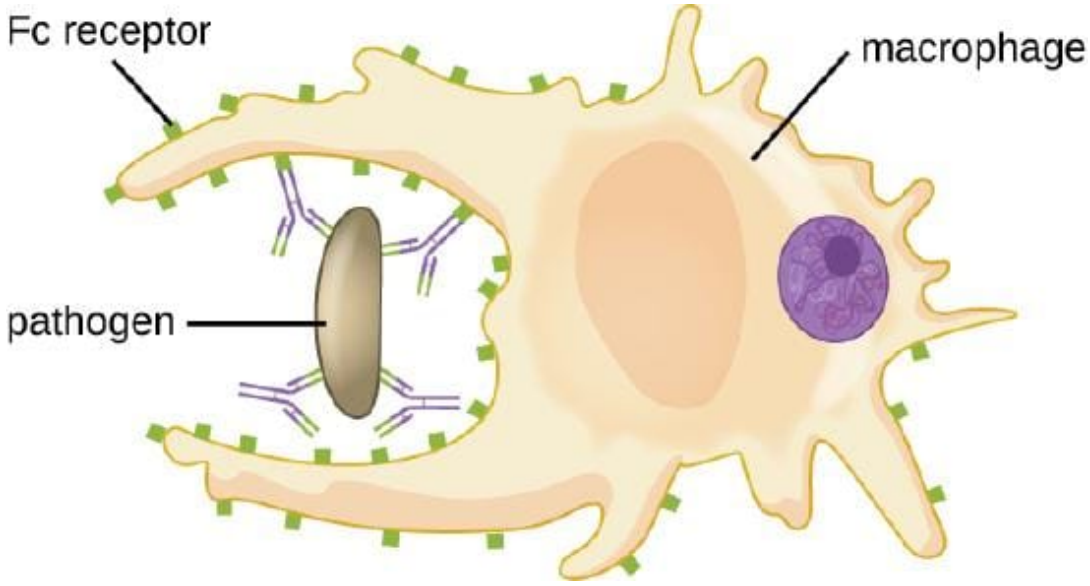


Figure 9.14.3**:** Antibodies serve as **opsonins** and inhibit infection by tagging pathogens for destruction by macrophages, dendritic cells, and neutrophils. These phagocytic cells use Fc receptors to bind to IgG-opsonized pathogens and initiate the first step of attachment before phagocytosis.

Agglutination — Clumping

Antibodies can link many pathogens together into a clump. Big clumps are easier for phagocytes to clean up and for organs like the spleen to filter out of the blood. **IgM** is especially good at this because each IgM has many binding sites (10 to be exact).

Agglutination can also occur with red blood cells (RBCs), as shown in the image below. This can happen during transfusion reactions, when the immune system reacts to incompatible blood types. You can find more details on this process on the last page of this Unit.

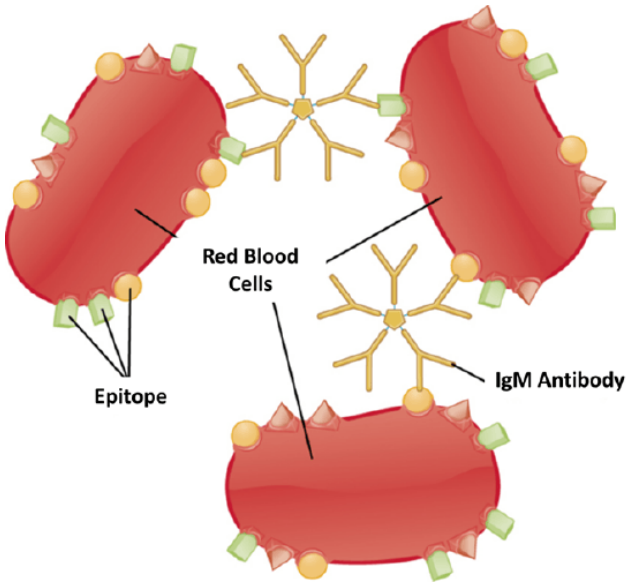


Figure 9.14.4**:** Antibodies, especially **IgM antibodies**, **agglutinate** RBCs by binding to epitopes on two or more of the RBCs

simultaneously.

Different classes of antibody play important roles in the body's defense against pathogens. These functions include neutralization of pathogens, opsonization for phagocytosis, agglutination, complement activation, and antibody-dependent cell-mediated cytotoxicity. For most of these functions, antibodies also provide an important link between adaptive specific immunity and innate nonspecific immunity.

Neutralization involves the binding of certain antibodies (IgG, IgM, or IgA) to epitopes on the surface of pathogens or toxins, preventing their attachment to cells. For example, Secretory IgA can bind to specific pathogens and block initial attachment to intestinal mucosal cells. Similarly, specific antibodies can bind to certain toxins, blocking them from attaching to target cells and thus neutralizing their toxic effects. Viruses can be neutralized and prevented from infecting a cell by the same mechanism (Figure).

Primary and Secondary Immune Responses

T cell–dependent activation of B cells is important for both the **primary** and **secondary** immune responses in adaptive immunity.

When the body is exposed to a **protein antigen for the first time**, it produces a **primary immune response**. This response begins with a **lag period** of about **10 days**, during which antibodies cannot yet be detected in the blood. This delay occurs because several steps must take place first. B cells must recognize the antigen, helper T cells must become activated, and the selected B cells must multiply and develop into antibody-producing cells.

At the end of this lag period, **plasma cells** begin producing antibodies. The first antibody that appears in the blood is **IgM**, which usually peaks about **two weeks after exposure**. Soon after, helper T cells stimulate **antibody class switching**, and B cells begin producing **IgG antibodies** instead. IgG levels continue to increase and usually reach their highest level about **three weeks after the first exposure**.

During the primary response, some of the activated B cells become **memory B cells**. These long-lived cells remain in the body and "remember" the antigen.

If the same antigen enters the body again, a **secondary immune response** occurs. This response is **much faster and stronger** than the primary response. The lag period is only a few days, and **IgG antibodies are produced in much larger amounts**. The antibodies produced during the secondary response also **bind more effectively** to the antigen. In addition, the plasma cells formed during this response live longer, so antibody levels remain elevated for a longer time.

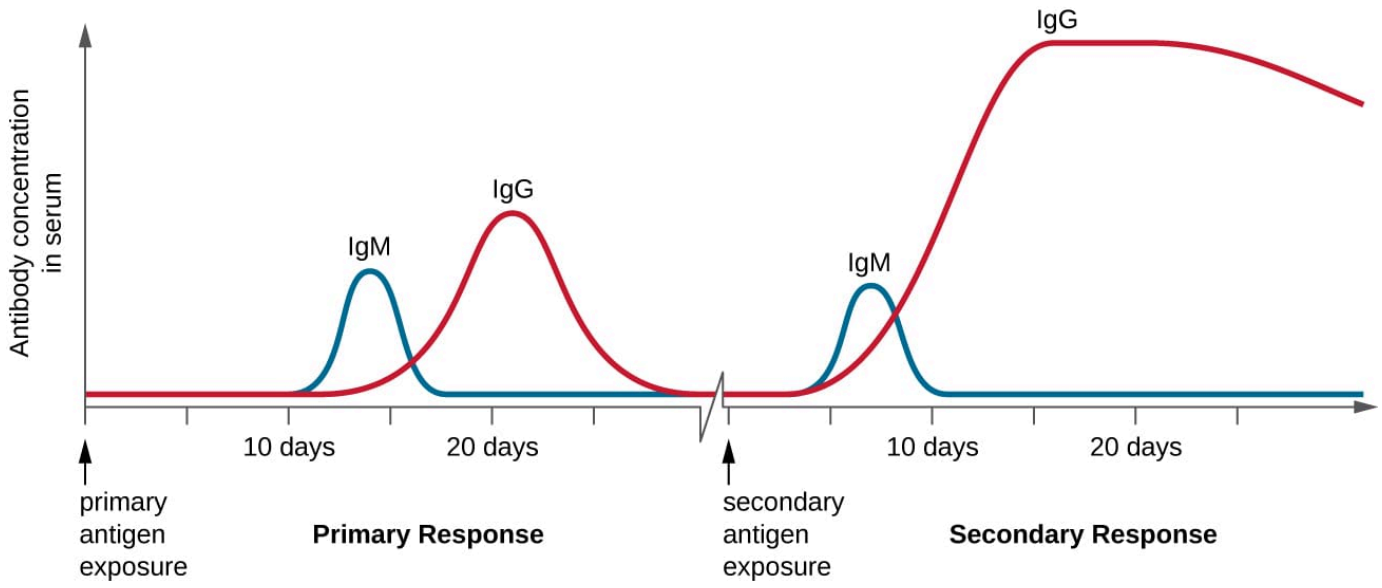


Figure 9.14.5: Primary and Secondary Responses. Compared to the primary response, the secondary antibody response

occurs much more quickly and produces antibody levels that are much higher and more sustained. The secondary response mostly involves IgG.

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9.15: Cell-Mediated Immune Response

Cell-mediated immunity uses T lymphocytes to recognize infected cells, coordinate immune responses, and destroy cells that contain pathogens.

Master this section and you'll be able to

- Explain the role of T lymphocytes in cell-mediated immunity.
- Describe how antigen presentation through MHC molecules activates T cells and leads to clonal selection and clonal expansion.
- Distinguish between helper T cells (CD4) and cytotoxic T cells (CD8) and explain their functions in the immune response.

Cell-mediated immunity is the part of the adaptive immune response that involves T lymphocytes, mainly **helper T cells (CD4 cells) and cytotoxic T cells (CD8 cells).** The term CD stands for Clusters of Differentiation, a system used to classify immune cells based on specific proteins found on their surface. These surface markers help scientists identify and distinguish between different types of immune cells.

T cells become activated in a way that is similar to B cells, but with **one important difference: T cells cannot recognize free antigens directly**. Instead, antigen-presenting cells must first capture a pathogen, break it into fragments, and display those fragments on their surface attached to major histocompatibility complex (MHC) molecules. You can think of the MHC molecule as a “silver platter” that presents the antigen fragment to the T cell. Only when the antigen is presented this way can the T cell recognize it and become activated. B cells, in contrast, can bind directly to free antigens without needing this presentation step.

When a T cell receptor matches a specific antigen fragment presented on an MHC molecule, that T cell becomes activated. This step again represents **clonal selection** (just like with the B cells), because only the T cells with receptors that fit that particular antigen are chosen to respond. Once activated, the selected T cell begins dividing rapidly by mitosis in a process you are familiar with as **clonal expansion**. Just like with the B cells, this produces many identical T cells, all carrying the same receptor and capable of recognizing the same antigen.

These cloned T cells then carry out different roles in the immune response. **Helper T cells** coordinate the immune response by activating other immune cells, including B cells and cytotoxic T cells. **Cytotoxic T cells** directly destroy infected or abnormal body cells that display the specific antigen.

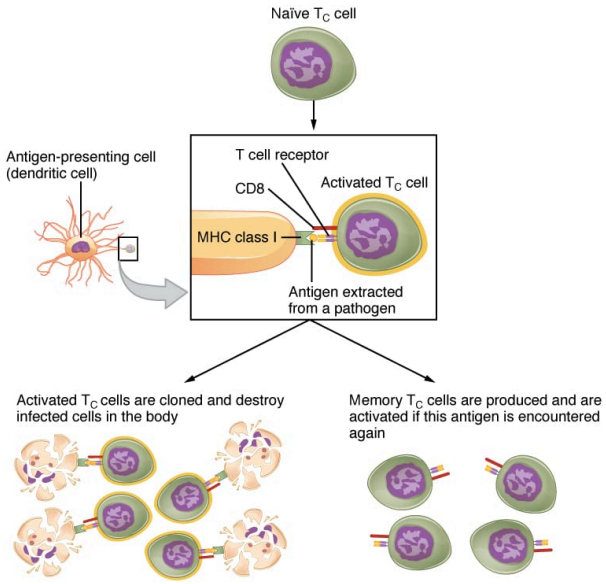


Figure 9.15.1: **Clonal Selection and Expansion of T Lymphocytes.** Stem cells differentiate into T cells with specific receptors,

called clones. The clones with receptors specific for antigens on the pathogen are selected for and expanded.

T Cell Types and their Functions

As stated above, mature T cells **display either the CD4 marker or the CD8 marker on their surface**, but not both. These CD markers also help T cells interact with antigen-presenting cells. The CD4 or CD8 molecule attaches to the MHC molecule on the antigen-presenting cell, while the T cell receptor binds to the antigen fragment that is displayed by the MHC molecule. In this way, the T cell and the antigen-presenting cell are held together at two points: the CD marker binds to the MHC molecule, and the T cell receptor binds to the antigen.

CD4 is typically found on helper T cells. These cells recognize antigens presented on MHC class II molecules and help coordinate the immune response by activating other immune cells, including B cells and cytotoxic T cells.

CD8 is found on cytotoxic T cells. These cells recognize antigens presented on MHC class I molecules and destroy infected or abnormal body cells.

Although the relationship is not absolutely perfect, CD4 T cells are generally associated with helper functions, while CD8 T cells are associated with cytotoxic functions.

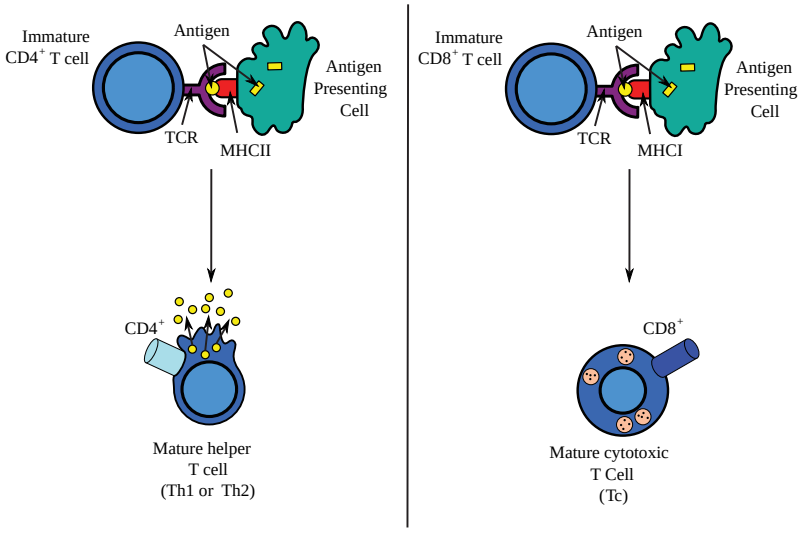


Figure 9.15.2: **Activation of Helper and Cytotoxic T Cells.** APCs display fragments of pathogens (epitopes) on their surface using major histocompatibility complex (MHC) molecules. On the left, a **naïve CD4 T cell** recognizes an antigen presented on an MHC II molecule through its T-cell receptor (TCR). This interaction activates the T cell and leads to the formation of a mature helper T cell (Th), which releases signaling molecules (cytokines) that coordinate the immune response. On the right, an **naïve CD8 T cell** recognizes an antigen presented on an MHC I molecule. After activation, it becomes a mature cytotoxic T cell (Tc), which can destroy infected or abnormal cells that display the same antigen.

Helper T Cells and their Cytokines

Helper T cells (Th cells) carry the **CD4 marker** and help coordinate the immune response by releasing **signaling molecules called cytokines**. These cytokines stimulate and guide the activity of other immune cells.

There are two main types of helper T cells:

Th1 cells mainly activate macrophages and support other T cells. They help strengthen the cell-mediated immune response that

destroys infected cells.

Th2 cells mainly interact with B cells. They stimulate B cells to divide and develop into plasma cells that produce antibodies. For most protein antigens, B cells need help from Th2 cells in order to produce large amounts of antibodies.

Cytotoxic T cells

Cytotoxic T cells (Tc cells or CD8 cells) are T cells that **kill infected or abnormal body cells**. They do this by releasing special molecules, such as **perforins and granzymes**, that trigger the target cell to undergo **apoptosis (programmed cell death)**.

This is especially important during **viral infections**. By destroying infected cells before the virus can finish replicating, cytotoxic T cells help prevent the virus from spreading. Each cytotoxic T cell can kill **multiple infected cells**, making them a powerful defense against viral diseases.

As more Tc cells are developed during an immune response, they overwhelm the ability of the virus to cause disease. In addition, each Tc cell can kill more than one target cell, making them especially effective. In fact, Tc cells are so important in the antiviral immune response that some scientists speculate that this was the main reason the adaptive immune response evolved in the first place.

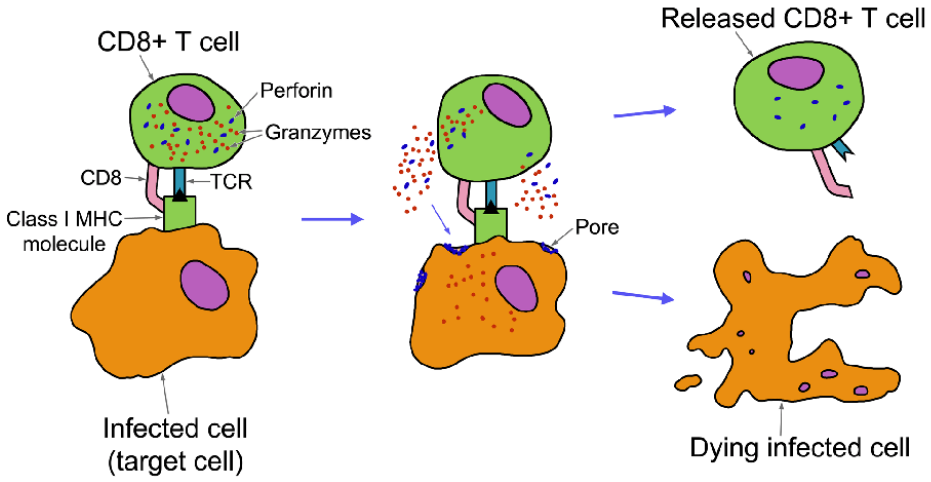


Figure 9.15.3: **Cytotoxic T Cell Killing of an Infected Cell.** A CD8 cytotoxic T cell recognizes an infected target cell when its T-cell receptor (TCR) binds to a foreign antigen displayed on an MHC class I molecule on the surface of the infected cell. After binding, the cytotoxic T cell releases toxic proteins called **perforin** and **granzymes**. Perforin forms pores in the target cell membrane, allowing granzymes to enter the cell. These molecules trigger processes that lead to the death of the infected cell. After delivering these molecules, the cytotoxic T cell detaches and can move on to attack other infected cells.

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9.16: Immune Dysfunction and Clinical Connections

Overview of how vaccines protect against disease and how immune system dysfunction can lead to immunodeficiency, autoimmune disorders, and allergic hypersensitivity reactions.

Master this section and you'll be able to

- Explain how vaccines protect against disease and describe the concept of herd immunity.
- Identify the three major types of immune system disorders: immunodeficiency, autoimmune disease, and hypersensitivity.
- Describe how HIV affects the immune system.
- Explain the basic mechanisms of autoimmune diseases and allergic reactions.

Vaccines: Preparing the Immune System for Future Battles

Vaccination helps protect people from communicable diseases by building immunity **before a person is exposed to the actual pathogen**. Vaccines work by exposing the immune system to a **weakened or harmless form of a pathogen**, or to specific molecules from the pathogen called **antigens**. This exposure allows the immune system to learn to recognize the pathogen and produce **memory B cells and T cells**. If the real pathogen enters the body later, these memory cells can respond quickly and often stop the infection before it causes serious illness.

Vaccination has been one of the **most effective public health tools in history**, preventing millions of deaths worldwide. Diseases such as **smallpox, polio, measles, and whooping cough** were once common causes of severe illness and death, but vaccination programs have dramatically reduced their spread.

Vaccines are highly effective, but they are **not perfect**. A small percentage of vaccinated people may still become infected, and some individuals cannot receive certain vaccines. This includes people with **weakened immune systems**, such as those undergoing cancer treatment, people with certain immune disorders, or very young infants who are not yet eligible for vaccination.

Because of this, protection also depends on **herd immunity**. Herd immunity occurs when a large portion of the population is immune to a disease, either through vaccination or previous infection. When enough people are immune, the pathogen has fewer opportunities to spread, which helps protect individuals who cannot be vaccinated. The percentage of immune individuals needed for herd immunity depends on how contagious the disease is. For example, **measles is extremely infectious**, so about **95% of the population must be immune** to prevent outbreaks.

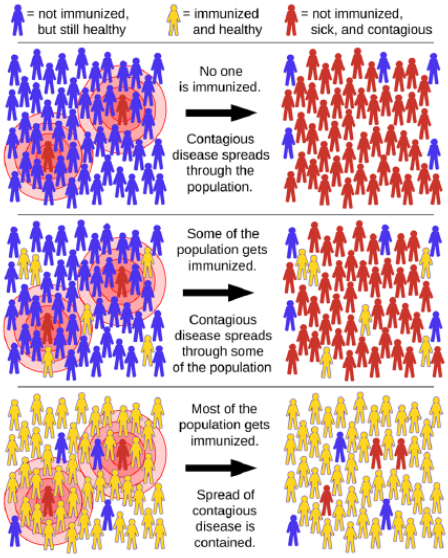


Figure 9.16.1: **Herd Immunity and Disease Spread.** When few people are vaccinated, contagious diseases spread easily through the population. As more individuals become immunized, transmission slows, and when most people are immune, the spread of the disease is largely contained, protecting even those who are not vaccinated.

In recent years, vaccine hesitancy has increased in some communities. Some people worry about possible side effects and may fear the risks of vaccination more than the diseases vaccines prevent. Like any medication or medical procedure, vaccines can cause side effects, but **most reactions are mild**, such as temporary soreness at the injection site or a low fever. Serious reactions are **very rare**. Some concerns are also based on misinformation. For example, the widely circulated claim that vaccines cause **autism** has been carefully studied and **repeatedly disproven by large scientific studies**.

When vaccination rates decline, diseases that were once under control can return. In recent years, several countries (including the US) have experienced outbreaks of **measles, whooping cough (pertussis), and other preventable diseases**. During the **COVID-19 pandemic**, many routine medical visits and childhood vaccinations were delayed, which contributed to lower vaccination coverage in some populations.

Overall, maintaining high vaccination rates helps protect **both individuals and communities**, making vaccines an essential part of modern public health.

The Three Major Types of Immune System Disorders

1) Immunodeficiency

If the immune system does not work properly, pathogens or abnormal cells can multiply and cause disease. This condition is called **immunodeficiency**. Immunodeficiency can be **inherited (present at birth)** or **acquired later in life**.

Acquired immunodeficiency can occur for several reasons, including **infection with certain pathogens (such as HIV), exposure to radiation or chemicals, malnutrition, medical treatments like chemotherapy, or extreme stress**. For example, radiation can destroy **lymphocytes**, which weakens the body's ability to fight infections and cancer.

Some people are born with **genetic disorders that affect the immune system**. One example is **Severe Combined Immunodeficiency (SCID)**, a condition in which important immune cells do not function properly. Another example is **neutropenia**, in which the body produces too few **neutrophils**, the most common type of phagocytic white blood cell. Without enough neutrophils, bacteria can spread more easily in the bloodstream and cause serious infections.

HIV and AIDS

Human Immunodeficiency Virus (HIV) is a virus that attacks the immune system. HIV mainly infects and destroys certain immune cells, especially **helper T cells (CD4 cells)**, which are important for coordinating immune responses.

Shortly after infection, a person may experience **flu-like symptoms**, such as fever, fatigue, and swollen lymph nodes. After this early stage, the infection may remain **without obvious symptoms for many years** while the virus slowly damages the immune system.

As the immune system becomes weaker, the body becomes more vulnerable to **opportunistic infections and certain cancers** that usually do not affect people with healthy immune systems. The most advanced stage of HIV infection is called **Acquired Immunodeficiency Syndrome (AIDS)**.

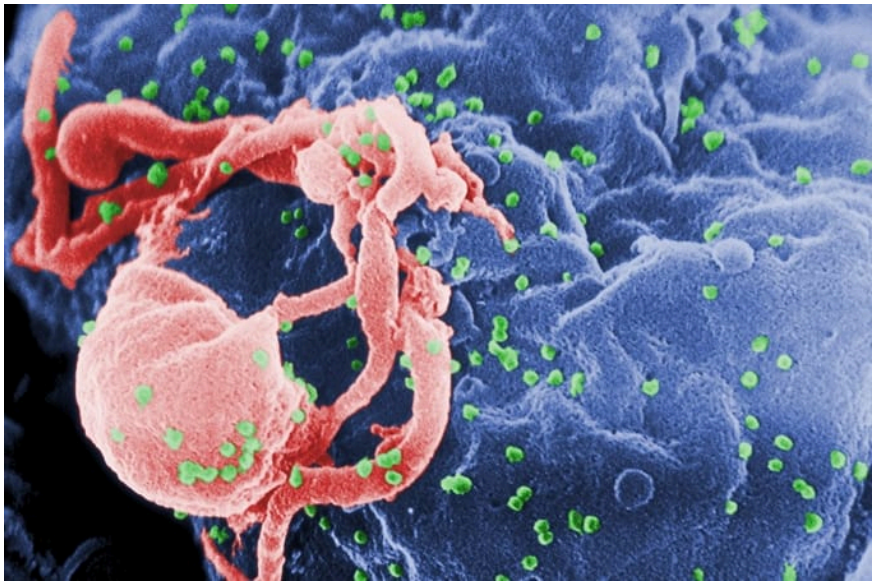


Figure 9.16.2: **Image of HIV.** Scanning electron micrograph of HIV-1 budding (in green, color added) from cultured lymphocyte. Multiple round bumps on cell surface represent sites of assembly and budding of HIV. During primary infection, the level of HIV may reach several million virus particles per milliliter of blood.

After **HIV enters the body**, the virus begins to multiply rapidly. During this early stage of infection, called the **acute phase**, large amounts of the virus circulate in the bloodstream. At the same time, the number of **CD4 T cells (helper T cells)** drops sharply. These cells are important because they help coordinate many immune responses.

The immune system responds by activating **cytotoxic T cells**, which kill cells infected with HIV. The surviving helper T cells start to produce **antibodies** against the virus. These responses can temporarily reduce the amount of virus in the blood and allow helper T cell levels to partially recover.

Over time, however, HIV continues to damage and destroy helper T cells. Because these cells are essential for coordinating immune defenses, their gradual loss weakens the immune system. As the number of CD4 T cells declines, the body becomes increasingly vulnerable to **opportunistic infections and certain cancers** that normally would not affect people with healthy immune systems.

2) Autoimmune Diseases

Autoimmune diseases occur when the immune system mistakenly attacks the body's own tissues. Normally, the immune system can distinguish between **"self" (the body's own cells)** and **"non-self" (pathogens)**. In autoimmune diseases, this recognition system fails, and the immune system treats parts of the body as if they were harmful invaders.

Although many individual autoimmune diseases are relatively rare, together they affect **millions of people**. It is estimated that about **5–8% of the U.S. population** has some form of autoimmune disease. Examples include **type 1 diabetes, multiple**

sclerosis, rheumatoid arthritis, and lupus.

Causes of Autoimmune Diseases

Scientists believe that autoimmune diseases are caused by a **combination of genetic and environmental factors**.

Some people inherit **genes that increase their risk** of developing autoimmune disorders. However, having these genes does not guarantee that a person will develop the disease. Studies of identical twins show that genetics explains only **about 25–40% of the risk**, meaning that environmental factors also play a major role.

Possible environmental triggers include:

- certain **infections** caused by bacteria or viruses
- **toxic chemicals** or pollutants
- **hormonal changes**
- **ultraviolet (UV) radiation** or other environmental exposures

Researchers are still working to understand exactly how these factors trigger autoimmune responses.

Treatment

Most treatments for autoimmune diseases focus on **reducing immune system activity**. These treatments often involve **immunosuppressive medications**, which help decrease the immune system's attack on the body's own tissues and reduce inflammation and symptoms.

3) Allergies — Hypersensitivity Reactions

An **allergy** is a hypersensitivity reaction in which the immune system responds to substances that are normally harmless. These substances are called **allergens** and may include things such as pollen, certain foods, insect venom, or medications.

Allergic reactions occur when the immune system produces a type of antibody called **Immunoglobulin E (IgE)**. These antibodies trigger **mast cells and basophils** to release chemicals such as **histamine**, which cause inflammation and the typical symptoms of an allergic reaction.

Common allergy symptoms include **itchy eyes, sneezing, runny nose, hives, or skin rashes**. Allergies can also contribute to conditions such as **asthma**. In some cases, allergies can cause a severe and potentially life-threatening reaction called **anaphylaxis**, which may occur after exposure to certain foods, medications, or insect stings.

Causes and Risk Factors

Allergies develop due to a combination of **genetic and environmental factors**. People with a family history of allergies are more likely to develop them. Environmental factors may also play a role, including exposure to allergens, pollution, infections early in life, and changes in diet.

Allergy Testing

Doctors can diagnose allergies using several types of tests. **Blood tests** can measure levels of allergen-specific IgE antibodies. Another common method is a **skin allergy test**, in which a very small amount of a suspected allergen is placed on or just under the skin. If the person is allergic, the area may become **red, swollen, or itchy**, indicating a hypersensitivity reaction.



Figure 9.16.3: **Skin allergy test (skin prick test).** In an intradermal allergy test, small amounts of potential allergens are introduced into the skin using tiny pricks. Areas that become red and swollen indicate an allergic reaction, helping doctors identify which substances trigger the patient's allergies.

Treatment

Treatment usually focuses on **avoiding known allergens** and reducing symptoms. Medications such as **antihistamines, decongestants, or corticosteroids** are often used to control allergic reactions. In severe cases, **epinephrine injections** are used to treat anaphylaxis. Some patients may also receive **immunotherapy**, in which small amounts of allergens are given over time to gradually reduce the immune system's sensitivity.

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9.17: Blood Types and Transfusions

Blood typing and transfusion safety depend on the interaction between antigens and antibodies.

Master this section and you'll be able to

- Explain how antigens and antibodies help the body recognize self and non-self.
- Describe how the ABO and Rh systems determine blood type and compatibility.
- Discuss why blood typing and cross-matching are essential for safe transfusions.

Antigens and Antibodies: How the Body Recognizes “Self” and “Non-Self”

Your immune system is constantly on the lookout for anything that does not belong in your body. To tell friend from foe, it relies on tiny molecular markers called **antigens**. An antigen is any molecule — most often a **protein** or carbohydrate attached to a protein — that can trigger an immune response. These markers are found on the surface of all cells, bacteria, and viruses, and the immune system can usually tell whether they belong to the body (“self”) or are foreign (“non-self”).

When the immune system detects an unfamiliar antigen, it responds by making special proteins called **antibodies**. These Y-shaped antibodies specifically recognize and bind to that antigen, marking it for destruction or neutralization. Each antibody fits its matching antigen like a lock and key, allowing the immune system to target invaders with great precision.

The antigen–antibody system is the foundation of immune defense and is also key to understanding many biological processes — including how **blood typing and transfusions** work, which you will explore next.

Antigens and Antibodies: The Key to Blood Typing and Transfusions

As mentioned above, every person’s red blood cells (RBCs) carry such specific surface markers called **antigens**. They act like “ID tags” that the immune system recognizes as belonging to the body. If a person receives blood containing unfamiliar antigens, the immune system sees them as **foreign** and attacks them using **antibodies** — also known as "**immunoglobulins**", these specialized proteins that circulate in the plasma and bind to their specific antigens.

In blood typing, we identify which antigens are present on a person's RBCs. Although red blood cells carry hundreds of different antigens, **only the ABO and Rh systems are routinely tested** because they are the most likely to trigger strong immune reactions during transfusion. Antibodies against A, B, or Rh antigens form naturally or easily after exposure to mismatched blood, leading to rapid and dangerous **clumping** (**agglutination**) of the RBCs. In contrast, antibodies to most other RBC antigens develop only after repeated transfusions or pregnancy, so they are screened for only when a patient has a history that increases that risk.

The ABO Blood Group System

If an individual is exposed to a blood group antigen (A or B) that is not recognized as self, the individual can become sensitized to that antigen. This will cause the immune system to make specific antibodies to a particular blood group antigen and form an **immunological memory** against that antigen. These antibodies can bind to antigens on the surface of transfused red blood cells (or other foreign tissue cells), often leading to destruction of the cells via recruitment of other components of the immune system.

Knowing a person’s blood type is essential for matching compatible blood for transfusions or organ transplants. The four main blood types — A, B, AB, and O — differ according to which **antigens** are present on the surface of the red blood cells and which **antibodies** circulate in the plasma.

Interestingly, in the **ABO system**, antibodies are **naturally present** in the plasma **from birth or early infancy** without prior exposure to other blood types. This happens because harmless bacteria in the digestive tract have surface molecules that resemble A and B antigens, prompting the immune system to make anti-A or anti-B antibodies automatically.

- Example: A person with type A blood has **anti-B antibodies** even if they have never received a transfusion.
- This is why a transfusion mismatch (like giving type B blood to a type A person) triggers an **immediate and severe reaction**—the antibodies are already there, ready to attack.

The antigen determines which blood types a person can **donate to**, while the antibody determines which types of blood their immune system will **reject** as foreign.

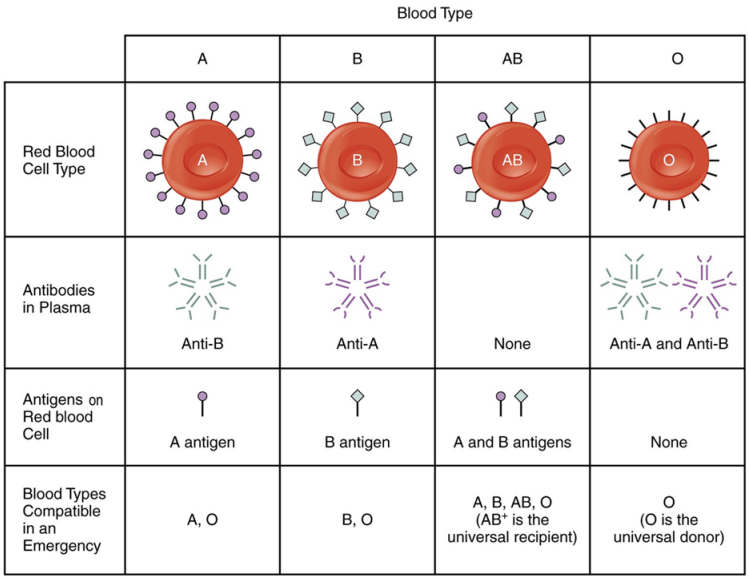


Figure 9.17.1: **Blood Type Classification.** Blood type (or blood group) is determined, in part, by the ABO blood group antigens present on RBCs.

- **Blood group A** individuals have the A antigen on the surface of their RBCs, and blood serum contains antibodies against the B antigen. Therefore, a group A individual can only receive blood from individuals of groups A or O types, and can donate blood to individuals of groups A or AB.
- **Blood group B** individuals have the B antigen on the surface of their RBCs, and blood serum containing antibodies against the A antigen. Therefore, a group B individual can only receive blood from individuals of groups B or O, and can donate blood to individuals of groups B or AB.
- **Blood Group AB** individuals have both A and B antigens on the surface of their RBCs, and their blood serum does not contain any antibodies against either A or B antigen. Therefore, an individual with type AB blood can receive blood from any group, but can only donate blood to another group AB individual. AB blood is also known as "**universal receiver**."
- **Blood group O** individuals do not have either A or B antigens on the surface of their RBCs, but their blood serum contains IgM antibodies against both A and B antigens. Therefore, a group O individual can only receive blood from a group O individual, but they can donate blood to individuals of any ABO blood group (i.e. A, B, O, or AB). O blood is also known as "**universal donor.**"

Blood types are inherited and represent genetic contributions from both parents. The gene that codes for blood type contains three alelles: IA and IB which give type A and B blood and are dominant, and i, which is recessive and codes type O. Children will have blood types similar to their parents based on inheritance. The i allele is far more commonly expressed in the gene pool than IA and IB, which is why type O blood is the most common type despite being a recessive phenotype. Type AB is the rarest because it is the combination of less commonly expressed alleles, and is the result of codominance between IA and IB alelles.

	Rh+	Rh-
Red Blood Cells		
Antigens		N/A
Antibodies	N/A	

Rhesus Factor

In addition to the ABO system, another important antigen called the **Rh factor** is either present (**Rh-positive**) or absent (**Rh-negative**) on the red blood cells. The **Rh factor** gets its name from the **Rhesus monkey**, in which it was first studied in the 1940s. Scientists then discovered a similar antigen on human red blood cells, calling it the **Rhesus D antigen**, often shortened to the **Rh(D) antigen.**

Together, the ABO and Rh systems form the familiar blood type labels such as A+, O–, or AB+.

In contrast to the antibodies in the ABO system, in the **Rh system**, people **do not naturally have anti-Rh antibodies**. These antibodies form **only after exposure** to Rh-positive blood, such as during a mismatched transfusion or pregnancy (when an Rh-negative mother carries an Rh-positive fetus).

- The **first exposure** usually causes no major problem because it simply "teaches" the immune system to recognize the Rh antigen.
- On **later exposures**, however, the newly made anti-Rh antibodies can attack Rh-positive red cells, leading to a dangerous immune reaction.

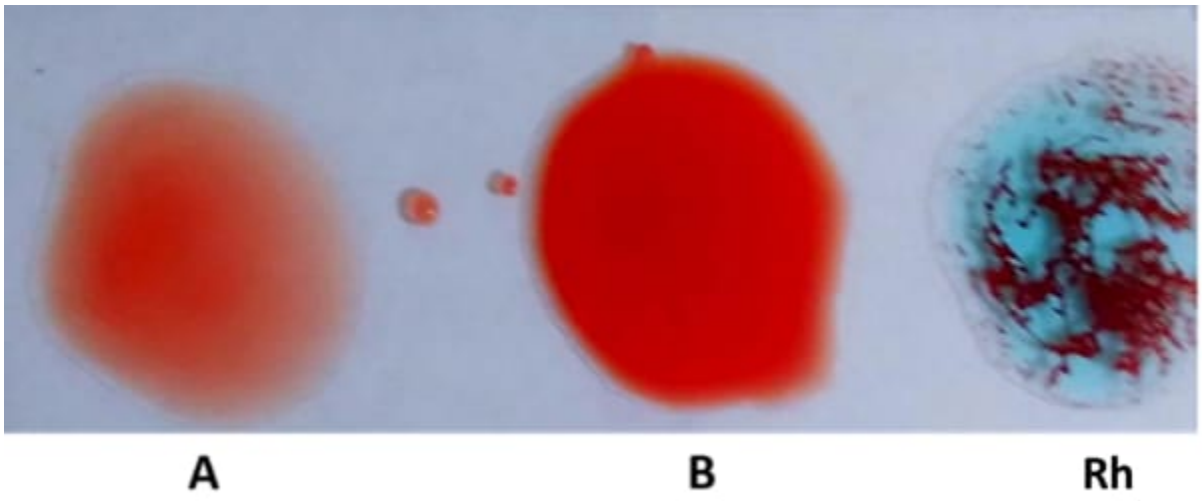


Figure 9.17.2: **Blood Typing Test Showing Agglutination with Anti-Rh Serum.**
This image shows a blood typing test using three antibody solutions: anti-A, anti-B, and anti-Rh (from left to right). Only the anti-Rh sample on the right shows visible clumping, or *agglutination*, indicating that this blood sample is **Rh-positive**. The absence

of clumping in the anti-A and anti-B wells means the sample lacks both A and B antigens, so the blood type is **O positive (O⊕)**.

Blood Transfusions

Transfusion medicine is extremely effective at treating those with severe blood loss. Transfusions are often a required component of major surgeries. Due to the different antigen blood types, blood must be cross-matched during processing to avoid potential complications, such as hemolytic reaction, renal failure, and death.

The Cross-Matching Process

Much of the routine work in a blood bank involves testing both donor and recipient blood to ensure that each patient receives blood that is compatible and safe. Several laboratory tests are used to **cross-match** donor and recipient samples, checking for any potential reaction between the two.

Ideally, patients receive their own blood or **type-specific** blood products to minimize the risk of a transfusion reaction. Cross-matching further reduces this risk, but in emergencies — when time is limited or the need for transfusion is unexpected — it may not always be possible to perform this testing in advance.

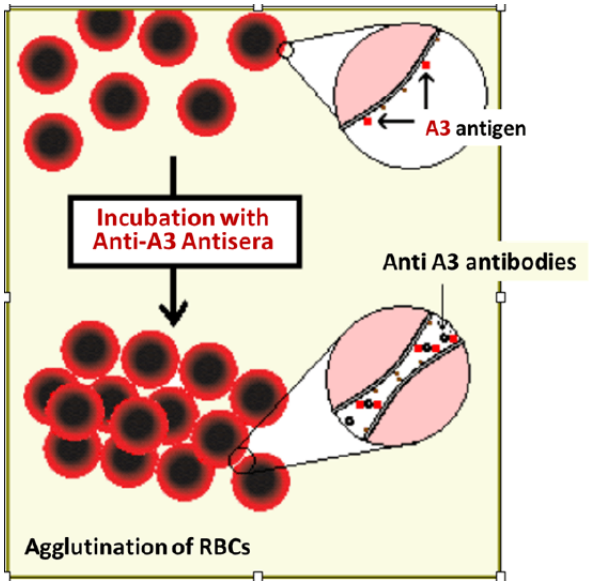


Figure 9.17.3: **Agglutinated RBC in Cross-Matching Test.** Red blood cells can agglutinate if the serum contains antibodies against the expressed surface antigen proteins. In this image, the blood serum contains anti-A3 antibodies, which attack and agglutinate type A blood.

Cross-matching involves mixing a sample of the recipient's serum with a sample of the donor's red blood cells and checking if the mixture agglutinates, or forms clumps. These clumps are the result of antibodies binding the red blood cells together. If agglutination is not obvious by direct vision, blood bank technicians check for agglutination with a microscope. If agglutination occurs, that particular donor's blood cannot be transfused to that particular recipient. In a blood bank, it is vital that all blood specimens are correctly identified, so labeling has been standardized using a barcode system known as ISBT 128. The blood group may be included on identification by military personnel in case they need an emergency blood transfusion.

If a patient receives blood during a transfusion that is not compatible with his or her blood type, severe problems can occur. **Acute hemolytic transfusion reactions** occur if donated blood cells are attacked by matching host antibodies. This can cause **shock-like symptoms, such as fever, hypotension, and disseminated intravascular coagulation** from immune system mediated endothelial damage. Transfusion reactions are also associated with **acute renal failure**. **Lung injury** is common as well, due to pulmonary edema from fluid overload if plasma volume becomes too high or neutrophil activation during a transfusion reaction. If the donated blood is contaminated with bacteria, it may induce septic shock in the patient.

Key Terms

- **antibodies**: Also known as an immunoglobulin (Ig), a large Y-shaped protein produced by B-cells that is used by the immune system to identify and neutralize foreign objects such as bacteria and viruses.
- **antigen**: A substance that induces an immune response, usually foreign.
- **hemolysis**: The destruction of red blood cells from pathological causes, such as infection or immune system mediated damage.
- **agglutinate**: The act of red blood cells clumping together due to antibody reactivity.

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10: CARDIOVASCULAR SYSTEM

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10.2: Heart Anatomy — Overview
10.3: Pericardium and the Heart Wall
10.4: Heart Anatomy - Details
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10.1: Overview of the Cardiovascular System

The cardiovascular system is the body's transport network, tirelessly moving blood through a closed circuit of vessels to deliver oxygen and nutrients to every cell while carrying away waste products like carbon dioxide. At its center is the heart, a muscular pump that beats over 100,000 times a day, propelling blood through arteries to the tissues and then back through veins to be reoxygenated in the lungs. Together, the heart and blood vessels maintain the continuous circulation that keeps organs functioning and the body in balance.

There are two distinct but linked circuits in the human blood circulation called the pulmonary and systemic circuits. Although both circuits transport blood and everything it carries, we can initially view the circuits from the point of view of gases. The **pulmonary circuit** transports blood to and from the lungs, where it picks up oxygen and delivers carbon dioxide for exhalation. The **systemic circuit** transports **oxygenated blood** to virtually all of the tissues of the body and returns relatively deoxygenated blood and carbon dioxide to the heart to be sent back to the pulmonary circulation.

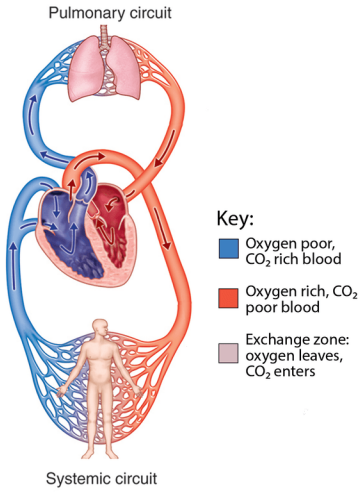
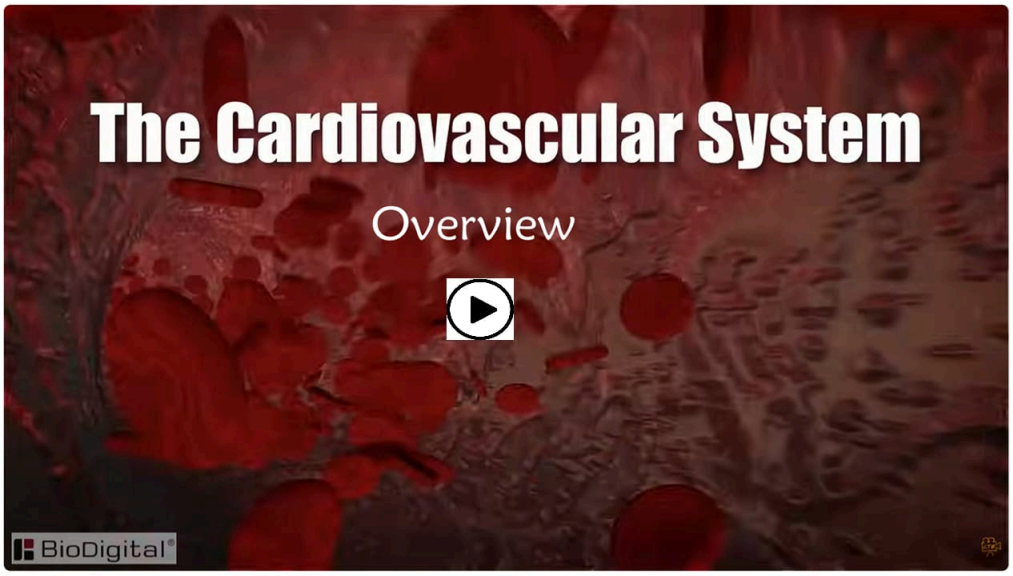


Figure 10.1.1: **Cardiovascular System Circuits.** The pulmonary circuit moves blood from the right side of the heart to the lungs and back to the heart. The systemic circuit moves blood from the left side of the heart to the head and body and returns it to the right side of the heart to repeat the cycle. The arrows indicate the direction of blood flow, and the colors show the relative levels of oxygen concentration. (Caption from OpenStax) *(Image Credit: "Systemic and Pulmonary Circuits" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Open Learning Initiative.)*

Beyond simple **transport**, the cardiovascular system plays an essential role in maintaining homeostasis. It has a vital role in regulating **body temperature**, **pH**, and **fluid balance**, and provides a **rapid communication pathway for hormones and immune cells.** When functioning properly, it adapts instantly to changes in activity, such as increasing cardiac output during exercise or conserving blood flow during rest. Because every organ depends on this system, understanding how it works — and what happens when it fails — is crucial to understanding human health and disease.

Cardiovascular Overview



Watch this video

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10.2: Heart Anatomy — Overview

The heart is a muscular double pump within the thoracic cavity that drives blood through two circuits — pulmonary and systemic.

Master this section and you'll be able to

- Describe the heart's location within the thoracic cavity.
- Describe the basic anatomy of the heart.
- Explain how the heart functions as a double pump.

You are about to explore the remarkable pump that propels the blood into and through the vessels. The heart functions as a "**double pump**," since its contraction develops the pressure that ejects blood into the major vessels for two separate circuits of blood flow: blood from the left side of the heart flows into the aorta for the **systemic circuit** and blood from the right side of the heart flows into the pulmonary trunk for the **pulmonary circuit**. From these vessels, blood is distributed to the remainder of the body. Although the connotation of the term "pump" suggests a mechanical device made of steel and plastic, the anatomical structure is a living, sophisticated muscle. As you read on, try to keep these twin concepts in mind: pump and muscle.

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

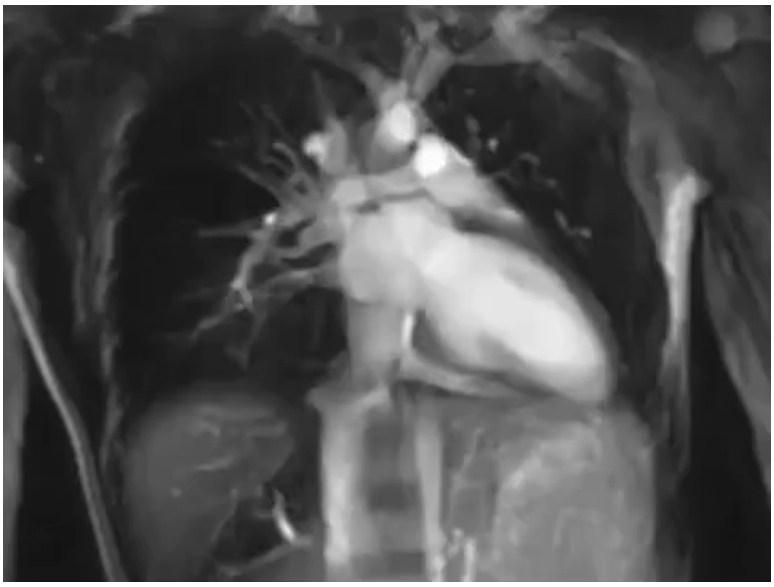


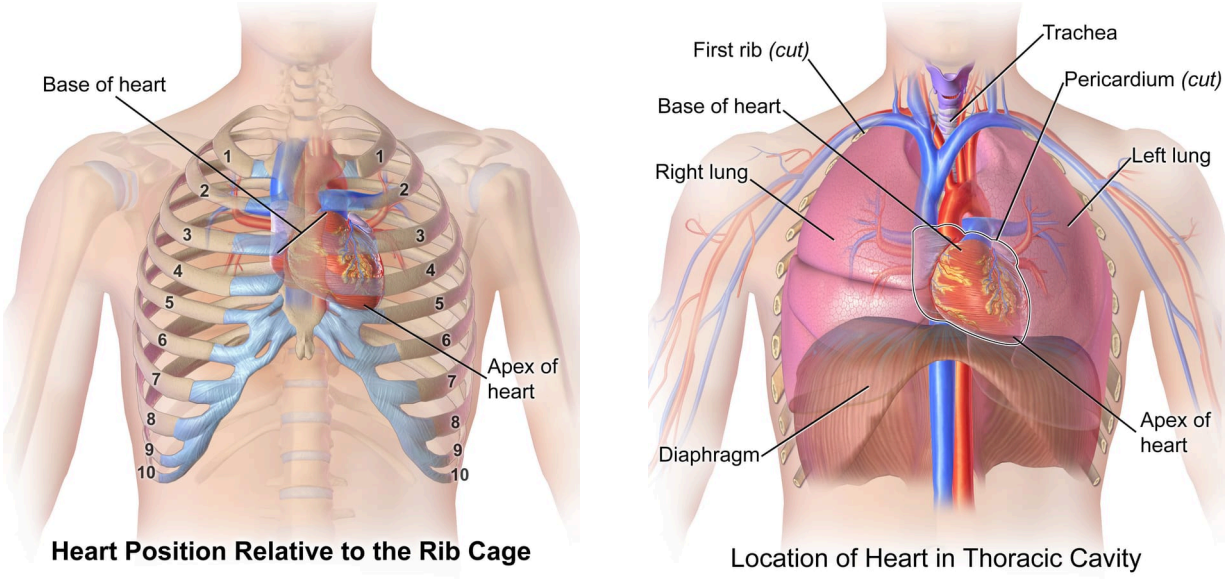
Figure 10.2.1: **Human Heart.** The real-time heartbeat of an adolescent human female visualized with Magnetic Resonance Imaging (MRI). (Image credit: "Heart MRI" by Alith3204 is licensed under CC BY-SA 4.0, via Wikimedia Commons)The human heart is the pump for the circulatory system, and along with the circulatory system is considered to be an organ of the cardiovascular system. It consists of four chambers and pumps blood through both systemic and pulmonary circulation to enable gas exchange and tissue oxygenation. The heart is located in the thoracic cavity between the lungs and protected by the rib cage.

Location of the Heart

The human heart is located within the thoracic cavity, medially between the lungs in the region known as the **mediastinum**. The mediastinum also includes the portions of the major blood vessels, the trachea, and the esophagus that are positioned between the lungs medially. Within the mediastinum, the heart is separated from the other mediastinal structures and is held in place by a tough wrapping known as the pericardium, or pericardial sac. The sac also limits the range of motion of the heart as it beats. The double layered pericardial sac creates a thin space surrounding the heart called the **pericardial cavity** that is filled with serous fluid to prevent friction as the heart beats.

The dorsal surface of the heart lies near the bodies of the vertebrae and its anterior surface sits deep to the sternum and costal cartilages. The great veins, the superior and inferior venae cavae, and the great arteries, the aorta and pulmonary trunk, are attached to the superior surface of the heart, called the **base**. The inferior tip of the heart, the **apex**, lies just to the left of the sternum between the junction of the fourth and fifth ribs.

The heart is also rotated slightly around its vertical axis such that more of the right side of the heart is visible in an anterior view while more of the left side is visible in a posterior view. There is a slight deviation of the apex to the left.



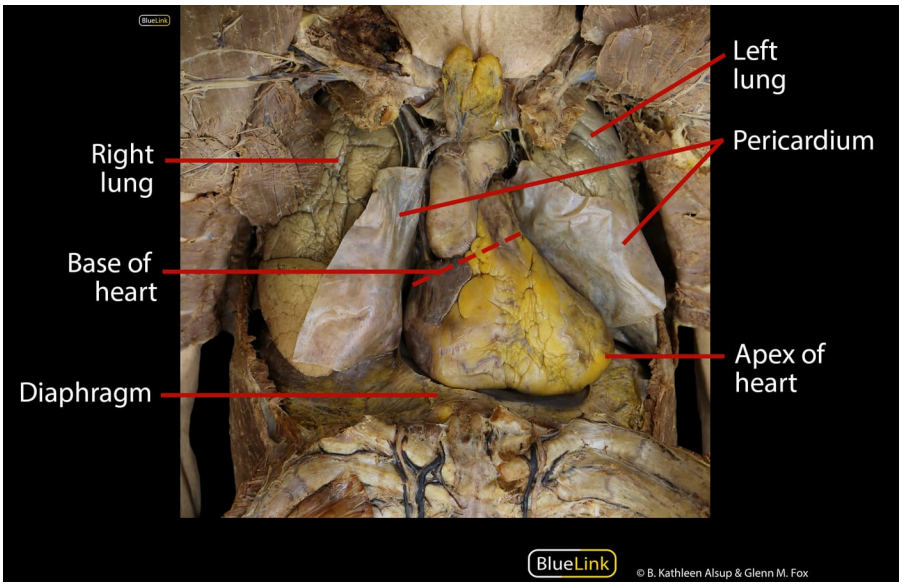


Figure 10.2.2: **Location of Heart in the Thorax.** The heart is located within the thoracic cavity, medially between the lungs in the mediastinum. It is about the size of a fist, is broad at the top, and tapers toward the base. (Caption from OpenStax) *(Image credits: "Blausen 0467 - Heart position relative to the rib cage - English labels" by Blausen.com staff (2014), license: CC BY. Source: "Medical gallery of Blausen Medical 2014" https://en.wikiversity.org/wiki/Wiki...n_Medical_2014 "Blausen 0458 - Heart position in the thoracic cavity - English labels" by Blausen.com staff (2014), license: CC BY. Source: "Medical gallery of Blausen Medical 2014" https://en.wikiversity.org/wiki/Wiki...n_Medical_2014. "Cadaver Heart" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Basic Heart Anatomy

The heart is a muscular double pump made up of **four chambers** separated into two sides. Each side has an **atrium**, which receives blood returning to the heart, and a **ventricle**, which pumps blood out. Valves between the atria and ventricles prevent

backflow, ensuring one-way movement of blood. A thick wall called the **septum** divides the right and left sides of the heart, keeping oxygen-poor and oxygen-rich blood separate.

The **right side** of the heart controls the **pulmonary circulation** — it receives deoxygenated blood from the body through the **superior and inferior vena cavae** and pumps it to the lungs through the **pulmonary arteries**.

The **left side** of the heart controls the **systemic circulation** — it receives oxygenated blood from the lungs through the **pulmonary veins** and pumps it to the rest of the body through the **aorta**. Valves at the exits of the ventricles (the pulmonary and aortic semilunar valves) prevent blood from flowing backward into the heart.

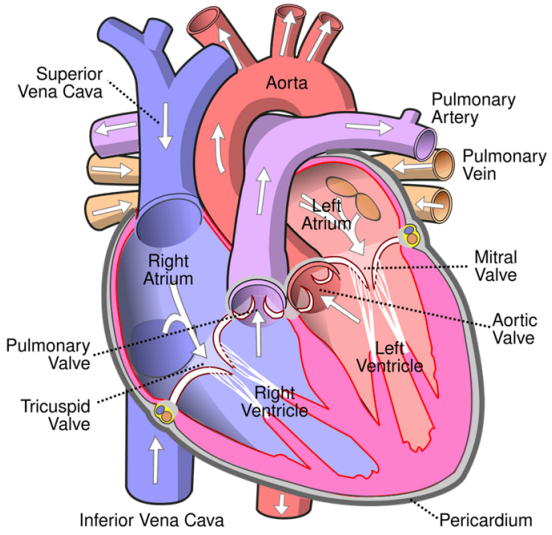


Figure 10.2.3: **The Human Heart**: The position of valves ensures proper directional flow of blood through the cardiac interior. Note the difference in the thickness of the muscled walls of the atrium and the left and right ventricle.

The heart has its own **conduction system** that coordinates each heartbeat. The **sinoatrial (SA) node**, located in the right atrium, acts as the natural pacemaker, sending electrical impulses that cause the atria to contract. The signal then passes to the **atrioventricular (AV) node**, which briefly delays the impulse before sending it down the **bundle of His**, **bundle branches**, and **Purkinje fibers**, triggering the ventricles to contract. Although the heart beats automatically, the **autonomic nervous system** can speed it up or slow it down as needed.

Finally, the heart has its own **blood supply** through the **coronary arteries**, which deliver oxygen and nutrients to the cardiac muscle itself—because the blood inside the chambers does not nourish the heart tissue directly.

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10.3: Pericardium and the Heart Wall

The heart is enclosed by the pericardial sac, which protects and supports the powerful myocardium as it drives the heart's continuous pumping action.

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

- Describe the layers and functions of the pericardium and the role of pericardial fluid.
- Identify the three layers of the heart wall and their functions.
- Explain why the left ventricle has a thicker wall than the right.

From Cover to Core: Pericardium

The heart is enclosed in a double-layered membrane called the **pericardium**, or **pericardial sac**. This membrane also surrounds the "roots" of the major blood vessels above the heart and attaches to the diaphragm below, helping to anchor the heart securely within the thoracic cavity as it beats continuously.

The pericardium, which literally translates as "around the heart," consists of two distinct sublayers: the sturdy outer **fibrous pericardium** and the inner **serous pericardium**. The fibrous pericardium is made of tough, dense irregular connective tissue that protects the heart and maintains its position in the thorax while also limiting the heart's motion during the heartbeat. The more delicate serous pericardium consists of two layers:

- the **parietal pericardium**, which is fused to the fibrous pericardium, and
- an inner **visceral pericardium**, or **epicardium**, which is fused to the heart and is also part of the heart wall.

The **pericardial cavity**, filled with lubricating serous fluid, lies between the epicardium and the parietal pericardium. The serous layers of the pericardium consist of a simple squamous epithelium anchored by a layer of areolar connective tissue. The areolar connective tissue connects the parietal pericardium to the fibrous pericardium and it connects the epicardium to the myocardium.

The epithelial tissue of the serous membranes secretes the **lubricating serous fluid** that fills the pericardial cavity and reduces friction as the heart contracts. Adipose connective tissue can also be found in the epicardium, particularly in the areas where blood vessels run along the heart's surface. Figure illustrates the pericardial membrane and the layers of the heart.

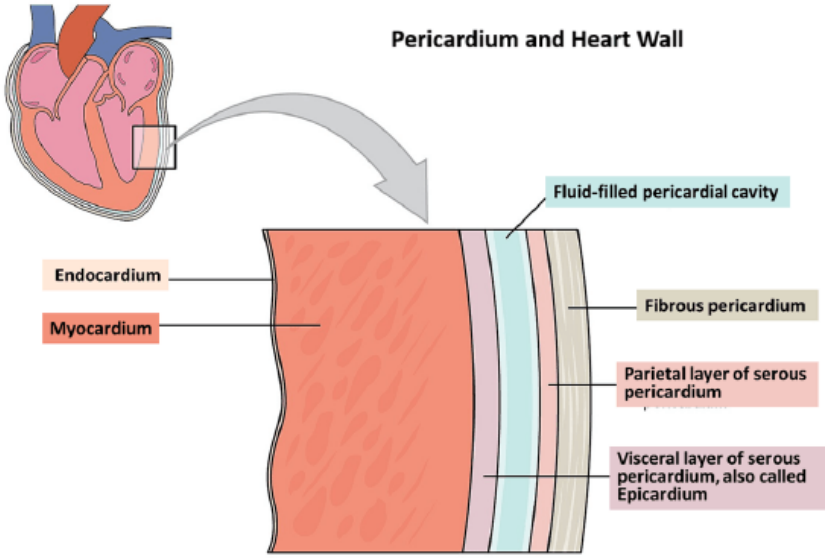
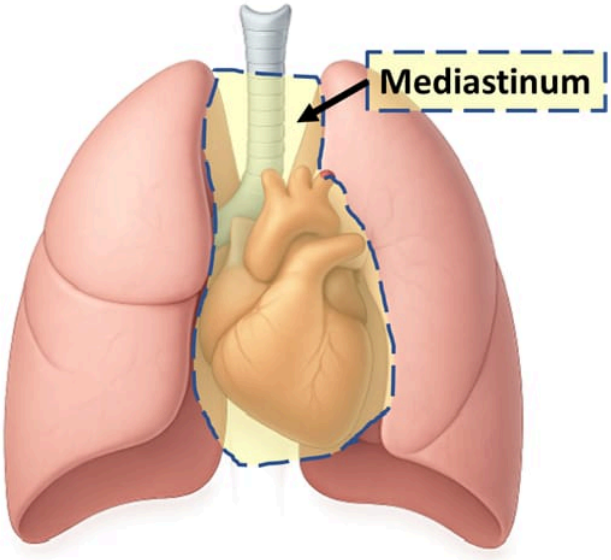


Figure 10.3.1: **Pericardial Membranes and Layers of the Heart Wall.** The pericardial membrane that surrounds the heart consists of three layers and the pericardial cavity. The heart wall also consists of three layers. The pericardial membrane and the heart wall share the epicardium. (Caption from OpenStax) *(Image credit: "Heart Wall" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Blausen.com staff (2014).)*



The pericardium is very important because it protects the heart from trauma, shock, stress, and even infections from the nearby lungs. It supports the heart and anchors it to the **mediastinum** — the central compartment of the thoracic cavity that lies between the lungs and contains the heart, major blood vessels, trachea, and esophagus — so it doesn't move within the body. The pericardium lubricates the heart and prevents it from becoming too large if blood volume is overloaded (though it will not prevent chronic heart enlargement).

Despite these functions, the pericardium is still vulnerable to problems of its own. **Pericarditis** is the term for inflammation in the pericardium, typically due to infection. Pericarditis is often a severe disease because it can constrict and apply pressure on the heart and work against its normal function. Pericarditis comes in many types depending on which tissue layer is infected.

From Cover to Core: Heart Wall

The wall of the heart is composed of three layers of unequal thickness. From superficial to deep, these are the **epicardium**, the **myocardium**, and the **endocardium** (see Figure above). The outermost layer of the wall of the heart is also the innermost layer of the pericardium, the **epicardium**, **or the visceral pericardium** discussed above.

The middle and thickest layer of the heart wall is the **myocardium**, which is composed mainly of **cardiac muscle** supported by small amounts of connective tissue. The contraction of this muscular layer generates the force needed to propel blood through both the pulmonary and systemic circuits. As with skeletal muscle, the more muscle fibers that contract, the greater the force produced.

The myocardium rests on a framework of dense connective tissue known as the **cardiac skeleton** (described later). This structure helps anchor the muscle fibers and supports the heart's valves. The arrangement of the cardiac muscle cells is both elegant and efficient: the fibers spiral and swirl around the chambers of the heart in complex **figure-8 patterns**. These loops wrap around the atria and the roots of the great vessels, while deeper layers encircle the ventricles and extend toward the apex. The outermost layers twist around both ventricles together.

This **spiraling pattern of muscle** ensures that when the heart contracts, it does not just squeeze but also twists, reducing the size of the chambers in a wringing motion that pushes blood efficiently **to the top of the heart** and into the arteries. *(See the figure below for the arrangement of myocardial fibers.)*

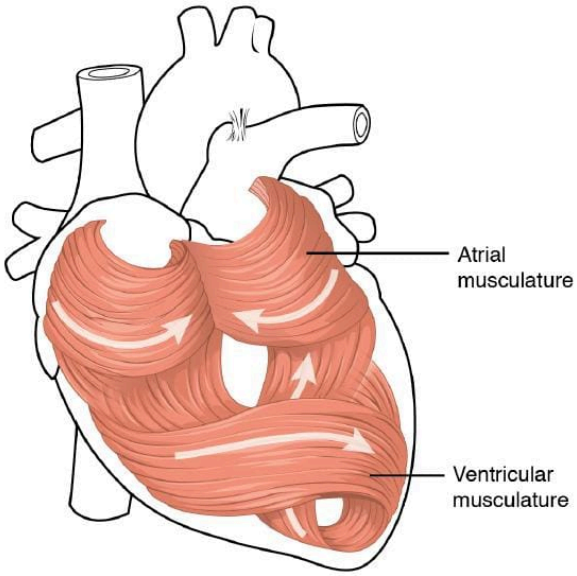


Figure 10.3.2: **Cardiac Musculature.** The swirling pattern of cardiac muscle tissue contributes significantly to the heart's ability to pump blood effectively. *(Image credit: "Heart Musculature" by OpenStax is licensed under CC BY 3.0.)*

Although both ventricles pump the same volume of blood with each heartbeat, their workloads are very different. The **left ventricle** must push blood through the long, high-resistance systemic circuit, so its muscular wall is much thicker and more powerful. In contrast, the **right ventricle** only sends blood a short distance to the lungs through the low-resistance pulmonary circuit and therefore does not need to generate as much force. As a result, the heart's left side appears more muscular when viewed in cross section. (*see figure below).*

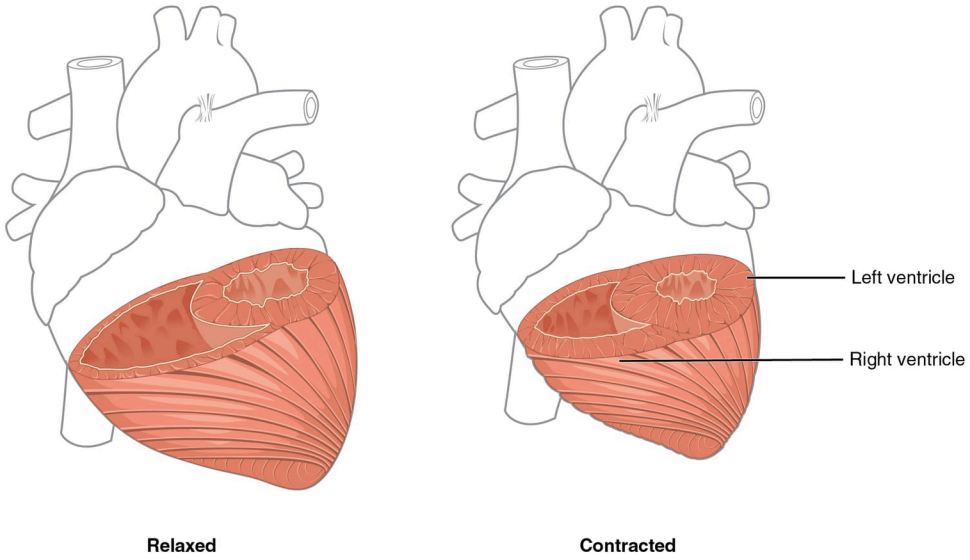


Figure 10.3.3: **Differences in Ventricular Muscle Thickness.** The myocardium in the left ventricle is significantly thicker than that of the right ventricle. In both relaxed and contracting states, also note the differences in the relative size of the lumens, the region inside each ventricle where the blood is contained. *(Image credit: "Ventricular Muscle Thickness" by OpenStax is licensed under CC BY 3.0.)*

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10.4: Heart Anatomy - Details

The heart's external and internal structures work together to move blood efficiently through its atria and ventricles, valves, and vessels, ensuring continuous circulation throughout the body.

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

- Identify the major external structures of the heart and describe how the atria, ventricles, and great vessels function in blood flow.
- Trace the pathway of blood through the heart, lungs, and body, distinguishing between pulmonary and systemic circuits.
- Explain how the septa, valves, chordae tendineae, and papillary muscles maintain one-way blood flow through the heart.

External Structures of the Heart

Atria and Ventricles

The heart contains four hollow chambers: **two atria** and **two ventricles**. The right and left atria are the thin-walled, superior chambers that receive blood returning to the heart. Although both atria can be seen from the front, most of the left atrium lies on the posterior side of the heart *(see Figures below)*.

Each atrium has a small, flap-like extension called an **auricle**, named for its resemblance to a human ear *(see Figure B below)*. The auricles act as expandable "pockets" that can temporarily hold extra blood during times of exertion, helping to relieve high pressure in the atria.

The two ventricles lie below the atria and make up most of the heart's mass. Their muscular walls are much thicker than those of the atria because they must generate enough force to pump blood into the arteries. The **right ventricle** forms most of the heart's anterior surface, while the **left ventricle** forms much of the posterior and left sides.

The heart is composed of four hollow chambers: two atria and two ventricles. The thin walled **right and left atria** are the two superior chambers. While both atria are visible from the anterior, the majority of the left atrium is seen on the posterior aspect. Each atrium has a superficial flap-like extension called an **auricle** because its shape resembles the external ear of a human. You may also hear them referred to as atrial appendages. The auricles can increase the atrial capacity at times of exertion by filling with blood and, thus, relieving high atrial pressure. The two ventricles are inferior to the atria and they form the largest portion of the heart. Their walls are significantly thicker than those of the atria as a large amount of muscle mass is needed to push the blood into the arteries. The **right ventricle** makes up the right side and much of the anterior portion of the heart, while the **left ventricle** makes up the left side and much of the posterior portion of the heart.

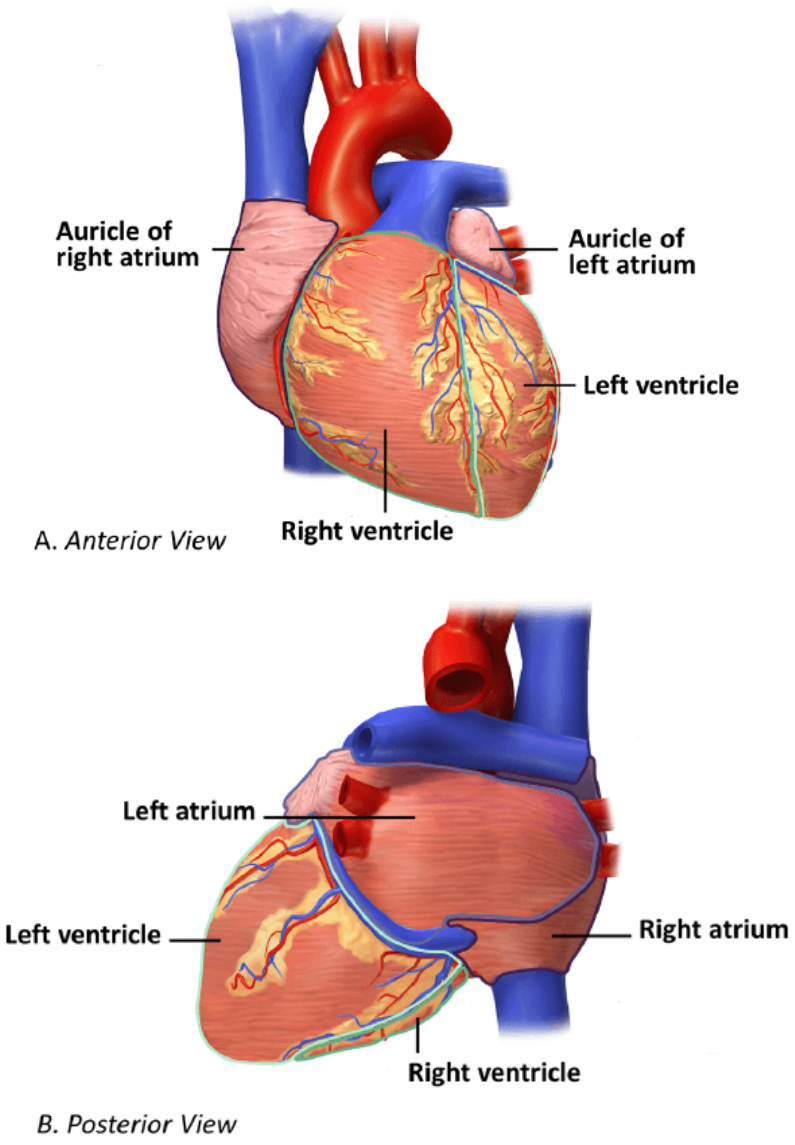


Figure 10.4.1: **Superficial Heart Anatomy.** Inside the pericardium, the surface features of the heart are visible. (Caption from OpenStax) *(Image credits: "Heart Chambers Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Heart Chambers Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

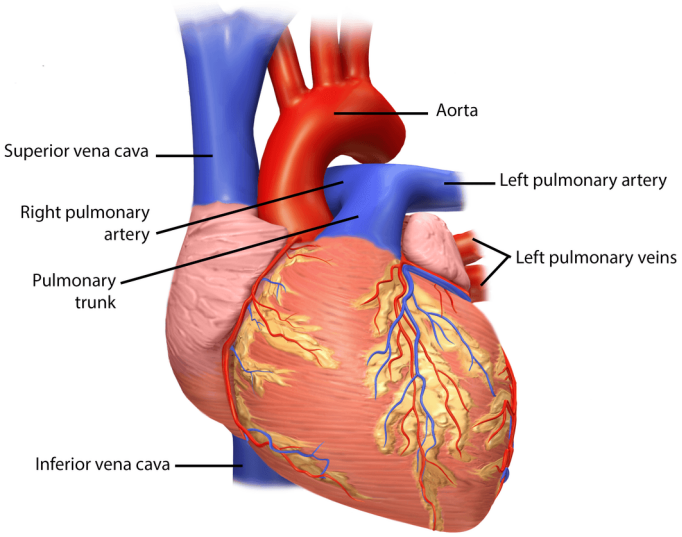
Great Vessels of the Heart

Blood enters and exits the heart through the body's largest arteries and veins, collectively called the *great vessels*. These major vessels include the **inferior vena cava**, **superior vena cava**, **pulmonary arteries**, **pulmonary veins**, and the **aorta** (See figure below).

The **pulmonary trunk** emerges from the right ventricle and quickly divides into the **right and left pulmonary arteries**, which carry deoxygenated blood to each lung. After passing through the lung capillaries, the now oxygen-rich blood returns to the heart through the **right and left pulmonary veins**, which empty into the **left atrium**. From there, blood flows into the **left ventricle**, from where it is pumped into the **aorta** — the largest and thickest artery in the body. The aorta distributes oxygenated blood to every organ through the systemic circuit.

Blood returning from the body completes its journey through two of the great vessels: the **superior vena cava**, which drains blood

from regions above the heart, and the **inferior vena cava**, which returns blood from regions below the heart. We will explore the structure of these vessels a little further on in this Chapter.



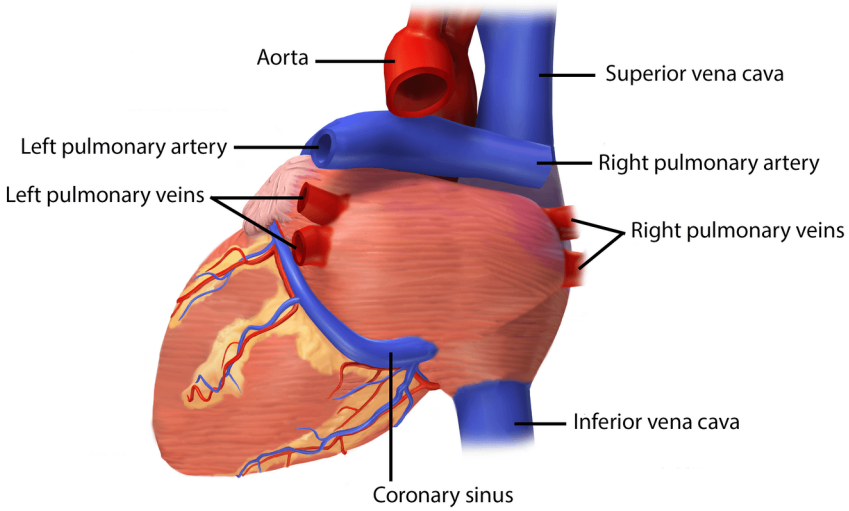


Figure 10.4.2: **Great Vessels of the Heart.** The base of the heart shows the location of the great vessels. Insert image caption. *(Image credits: "Great Vessels of the Heart, Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Great Vessels of the Heart, Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

Coronary Arteries: Fueling the Heart

The heart may pump blood to every cell in the body, but it also needs its own dedicated blood supply. The **coronary arteries** deliver oxygen-rich blood to the **myocardium** and other tissues of the heart itself.

Immediately after the **aorta** emerges from the **left ventricle**, it gives rise to the **right and left coronary arteries**.

The **left coronary artery (LCA)** supplies blood to most of the **left side of the heart** — including the **left atrium**, **left ventricle**, and **interventricular septum**. It passes behind the **pulmonary trunk** and quickly branches into two major arteries:

- The **circumflex artery**, which follows the **coronary sulcus** to the left and eventually connects with small branches of the right coronary artery.
- The **anterior interventricular artery**, also called the **left anterior descending artery (LAD)**, which travels along the **anterior interventricular sulcus** toward the **apex** of the heart. Along its route, it gives rise to smaller branches that form tiny **anastomoses** (connections) with branches of the **posterior interventricular artery**. These interconnections can allow limited rerouting of blood flow if a vessel is partially blocked. However, in the heart, these connections are very small — so a coronary artery blockage can still lead to **myocardial infarction (heart attack)** in the affected area.

The **right coronary artery (RCA)** travels along the **coronary sulcus** and supplies the **right atrium**, portions of both **ventricles**, and parts of the **cardiac conduction system**. On the posterior surface of the heart, it curves downward and becomes the **posterior interventricular artery** (or **posterior descending artery, PDA**). This artery runs along the **posterior interventricular sulcus** toward the apex, supplying the back of the heart and the posterior portion of the septum.

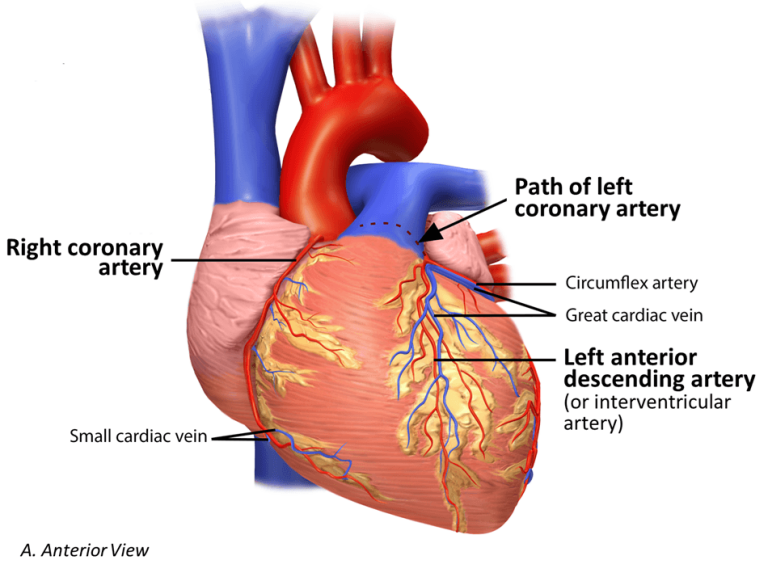


Figure \({10{.}4{.}\eatSpaces{3\): **Coronary Arteries of the Heart.** *(Image credits: "Coronary Vessels, Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Coronary Vessels, Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

Interactive Element

Explore a model of the heart in 3D:

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

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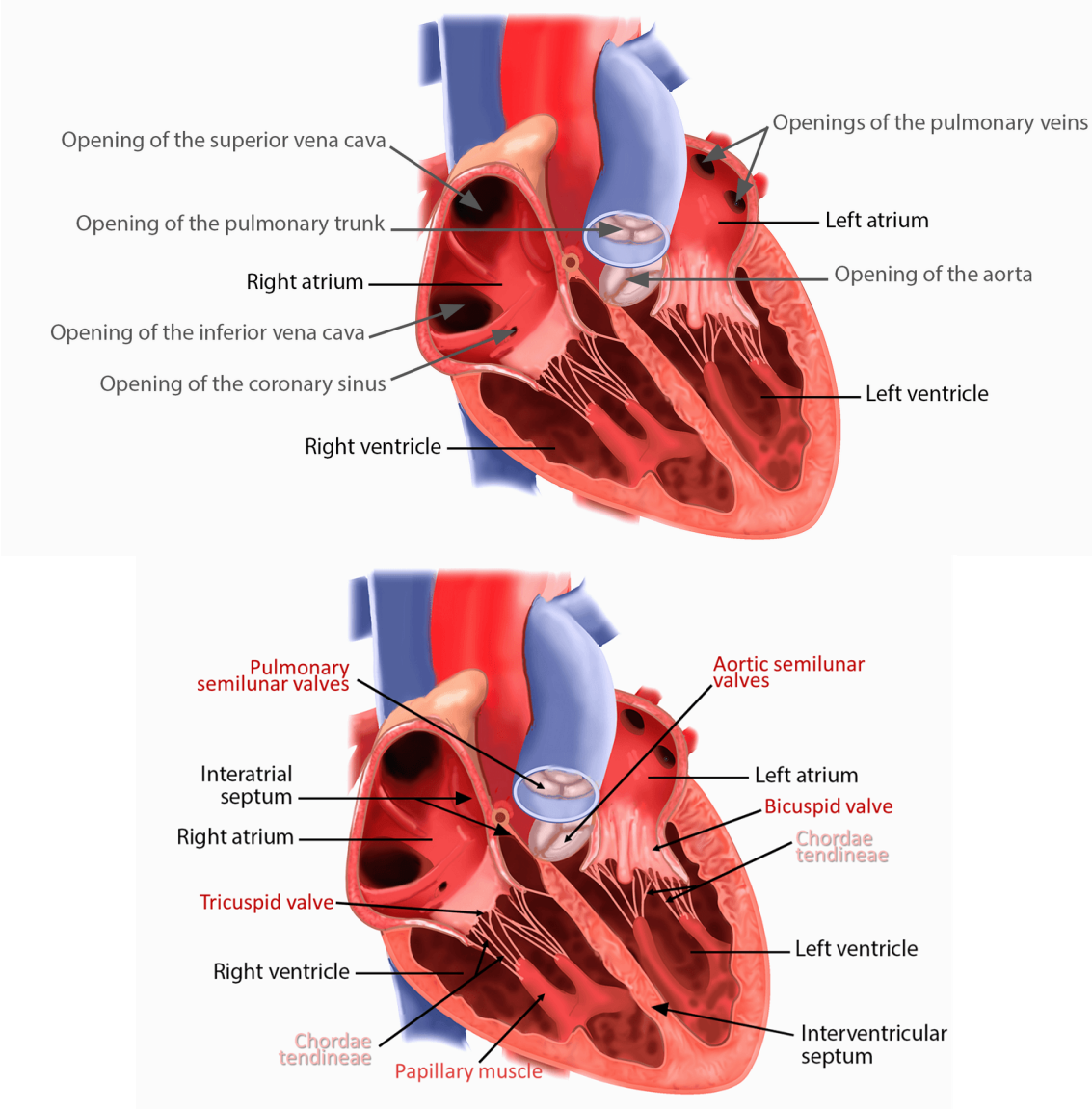
Internal Structures of the Heart

Muscular walls called **septa** divide the heart into right and left sides. The term *septum* (plural *septa*) comes from the Latin for

“something that encloses.” Each septum is a continuation of the **myocardium** lined with **endocardium**.

The **interatrial septum** separates the two atria and contains a shallow depression called the **fossa ovalis**, a remnant of the fetal **foramen ovale** that once allowed blood to pass directly from the right to the left atrium, bypassing the lungs. This opening closes shortly after birth as normal circulation begins. The **interventricular septum**, which separates the ventricles, is thicker because the ventricles generate much higher pressure during contraction.

The **atrioventricular septum** separates the atria from the ventricles and contains four openings that allow blood flow between chambers and into the major arteries. Each opening is guarded by a **valve** that ensures one-way flow. The **atrioventricular (AV) valves** are reinforced by strands of connective tissue called **chordae tendineae** (“heart strings”), which anchor each valve flap to a **papillary muscle** on the ventricular wall. At the exits of the ventricles, the **semilunar valves**—each with three small cusps—control blood flow into the pulmonary trunk and aorta.



Figures \(\PageIndex{4\): **Interior Structures of the Heart.** This anterior view of the heart shows the four chambers, the great vessels, the valves, the chordae tendinae , and the papillary muscles. The presence of the pulmonary trunk and aorta covers the interatrial septum, and the atrioventricular septum is cut away to show the atrioventricular valves. (Caption from OpenStax) *(Image credits: "Interior Structures of the Heart - illustration with multiple label sets" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Slagter - Drawing Anatomy of the heart and large vessels - no labels" by Ron Slagter, license: CC BY-NC-SA.)*

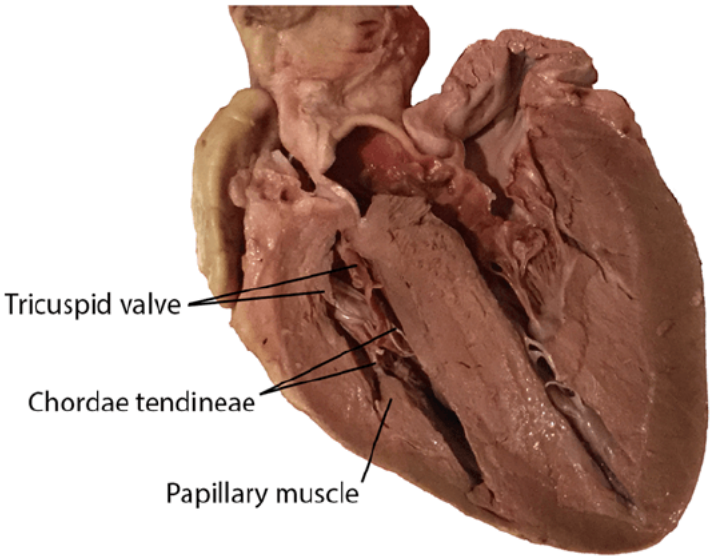
Right Atrium

The **right atrium** receives blood returning from the body through three large veins: the **superior vena cava**, **inferior vena cava**, and **coronary sinus**.

- The **superior vena cava** drains the head, neck, upper limbs, and thoracic region.
- The **inferior vena cava** returns blood from below the diaphragm—the lower limbs and abdominopelvic cavity.
- The **coronary sinus**, a thin-walled vein on the posterior heart, collects blood from the myocardium itself.

The atria receive venous blood almost continuously, so the heart can keep filling even while the ventricles are contracting. Most ventricular filling happens while the atria are relaxed, but they also contract briefly to push the last bit of blood into the ventricles before the latter contract. The opening between the right atrium and right ventricle is controlled by the **tricuspid valve**.

The atria receive venous blood on a nearly continuous basis, allowing the heart to continue to receive blood even while the ventricles are contracting. While most ventricular filling occurs while the atria are relaxed, they do demonstrate a contractile phase and actively pump blood into the ventricles just prior to ventricular contraction. The opening between the right atrium and right ventricle is guarded by the **tricuspid valve**.



Right Ventricle

The right ventricle receives blood from the right atrium through the tricuspid valve (also called the right atrioventricular valve). Three papillary muscles in the right ventricle anchor the three flaps of this valve.

When the ventricular myocardium contracts, pressure within the ventricle increases and blood flows toward lower-pressure areas — the pulmonary trunk and the atrium. To prevent backflow into the atrium, the rising pressure pushes the tricuspid valve flaps closed. Simultaneously, the papillary muscles contract, pulling on the chordae tendineae to keep the valve flaps from everting into the atria. This coordination prevents regurgitation of blood during ventricular contraction.

When the right ventricle contracts, it ejects blood into the pulmonary trunk, which branches into the left and right pulmonary arteries that carry deoxygenated blood to each lung. At the base of the pulmonary trunk is the pulmonary semilunar valve that prevents backflow from the pulmonary trunk when the ventricle relaxes.

Left Atrium

After gas exchange occurs in the lungs, oxygenated blood returns to the left atrium through **four pulmonary veins.** Blood flows almost continuously from the pulmonary veins into the atrium, which serves as a receiving chamber, and then through the open **bicuspid (mitral or left atrioventricular) valve** into the left ventricle. Most ventricular filling occurs passively while both chambers are relaxed, but near the end of this phase — just as on the right side — the left atrium contracts to push into the ventricle the last 20% of of the blood.

Left Ventricle

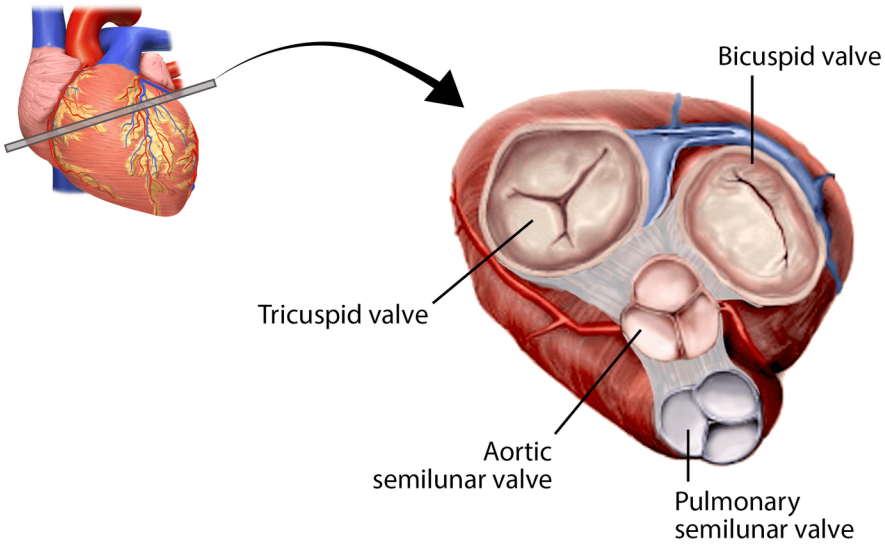
Although both ventricles pump the same volume of blood, the left ventricle has a much thicker myocardium because it must generate greater force to propel blood through the systemic circuit and upward to the brain against gravity. The left ventricle contains prominent trabeculae carneae, and its bicuspid valve flaps are anchored to two papillary muscles by the chordae tendineae. Again, this structure ensures the valve closes securely during contraction as blood is ejected into the aorta through the aortic semilunar valve.

Heart Valves

A transverse section through the heart just above the atrioventricular septum reveals all four valves in the same plane *(see figure below)*. These valves ensure that blood flows in only one direction through the heart.

Between the right atrium and right ventricle lies the **right atrioventricular (tricuspid) valve**. It has three flaps, or leaflets, formed from endocardium strengthened with dense connective tissue. Each flap is anchored by **several chordae tendineae to papillary muscles projecting from the ventricular wall.**

At the opening between the left atrium and left ventricle is the **left atrioventricular valve, commonly called the mitral valve (or bicuspid valve).** Clinically, “mitral valve” is preferred since the number of cusps can vary among individuals. The mitral valve’s cusps are also attached by chordae tendineae, this time to two papillary muscles that extend from the ventricular wall.



Figures \(\PageIndex{5}\): **Heart Valves.** With the atria and major vessels removed, all four valves are clearly visible. (Caption from OpenStax) *(Image credit: "Valves and the Cardiac Skeleton" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of originals "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc. and OLI - Drawing Valves of the heart from anterior and cross-section - English labels" by Open Learning Initiative.)*

Pathway of Blood Through the Heart

The **right ventricle** pumps **deoxygenated blood** into the **pulmonary trunk**, which travels upward in front of the aorta and left atrium before splitting into the **right and left pulmonary arteries**.

- The **right pulmonary artery** carries blood to the right lung.
- The **left pulmonary artery** carries blood to the left lung.

Inside the lungs, these arteries branch repeatedly until they reach the **pulmonary capillaries**, where **gas exchange** occurs — **carbon dioxide** leaves the blood and **oxygen** enters. The pulmonary trunk and arteries are unique because they are the only arteries in the body that carry deoxygenated blood after birth.

Freshly oxygenated blood then returns from the lungs through the **pulmonary veins**, which are the only veins that carry oxygen-rich blood. These veins empty into the **left atrium**, which sends the blood into the **left ventricle**. From there, the **left ventricle** pumps oxygenated blood into the **aorta**, which arches over the top of the heart and then descends to deliver blood throughout the body via the **systemic circuit**.

In the **systemic capillaries**, oxygen and nutrients move out of the blood and into body cells, while **carbon dioxide and waste products** move into the blood. The now deoxygenated blood flows into small veins (**venules**), which merge into larger veins and finally drain into the two main systemic veins: the **superior vena cava** and **inferior vena cava**. These return the blood to the **right atrium**, completing the cycle (See figure below).

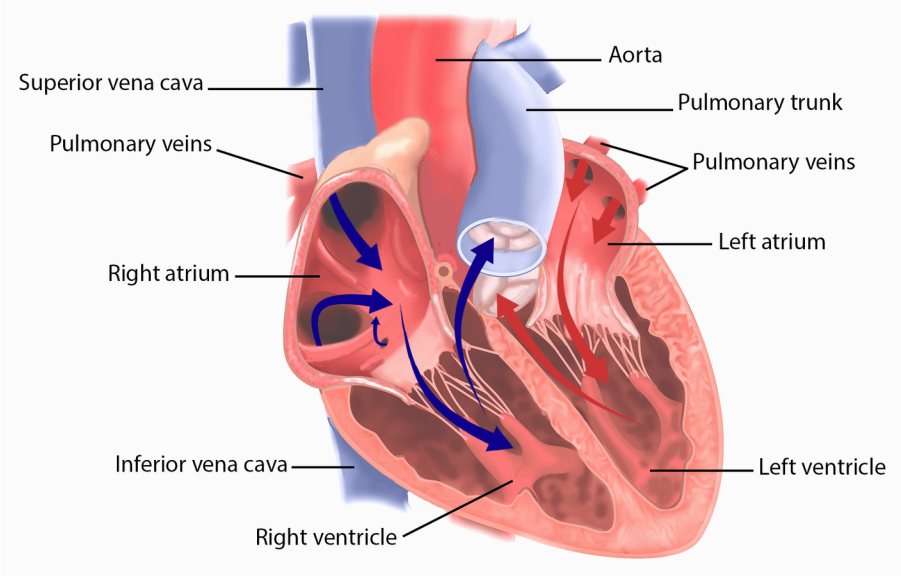


Figure Extra close brace or missing open brace : Circulation Through the Heart. Blood flows from the atria (right and left) to the ventricles (right and left), where it is pumped into the pulmonary circuit (from right ventricle) and systemic circuit (from left ventricle). *(Image credits: "Circulation Through the Heart" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Slagter - Drawing Anatomy of the heart and large vessels - no labels" by Ron Slagter, license: CC BY-NC-SA.)*

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10.5: Generation and Transmission of Cardiac Impulses

Specialized cardiac cells generate and transmit electrical impulses that coordinate the heart's rhythmic contractions.

Master this section and you'll be able to:

- Differentiate between myocardial contractile and conducting cells and their roles in the heartbeat.
- Explain what the term "pacemaker cells" means.
- Trace the cardiac conduction pathway from the SA node to the Purkinje fibers.
- Summarize how the nervous and endocrine systems influence heart beats.

Intrinsic Regulation: Pacemaker Cells

Cardiac muscle cells are unique muscle cells found only in the heart, and they play a crucial role in keeping the heart beating and blood circulating throughout the body.

There are two major types of cardiac muscle cells:

1. **Myocardial contractile cells:** they make up most of the heart and generate the force for pumping blood.

2. **Myocardial conducting cells:** these cells account for only about 1% of the heart's cells, but they are specialized to generate and rapidly transmit electrical impulses, rather like a built-in neuron network allowing the heart to synchronize contractions. Within the group of myocardial conducting cells is a very important subset known as **autorhytmic** or **pacemaker cells.**

So, while **contractile cells** focus on contraction, **conducting** and **pacemaker cells** are designed to start and propagate action potentials that travel through the heart and trigger those contractions.

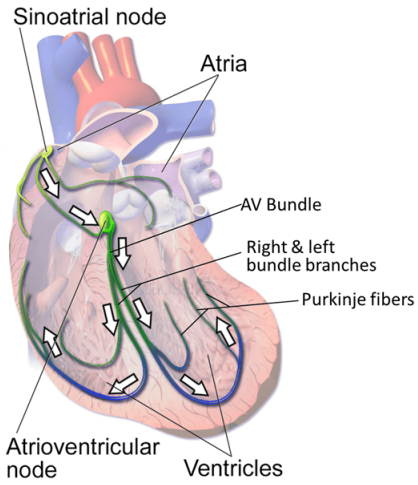
The main cluster of pacemaker cells is found in the **sinoatrial (SA) node**, the "natural pacemaker" of the heart located in the right atrium. Pacemaker cells can generate their own electrical impulses without any external stimulus — this property is called "**autorhythmicity**". These impulses set the pace for the heart's rhythm by being the fastest cells in the heart and drive the timing for all other cells. If any part of the system is damaged or blocked, other conducting cells can act as backup pacemakers

As you have already learned, normal cardiac rhythm is established by the sinoatrial (SA) node, which is why it is called the heart's natural pacemaker. It generates rhythmic electrical impulses that spread through the atria, triggering their contraction. The signal then travels to the **atrioventricular (AV) node**, where it briefly pauses before continuing through the heart's specialized **conduction pathways:**

1. **Atrioventricular (AV) bundle**, or **bundle of His**
2. **Right and left bundle branches**
3. **Purkinje fibers**

Working together, the SA node, AV node, and these pathways form the **heart's conduction system** — an intrinsic wiring network that ensures each heartbeat occurs in a precise, coordinated sequence.

Cardiac Conduction System



Electrical Conduction System of the Heart

Sinoatrial (SA) Node

The specialized myocardial conducting cells located in the upper posterior wall of the right atrium, near the opening of the superior vena cava make up the **SA node.** Because it has the fastest natural rate of depolarization, the SA node acts as the heart's **pacemaker**, initiating each heartbeat and setting the **sinus rhythm**, or normal electrical pattern.

From the SA node, the electrical impulse spreads across the atrial muscle cells and toward the **atrioventricular (AV) node** through what is known as **internodal pathways,** allowing both atria to contract at nearly the same time. This synchronized atrial contraction ensures efficient filling of the ventricles before they contract. The impulse takes about **50 milliseconds (ms)** to travel from the SA node to the AV node.

Atrioventricular (AV) Node

The **AV node** is another cluster of specialized myocardial conducting cells located in the lower part of the right atrium, within the **atrioventricular septum**. The **fibrous skeleton** of the heart — a dense connective tissue framework that surrounds the valves — acts as an electrical **insulator**, preventing impulses from passing directly from the atria to the ventricles. The only route for the signal to continue is through the AV node.

When the impulse reaches the AV node, it slows down briefly before moving on to the **AV bundle.** This delay, lasting about **100 milliseconds (ms)**, occurs because the cells in the AV node are smaller and conduct signals more slowly. The pause is essential — it gives the atria time to complete their contraction and push blood into the ventricles before ventricular contraction begins.

Atrioventricular Bundle (Bundle of His), Bundle Branches, and Purkinje Fibers

The **AV bundle**, also called the **bundle of His**, arises from the AV node and passes through the **interventricular septum** before dividing into the **right** and **left bundle branches**. The right branch conducts impulses to the right ventricle, while the thicker left branch supplies the left ventricle. Because the left ventricle is much larger and more muscular, its bundle branch is correspondingly broader. Both branches extend toward the **apex of the heart**, where they connect with the **Purkinje fibers**. The signal travels through this portion of the pathway in about **25 milliseconds (ms)**.

The **Purkinje fibers** are specialized conducting cells that deliver the electrical impulse rapidly to the ventricular myocardial cells. These fibers branch extensively through the ventricular walls, beginning at the **apex** and spreading upward toward the

atrioventricular septum and **base of the heart.** Their very fast conduction speed allows the impulse to reach all ventricular muscle cells in roughly **75 ms**. Contraction begins at the apex and moves upward — much like squeezing toothpaste from the bottom — so blood is efficiently pushed out of the ventricles into the **aorta** and **pulmonary trunk**. From the initial depolarization at the SA node , the entire process takes about **225 ms**.

From the moment the **SA node** fires **to the full activation of the ventricles**, only about **225 milliseconds** pass — less than **one-quarter of a second**. In that blink of time, the electrical signal travels through every chamber of the heart, coordinating the precise sequence of contractions that keep blood flowing smoothly. In other words, your heart's entire electrical "conversation" for each beat happens faster than you can snap your fingers.

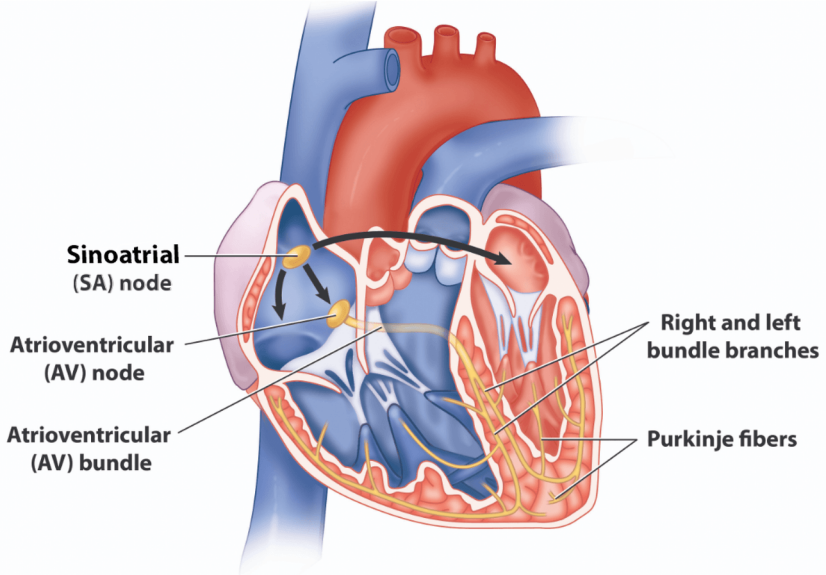


Figure 10.5.1: **Conducting System of the Heart.** The initiation of an action potential at the sinoatrial (SA) node spreads throughout the atria reaching the atrioventricular (AV) node, AV bundle (bundle of His), bundle branches, and ultimately Purkinje fibers. *(Image credit: "Conducting System of the Heart" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

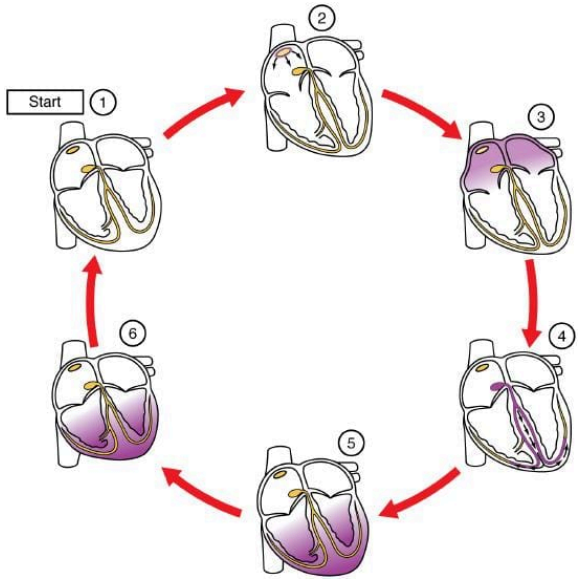


Figure 10.5.2: **Cardiac Conduction.** (1) The sinoatrial (SA) node and the remainder of the conducting system are at rest. (2) The SA node initiates the electrical wave, which sweeps across the atria. (3) After reaching the atrioventricular node the impulse is transmitted to the atrioventricular bundle. (4) The impulse travels through the atrioventricular bundle and bundle branches to the Purkinje fibers. (5) The impulse spreads to the contractile fibers of the ventricle. (6) Ventricular contraction begins. *(Image credit: "Cardiac Conduction" by OpenStax is licensed under CC BY 3.0.)*

Extrinsic Regulation: Nervous and Hormonal Control of the Heartbeat

The **sinoatrial (SA) node** normally generates electrical impulses about **80 to 100 times per minute**, but your resting heart rate is usually slower — around **60 to 80 beats per minute** — because the **parasympathetic nervous system** continuously keeps the heart rate in check.

The **autonomic nervous system (ANS)** constantly adjusts heart activity to match the body's needs:

- **Sympathetic stimulation** (the "fight or flight" response) speeds up the rate of depolarization in the SA node, causing the heart to beat faster and with greater force.
- **Parasympathetic stimulation** (the "rest and digest" response) slows the depolarization rate, reducing heart rate and conserving energy when the body is relaxed.

Hormones can also influence the heart's rhythm. During times of stress or excitement, the adrenal glands release **epinephrine (adrenaline)** into the bloodstream. This hormone has effects similar to sympathetic stimulation — they increase the heart rate, strengthen contractions, and help the body respond quickly to challenges.

Additionally, **thyroid hormones**, which regulate metabolism, can also increase the heart rate over the long term if present at higher levels.

Together, the nervous and endocrine systems act as a finely tuned control system, allowing the heart to accelerate when you sprint up stairs and slowing it when you settle into taking a nap.

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10.6: Electrocardiogram (ECG)

An electrocardiogram, or ECG, is a recording of the heart's electrical activity as a graph over a period of time.

Master this section and you'll be able to:

- Describe how ECG electrodes detect the heart's electrical activity and why a 12-lead ECG is better than a 3 or 5 lead ECG.
- Identify the main ECG waves, segments, and intervals and relate them to specific cardiac events.
- Interpret normal and abnormal ECG patterns to recognize common arrhythmias.

From Electrodes to Insights: Understanding the ECG

Electrical signals produced by the heart can be captured through the strategic positioning of electrodes on specific areas of the body. This process of tracking the heart's electrical activity is referred to as an **electrocardiogram** (**ECG**), also sometimes abbreviated as **EKG** (with "K" representing "kardiology," the German term for cardiology). Unlike recording signals from individual muscle fibers, a standard ECG showcases the overall fluctuations in electrical current flow, offering a comprehensive view of heart function.

The ECG graph can show the heart's **rate** and **rhythm**. It can also detect **enlargement** of the heart, or the presence of current or past **heart attacks,** making it a key tool for diagnosing cardiac conditions.

The ECG works by detecting and amplifying tiny electrical changes on the skin that occur during heart muscle depolarization. The output for the ECG forms a graph that shows several different waves, each corresponding to a different electrical and mechanical event within the heart. Changes in these waves are used to identify problems with the different phases of heart activity.

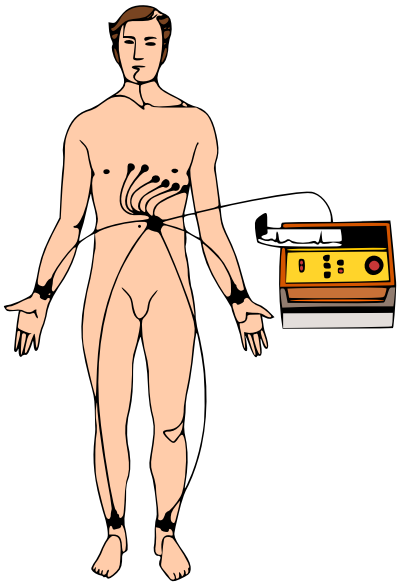
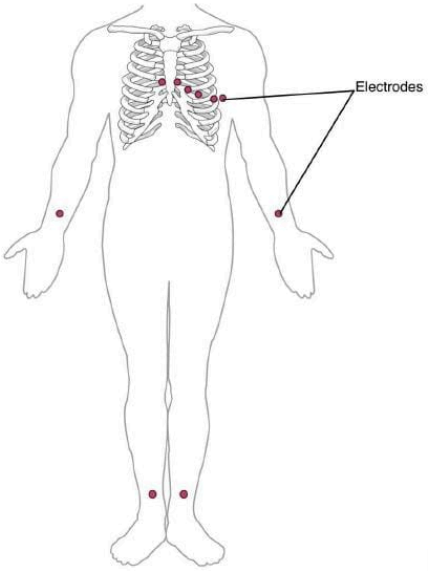


Figure 10.6.1: **ECG.** Illustration of a patient undergoing a 12-lead ECG.

A **12-lead ECG** records the electrical activity of the heart from **12 different perspectives**, or *leads*, using **10 electrodes** placed on specific parts of the body. Despite the name, there are not 12 wires — just 10 electrodes that capture enough information for the ECG machine to calculate 12 unique electrical views of the heart. An ECG can also just use 3 or 5 leads, instead of 12 leads. The level of detail an ECG provides increases with the number of leads used.

*What are "**leads**"?* In ECG terminology, a **lead** is not a wire — it is an *electrical viewpoint* of the heart. Each lead measures the heart's electrical signals from a particular angle. Together, the **12 leads** create a complete picture of how electrical impulses travel through the heart, helping to identify **arrhythmias** (irregular rhythms), **heart muscle damage**, or **myocardial infarctions** *(*heart attacks).

The figure below shows the standard placement of the **10 ECG electrodes** (4 limb electrodes and 6 chest electrodes) in a 12-lead ECG: six electrodes are placed on the chest, and four electrodes are placed on the limbs. Just imagine the purpose to be taking 12 photographs of the heart at once — from different spots around your body — to see how well it is beating and where any problem might be hiding.



Limb electrodes:

- Right arm (RA)
- Left arm (LA)
- Right leg (RL) – serves mainly as a ground or reference
- Left leg (LL)

Chest (precordial) electrodes:

- **V1** – right side of sternum, 4th intercostal space
- **V2** – left side of sternum, 4th intercostal space
- **V3** – midway between V2 and V4
- **V4** – 5th intercostal space, midclavicular line
- **V5** – level with V4, anterior axillary line
- **V6** – level with V5, midaxillary line

Interpreting the ECG Waves and Intervals

When you look at an ECG, you are essentially seeing the heart's **electrical story** drawn out on paper (or a screen). Each small

bump or spike represents a coordinated wave of electrical activity that triggers specific parts of the heart to contract. The three main features of a normal ECG tracing are the **P wave**, the **QRS complex**, and the **T wave.**

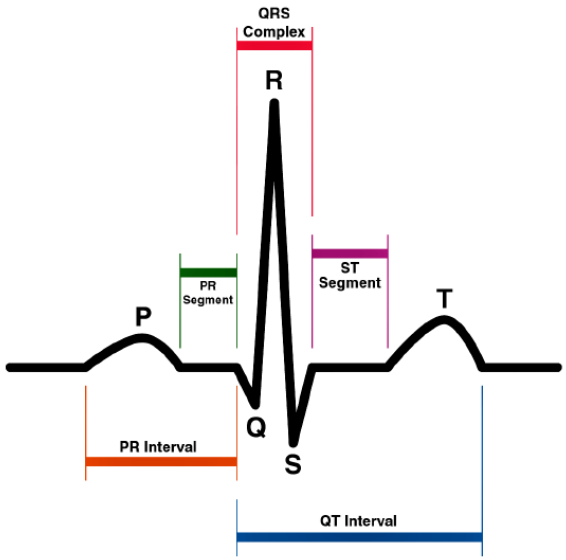


Figure 10.6.2: **Electrocardiogram.** A normal tracing shows the P wave, QRS complex, and T wave. Also indicated are the PR, QT, QRS, and ST intervals, plus the P-R and S-T segments.

The P Wave

The first feature on an ECG is the **P wave**, a small, rounded upward deflection that represents **atrial depolarization** — the electrical signal that triggers **atrial contraction** (*atrial systole*). This wave appears first because the heartbeat begins in the **sinoatrial (SA) node**, the heart's natural pacemaker, located in the right atrium. From there, the impulse travels across the atria. This contraction pushes blood into the ventricles, completing the filling phase of the cardiac cycle.

Because the atria are relatively small and thin-walled, the P wave is gentle and modest in size compared to the tall spike of the QRS complex. However, this small signal carries important diagnostic value. Changes in the **height or shape** of the P wave can indicate imbalances in **potassium ion concentration**, which affect the excitability of cardiac muscle cells.

If there is no distinct **P wave**, but rather there are chaotic "fibrillatory" waves, it may suggest **atrial fibrillation**, a condition in which the atria quiver instead of contracting rhythmically. In atrial fibrillation, the ventricles do not fill efficiently during diastole, but the condition is usually not immediately life-threatening on its own.

The QRS Complex

Next comes the **QRS complex**, a sharp, tall spike that represents **ventricular depolarization** — the electrical event that triggers **ventricular contraction** (ventricular systole). It is composed of three parts: the small downward **Q wave**, the tall upward **R wave**, and the following downward **S wave**. Because the ventricles contain much more muscle tissue than the atria, this electrical signal is stronger, faster, and more dramatic — truly the *star of the ECG show*.

The QRS complex corresponds to the movement of action potentials traveling from the **AV node**, down the **bundle of His**, through the **right and left bundle branches**, and out to the **Purkinje fibers** that spread the impulse through the ventricular walls. This rapid, coordinated wave of depolarization causes the ventricles to contract and pump blood forcefully into the **pulmonary trunk** and **aorta**.

Clinically, the QRS complex provides vital information about ventricular function. A wider, taller, or oddly shaped QRS may signal **ventricular hypertrophy**, **conduction abnormalities**, or a **myocardial infarction** (heart attack), all of which alter how the

depolarization wave travels through the heart muscle.

The T Wave

After the excitement of ventricular contraction, the **T wave** appears — a broad, rounded deflection that represents **ventricular repolarization**, or the electrical "reset" phase that prepares the ventricles for the next heartbeat. During this time, the ventricles relax and refill with blood, readying themselves for the next cycle of depolarization and contraction.

Interestingly, **atrial repolarization** is not seen as a distinctive wave, since it is hidden within the much larger QRS complex. The strong electrical signal generated by the ventricles effectively masks the smaller recovery wave from the atria, making it invisible on a standard ECG tracing.

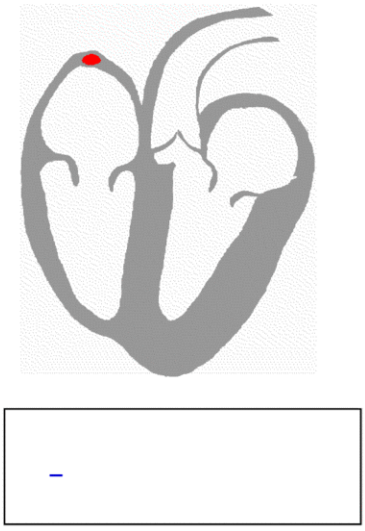


Figure 10.6.3: **Animation of a Normal ECG Wave**. The red lines represent the movement of the electrical signal through the heart.

Segments and Intervals

Beyond the main waves, the ECG also includes **segments** and **intervals**, which help clinicians understand the timing of cardiac events.

- A **segment** is the flat line between two waves.
- An **interval** includes one or more waves plus the connecting segment.

For example:

- The **P–R segment** extends from the end of the P wave to the beginning of the QRS complex and represents the brief pause as the electrical signal travels through the AV node.
- The **P–R interval**, which includes the P wave and the PR segment, measures the time between the start of atrial depolarization and the beginning of ventricular depolarization—about **0.16 seconds** in a healthy heart.

Another key measure is the **Q–T interval**, lasting roughly **0.35 seconds**, which represents the total time for the ventricles to depolarize and then repolarize — that is, the duration of ventricular contraction and recovery.

Timing the Contractions

Electrical activity always comes *before* the mechanical contraction of heart muscle. About **25 milliseconds** after the P wave begins, the atria start to contract. The ventricles follow suit shortly after, beginning their contraction near the **peak of the R wave** in the QRS complex.

Clinically, the **P–R interval** is one of the most important measurements on an ECG. It tells doctors how long it takes for an electrical impulse to travel from the atria to the ventricles. A longer or shorter PR interval can indicate problems with conduction — like a heart block or abnormal rhythm.

Quick Reference: Major ECG Waves and Intervals and their Functional Significance.

Wave / Interval	What It Represents	What's Happening in the Heart
P wave	Atrial depolarization	The atria contract, pushing blood into the ventricles.
QRS complex	Ventricular depolarization	The ventricles contract powerfully, sending blood to the lungs and body. Atrial repolarization happens here too but is hidden under the strong ventricular signal.
T wave	Ventricular repolarization	The ventricles reset electrically and prepare for the next beat.
P–R segment	Signal delay at AV node	The impulse pauses briefly to allow the ventricles to fill completely before they contract.
P–R interval	Atrial depolarization → start of ventricular depolarization	Measures how long it takes the signal to travel from the atria to the ventricles (about 0.16 seconds).
Q–T interval	Full cycle of ventricular activity	Time from the start of ventricular contraction to the end of repolarization (about 0.35 seconds).

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Decoding Disturbances: ECG Patterns of Arrhythmia

As mentioned above, ECGs provide a window into the electrical activity of the heart, allowing clinicians and scientists to identify disturbances in its normal rhythm known as **arrhythmias**. These disruptions arise when the heart's conduction system fails to generate or transmit impulses properly, resulting in beats that are too fast, too slow, or irregular. While some arrhythmias cause minimal physiological impact, others — such as ventricular fibrillation — can rapidly lead to circulatory collapse and cardiac arrest. Understanding how to interpret ECG patterns associated with different types of arrhythmias is therefore essential for diagnosing underlying conduction abnormalities and guiding appropriate clinical intervention.

Ventricular Fibrillation

When an ECG shows no identifiable P waves, QRS complexes, or T waves, it indicates **ventricular fibrillation (VF)** — a severe, life-threatening arrhythmia. During VF, the ventricles quiver rapidly and irregularly instead of contracting in a coordinated way. As a result, the heart cannot pump blood effectively and essentially acts as a mass of disorganized muscle activity.

Ventricular fibrillation leads to **sudden cardiac death within minutes** unless electrical resuscitation with an automated external defibrillator (AED) is performed immediately. VF often occurs in association with **myocardial infarction** or **heart failure** and is thought to result from **re-entry of action potentials** from the ventricular muscle back into the conduction pathway (such as the AV node), triggering rapid, chaotic impulses that prevent effective pumping.

Each tracing in the figure below shows a different type of **abnormal rhythm**. Some, like **partial or complete heart block**, interfere with the conduction of signals between the atria and ventricles. Others, such as **atrial or ventricular fibrillation**, involve chaotic electrical activity that prevents coordinated contraction. By examining how the P waves, QRS complexes, and T waves appear — or disappear — clinicians can identify the type of arrhythmia and predict how it affects the heart rate and the ability of the heart to pump blood effectively.

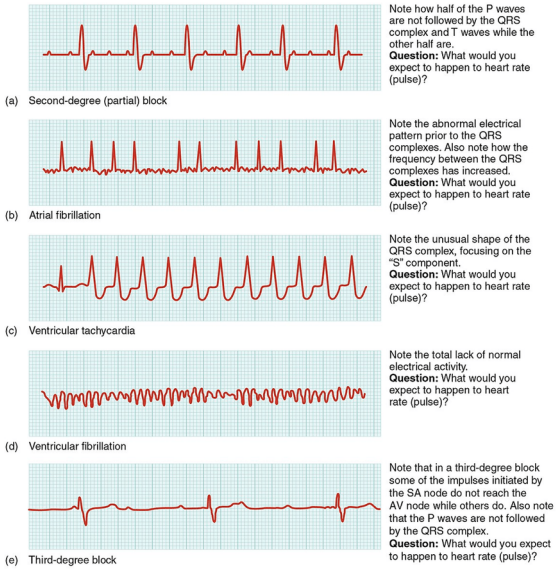


Figure 10.6.4: Electrocardiogram (ECG) Tracings demonstrating Five Distinct Types of Cardiac Arrhythmias. Review the accompanying descriptions and verify that each explanation corresponds appropriately to the pattern displayed.

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- 17.4B: Electrocardiogram and Correlation of ECG Waves with Systole by Boundless (now LumenLearning) is licensed CC BY-SA 4.0.

10.7: Cardiac Cycle

The cardiac cycle describes the heart's phases of contraction and relaxation that drive blood flow throughout the body.

Master this section and you'll be able to:

- Summarize the events of the cardiac cycle
- Compare atrial and ventricular systole and diastole
- Relate the ECG waves to the electrical and mechanical events of the cardiac cycle.
- Explain how pressure changes within the heart control valve opening and blood flow.

The **cardiac cycle** refers to the complete sequence of mechanical events that occur in the heart during one heartbeat. It begins with atrial contraction and concludes with ventricular relaxation. These mechanical events are initiated and regulated by the heart's electrical activity, as illustrated in the electrocardiogram (ECG), which displays a repeating pattern of waves — the P wave, QRS complex, and T wave — corresponding to distinct phases of cardiac excitation and recovery.

Heart rate is the term used to describe the frequency of the cardiac cycle.

The period of contraction that the heart undergoes while it pumps blood is called **systole**. The period of relaxation that occurs as the chambers fill with blood is called **diastole**. Both the atria and ventricles undergo systole and diastole, and it is essential that these components be carefully regulated and coordinated to ensure blood is pumped efficiently to the body.

Fluids, whether gases or liquids, are materials that **flow according to pressure gradients** — that is, they move from regions that are higher in pressure to regions that are lower in pressure. Accordingly, when the heart chambers are relaxed (diastole), blood will flow into the atria from the veins, which are higher in pressure. As blood flows into the atria, the pressure will rise, so the blood will initially move passively from the atria into the ventricles. When the action potential triggers the muscles in the atria to contract (atrial systole), the pressure within the atria rises further, pumping blood into the ventricles. During ventricular systole, pressure rises in the ventricles, pumping blood into the pulmonary trunk from the right ventricle and into the aorta from the left ventricle. Again, as you consider this flow and relate it to the conduction pathway, the elegance of the system should become apparent.

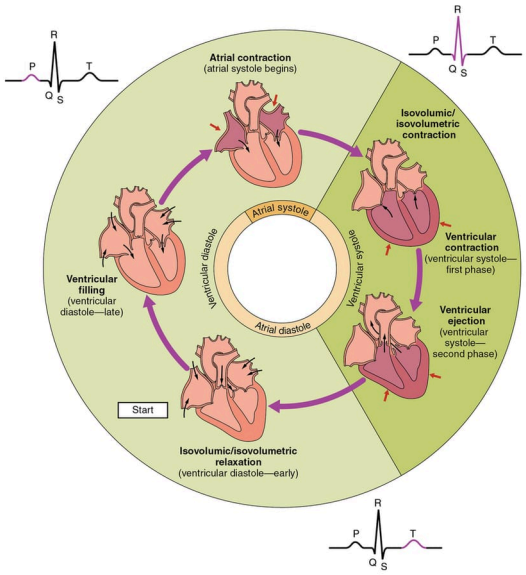
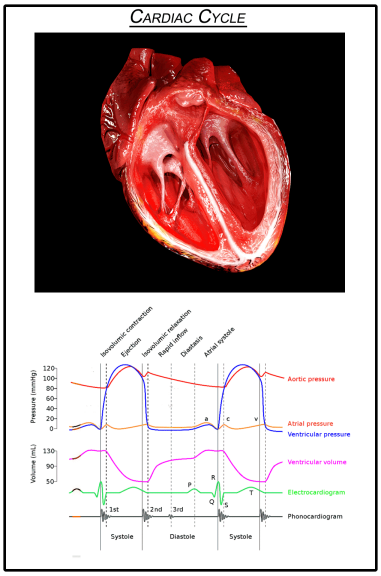


Figure 10.7.1: **Overview of the Cardiac Cycle.** The cardiac cycle begins with atrial systole and progresses to ventricular systole, atrial diastole, and ventricular diastole, when the cycle begins again. Correlations to the ECG are highlighted.

Interactive Element



Phases of the Cardiac Cycle

The **cardiac cycle** describes the complete sequence of events that occur in the heart during one heartbeat—from the beginning of atrial contraction to the end of ventricular relaxation. It includes alternating periods of contraction (*systole*) and relaxation (*diastole*) that move blood efficiently through the heart and into the circulation.

Ventricular and Atrial Diastole

At the start of the cycle, both the atria and ventricles are relaxed. Blood flows into the right atrium from the **superior and inferior venae cavae and the coronary sinus**, **and into the left atrium from the four pulmonary veins.** The atrioventricular (AV) valves — the tricuspid and mitra l— are open, allowing blood to passively flow into the ventricles. About 70–80 percent of ventricular filling occurs during this time. The pulmonary and aortic semilunar valves are closed, preventing any backflow into the ventricles.

Atrial Systole and Diastole

Depolarization of the atria (seen as the **P wave** on an ECG) triggers atrial contraction, or **atrial systole**. The atria contract from top to bottom, increasing pressure and pushing the remaining 20–30 percent of blood into the ventricles — this is known as the **atrial kick**. Atrial systole lasts about 100 milliseconds and ends just before ventricular contraction begins. The atria then relax and enter **atrial diastole**.

Ventricular Systole

Ventricular systole (represented by the **QRS complex** on the ECG) occurs in two phases and lasts about 270 milliseconds. At the start, the ventricles contain roughly 130 mL of blood, called the **end-diastolic volume (EDV)** or *preload*.

- **Isovolumic contraction phase:** The ventricles contract, pressure rises, and the tricuspid and mitral valves close, producing the **first heart sound (“lub”).** Because the semilunar valves remain closed, no blood leaves the heart, so ventricular volume remains constant.

- **Ventricular ejection phase:** Once ventricular pressure exceeds that in the pulmonary trunk and aorta, the semilunar valves open and blood is ejected. Both ventricles pump the same amount of blood, called the **stroke volume**, **typically 70–80 mL.** About 50–60 mL remain in the ventricle after contraction, known as the **end-systolic volume (ESV)**.

Ventricular Diastole

Ventricular relaxation follows repolarization of the ventricles, represented by the **T wave** on the ECG, and lasts about 430 milliseconds.

- **Isovolumic relaxation phase:** As the ventricles relax, pressure falls below that in the pulmonary trunk and aorta, causing the semilunar valves to close — producing the **second heart sound ("dup").** The AV valves remain closed, so ventricular volume does not change.
- **Late ventricular diastole:** As relaxation continues, ventricular pressure drops below atrial pressure. The tricuspid and mitral valves open, allowing blood to flow from the atria into the ventricles. Both chambers are again in diastole, the semilunar valves remain closed, and the cycle begins anew.

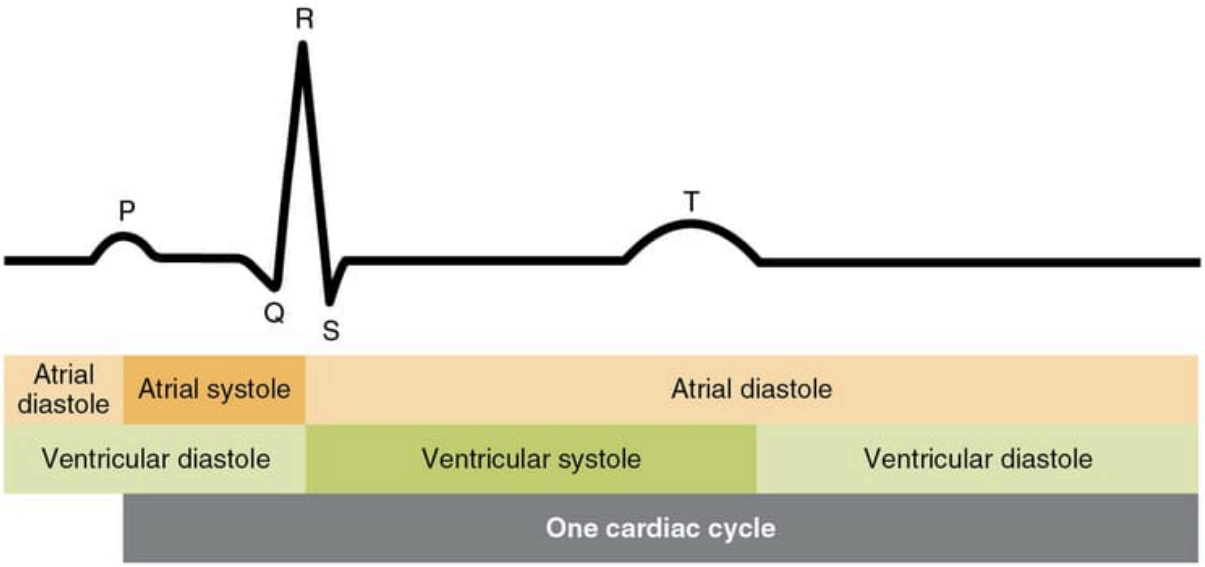


Figure 10.7.2: **Relationship between the Cardiac Cycle and ECG.** Initially, both the atria and ventricles are relaxed (diastole). The P wave represents depolarization of the atria and is followed by atrial contraction (systole). Atrial systole extends until the QRS complex, at which point, the atria relax. The QRS complex represents depolarization of the ventricles and is followed by ventricular contraction. The T wave represents the repolarization of the ventricles and marks the beginning of the ventricular relaxation.

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10.8: Heart Sounds

The two major heart sounds are “lub” (from the closure of AV valves) and “dub: (from the closure of aortic and pulmonary valves).

Master this section and you'll be able to:

- Describe how normal heart sounds (S_1 and S_2) are produced and what valve events correspond to each.
- Explain heart murmur as a common abnormal heart sound and explain what it indicates about cardiac function.



Listening to the heart is a simple, inexpensive, and informative way to assess cardiac function. Unlike the ECG, which records the heart’s electrical activity, this test relies on sound. You have already learned about the familiar “lub-dub” rhythm heard through a stethoscope. These sounds are not produced by the actual contractions of the heart but by the closing of its valves, which create vibrations in the blood and surrounding heart tissues.

Listening to heart sounds, a process called **auscultation**, allows clinicians to assess how effectively the valves are opening and closing and to detect abnormalities such as murmurs that may indicate turbulent blood flow or valve disease.

S1

The first heart sound, **S_1 (“lub”)**, occurs when the **atrioventricular (AV) valves — the tricuspid and mitral valves — close** following ventricular systole at the start of ventricular systole (contraction). There is a very slight split between the closure of the mitral and tricuspid valves, but it is not long enough to create multiple sounds.

S2

The second heart sound, **S_2 (“dub”)**, follows when the **semilunar valves — the aortic and pulmonary valves — close** as the ventricles relax at the beginning of diastole, following ventricular systole. S2 is split because aortic valve closure occurs before pulmonary valve closure. During inspiration (breathing in) there is slightly increased blood return to the right side of the heart, which causes the pulmonary valve to stay open slightly longer than the aortic valve. Due to this, the naming convention is to divide the second sound into two second sounds, A2 (aortic), and P2 (pulmonary). The time between A2 and P2 is variable depending on the respiratory rate, but the split is generally only prominent in children during inspiration. In adults and during expiration, the split is usually not long enough to suggest two sounds.

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Abnormal Heart Sounds

Abnormal heart sounds arise when normal cardiac flow or function is disrupted. **Heart murmurs** are the most common example, produced by **turbulent blood** flow through the heart or its valves. This turbulence often results from **valve abnormalities**:

- If a valve **fails to close completely,** blood leaks backward in a condition called ***regurgitation.***
- If it does not open fully, the narrowing is termed ***stenosis***.

Murmurs have a characteristic “whooshing” or “slosh” quality and are classified by their intensity (graded 1–6), pitch, configuration, location, and timing within the cardiac cycle.

Other abnormal heart sounds, such as **S3** and **S4**, are not caused by valve defects but by abnormal ventricular mechanics. An **S3** sound occurs just after the normal “lub-dub” and is linked to rapid ventricular filling in an overly compliant or weakened ventricle, often seen in heart failure. An **S4** sound occurs just before the “lub-dub” and results from forceful atrial contraction into a stiff or hypertrophied ventricle. These extra sounds generally indicate more significant cardiac dysfunction than typical murmurs.

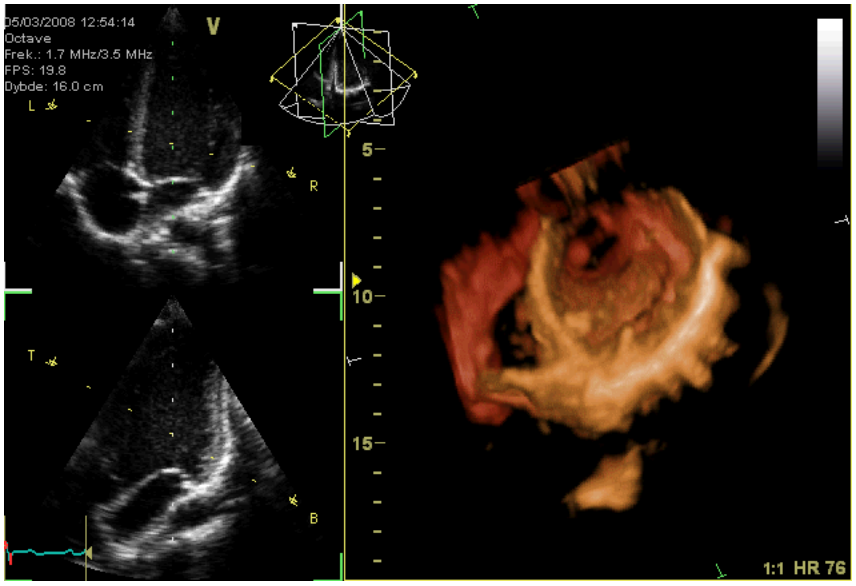


Figure 10.8.1: **Opening and Closing of Heart Valves**: The closing of the heart valves generates the “lub, dub” sounds that can be heard though a stethoscope.

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10.9: Blood Vessel Structure and Function

Blood vessels form a closed network of arteries, veins, and capillaries that transport blood throughout the body, allowing oxygen, nutrients, and wastes to be exchanged between the blood and tissues.

Master this section and you'll be able to:

- Differentiate among the structure of arteries, veins, and capillaries.
- Distinguish the locations of oxygen-rich and oxygen-poor blood in circulation.
- List the functions of blood vessels.

Blood vessels are essential components of both the systemic and pulmonary circulatory systems, forming the network that distributes blood throughout the body. There are three primary types of vessels, each specialized for its role in blood transport.

Arteries carry blood away from the heart under high pressure. They branch into smaller **arterioles**, which further divide into microscopic **capillaries**. Capillaries form vast networks that allow the exchange of gases, nutrients, and wastes between the blood and surrounding tissues — an exchange vital for maintaining homeostasis.

After exchange occurs, blood flows from the capillaries into small **venules**, which merge to form larger **veins** that return blood to the heart. Along the way, **anastomoses**—junctions where vessels interconnect — help provide alternate routes for blood flow in case of blockages or vessel damage.

Blood Vessel Structure

Different types of blood vessels vary in their structure according to their function, but they share a similar basic organization. Each vessel contains a **lumen**, the hollow central passageway through which blood flows. Surrounding the lumen are layers of tissue that help regulate blood flow and pressure. Arteries and arterioles have much thicker, more elastic, and muscular walls than veins and venules because they are located closer to the heart and must withstand the strong, pulsing pressure of blood being pumped out during each heartbeat. This structural reinforcement helps maintain their shape, giving arterial lumens a rounder appearance in cross section. In contrast, veins experience much lower pressure as they return blood to the heart, so their walls are thinner and their lumens often appear larger and more irregular in shape.

Structurally, **arteries and veins** share a similar design composed of **three distinct layers**, or **tunics**, that provide strength, elasticity, and control over vessel diameter.

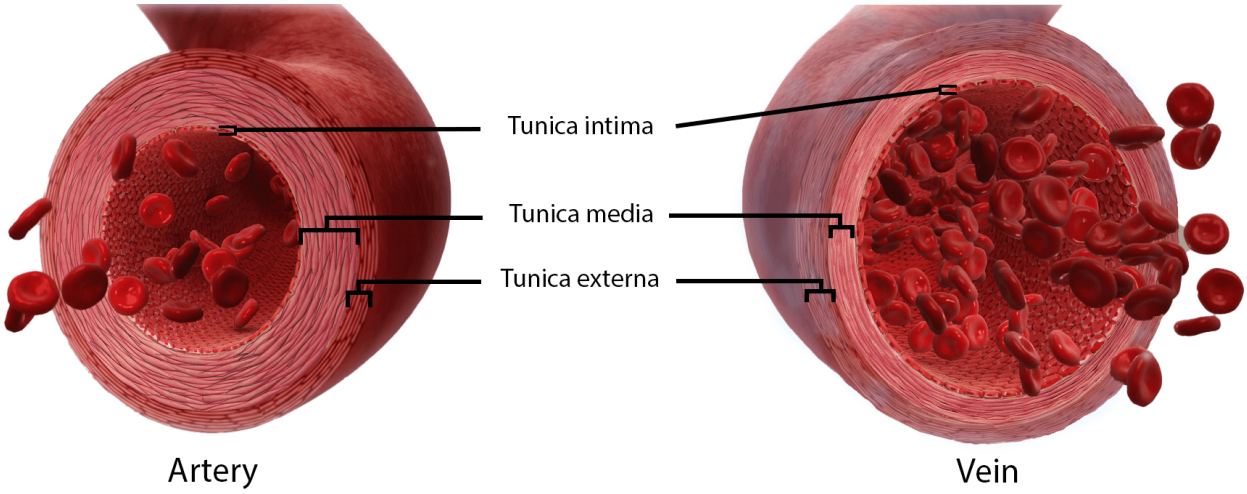
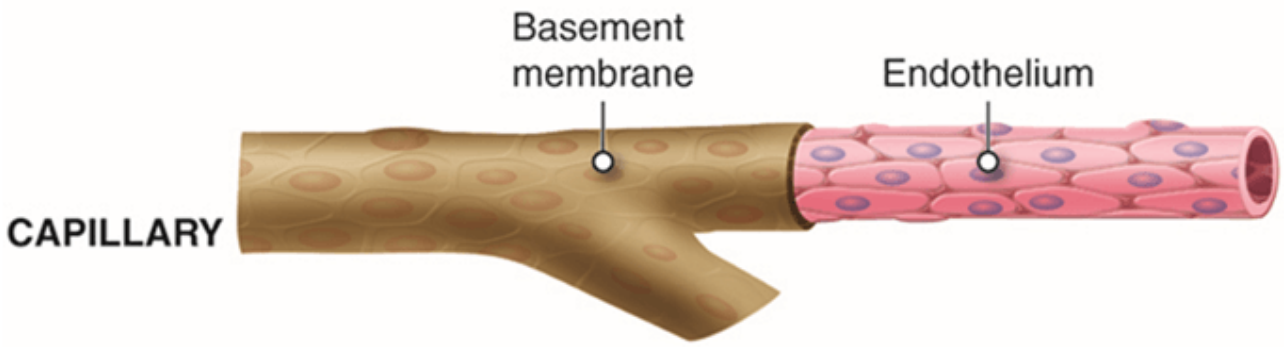


Figure 10.9.1: **Structure of Blood Vessel Wall.** The walls of arteries and veins share the same general features, but the muscular layer of arteries is much thicker because of the higher pressure of the blood that flows through them. *(Image Credit: "Tunics of Arteries and Veins" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

In contrast, **capillaries** consist of only a single layer of endothelial cells, allowing substances to move easily across their thin walls.



The Three Tunics

Tunica Intima

The **tunica intima** is the innermost and thinnest layer of a blood vessel. It is made up of a smooth sheet of **endothelial cells**, creating a friction-free surface so blood can flow easily. Beneath this layer lies a thin **subendothelial layer** of connective tissue for structural support. In small vessels such as arterioles and venules, this layer may be only a single cell thick, while in large arteries like the **aorta**, it can be much more substantial. The tunica intima is bordered by a delicate **elastic membrane** that helps the vessel stretch slightly with each heartbeat.

In **capillaries**, the structure is simplified to just this single layer of endothelial cells and a thin connective base — perfect for rapid exchange of gases, nutrients, and wastes.

Tunica Media

The **tunica media**, the middle layer, is the "**muscle**" of the vessel wall. It contains **smooth muscle cells**, **elastic fibers**, and **connective tissue** arranged in circular layers. This layer is **much thicker in arteries** than in veins because arteries must withstand and regulate the higher pressure of blood pumped from the heart.
By contracting or relaxing, the smooth muscle of the tunica media adjusts the **diameter** of the artery, which in turn helps regulate **blood pressure** and **blood flow**. Veins, on the other hand, have fewer elastic fibers and thinner walls since they operate under much lower pressure.

Tunica Externa

The **tunica externa** (also called the **tunica adventitia**) is the outermost protective layer. It is made mostly of **connective tissue fibers** that anchor the vessel to surrounding structures, preventing it from moving or collapsing. In veins, this layer tends to be **thicker**, offering added support and protection — especially because **many veins lie closer to the body's surface.** Larger vessels may also contain small blood vessels within this layer, called **vasa vasorum**, which literally means "vessels of the vessels."

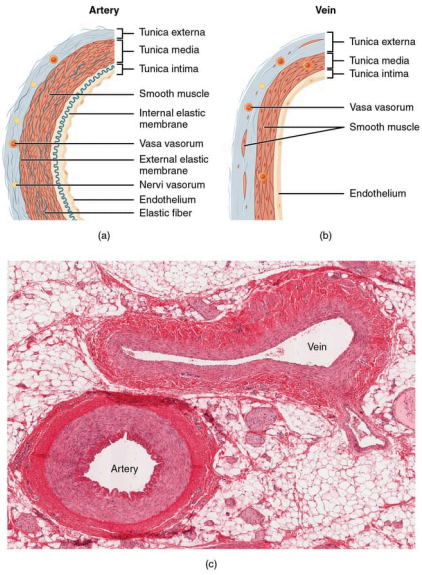


Figure 10.9.2: **Structure of Arteries and Veins.**
(a) Arteries have thick, elastic walls with a prominent tunica media of smooth muscle and elastic fibers that maintain high pressure as blood flows away from the heart.
(b) Veins have thinner walls, less smooth muscle and elasticity, and a larger lumen, allowing them to expand easily as they return blood to the heart.
(c) In the micrograph, the artery appears round with a thick wall, while the vein has a thinner wall and an irregular lumen. (Image credit: OpenStax, CC BY 4.0.)

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Structural Comparison of Arteries, Veins, and Capillaries

Feature	Arteries	Veins	Capillaries
General appearance	Thick walls with small lumens; usually appear rounded in cross-section.	Thin walls with large lumens; often appear flattened or irregular in shape.	Single-cell tube the width of one RBC.
Tunica intima	Endothelium usually appears wavy due to constriction of smooth muscle. Internal elastic membrane present in larger vessels.	Endothelium appears smooth. Internal elastic membrane often absent.	Single layer of endothelial cells: ideal for diffusion.
Tunica media	Thickest layer; composed of smooth muscle and abundant elastic fibers to withstand and regulate high pressure. Nervi vasorum and vasa vasorum (small nerves and blood vessels) present.	Thinner than in arteries; fewer elastic fibers and less smooth muscle since veins operate under low pressure. Nervi vasorum and vasa vasorum present.	**Absent**

Feature	Arteries	Veins	Capillaries
Tunica externa	Thinner than the tunica media. Collagen and elastic fibers provide structural support. Nervi vasorum and vasa vasorum present	Thickest layer; composed mainly of connective tissue that protects and anchors veins, preventing collapse. Nervi vasorum and vasa vasorum present	**Absent** — replaced by a thin basement membrane.

Valves

A key structural difference between arteries and veins is the presence of valves. Arteries carry blood under high pressure from the heart, which prevents backflow. After blood passes through the capillaries, pressure drops, making backflow possible in veins. To prevent this, veins contain one-way valves that ensure blood flows only toward the heart.

Blood Vessel Function

Blood vessels form a vast network that transports blood throughout the body, ensuring that **oxygen, nutrients, hormones**, and **immune cells reach every tissue** while **carrying away carbon dioxide and other metabolic wastes.** Together, arteries, veins, and capillaries keep the body's internal environment stable and supplied.

Arteries

Arteries carry blood **away from the heart**, usually rich in oxygen — except for the **pulmonary arteries**, which carry oxygen-poor blood to the lungs. Their thick, muscular, and elastic walls allow them to withstand the high pressure created by the heart's pumping action.

As arteries branch into smaller **arterioles**, smooth muscle in their walls can constrict or relax to regulate **blood flow** and **pressure**, directing blood where it is most needed.

Veins

Veins return blood **toward the heart**, usually low in oxygen — except for the **pulmonary veins**, which carry freshly oxygenated blood from the lungs. Veins have **thinner, more flexible walls** than arteries and can hold a larger volume of blood, acting as **reservoirs** (a property known as *capacitance*).

Because blood in veins moves under lower pressure, many veins — especially in the arms and legs — contain **valves** that prevent backflow and help blood move upward toward the heart despite gravity.

Capillaries

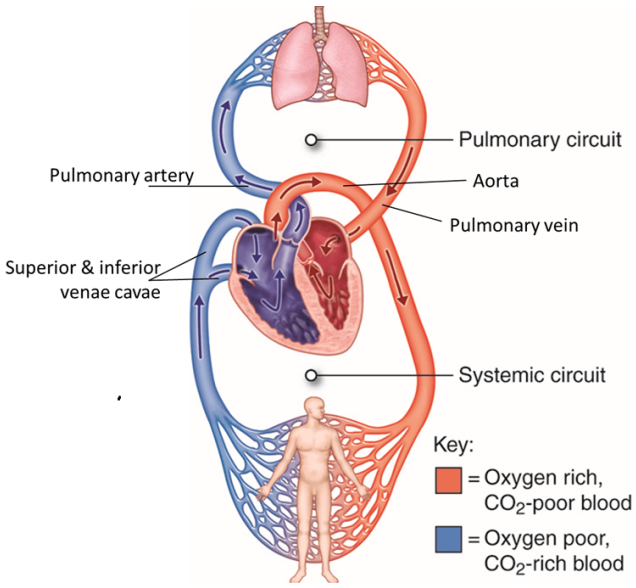
Capillaries are the tiniest blood vessels, forming a delicate network that connects arterioles and venules. Each capillary is a **single-cell-thick tube** made of endothelial cells, perfectly designed for **exchange**. Oxygen, nutrients, and hormones pass from the blood into surrounding tissues, while carbon dioxide and wastes move in the opposite direction. This continuous exchange keeps every cell nourished and functional.

Gas Transfer and Circulatory Pathways

The circulatory system is divided into two interconnected circuits: the **systemic circulation** and the **pulmonary circulation**.

In the **systemic circulation**, blood leaves the **left ventricle** through the **aorta**, carrying **oxygen-rich blood** (about 95–100% oxygen) to all body tissues. Within the **capillary networks**, gas exchange occurs — oxygen diffuses into tissues, while carbon dioxide, a waste product of cellular respiration, diffuses into the blood. The now **oxygen-poor blood** (about 75% oxygen) returns through the **venules** and **veins** to the **right atrium** of the heart.

The **pulmonary circulation** then reoxygenates this blood. From the **right ventricle**, blood travels through the **pulmonary arteries** — the only arteries in the body that carry **deoxygenated blood** — to the **lungs**. There, the capillaries surrounding the thin-walled **alveoli** allow for the rapid release of carbon dioxide and uptake of oxygen. The freshly oxygenated blood then returns to the **left atrium** through the **pulmonary veins** — the only veins that carry **oxygenated blood** — completing the circuit.



Key Point

Arteries and veins are defined not by their oxygen content but by the **direction of blood flow**:

- **Arteries** always carry blood *away* from the heart.
- **Veins** always carry blood *toward* the heart.

Figure 10.9.3: **Pulmonary and Systemic Circulation.** This diagram shows the dual circulatory pathways of the human cardiovascular system. The **pulmonary circuit** (shown in blue) carries oxygen-poor, carbon dioxide–rich blood from the right side of the heart to the lungs, where gas exchange occurs. The **systemic circuit** (shown in red) transports oxygen-rich, carbon dioxide–poor blood from the left side of the heart through the aorta to the body's tissues. After delivering oxygen and nutrients, blood returns to the heart through systemic veins to repeat the cycle. *(Image credit: modification of work by OpenStax, licensed under CC BY 4.0.)*

Additional Functional Highlights

- Blood vessels **help regulate blood pressure** by contracting or relaxing — **vasoconstriction** and **vasodilation** — which adjusts the resistance to blood flow.
- They are involved in **thermoregulation**, directing blood flow to the skin for heat loss or retaining it to preserve warmth. This allows for the maintenance of a constant internal temperature of an organism independent of the temperature of the environment.

- Blood vessels play a role in **distributing immune cells and clotting factors** as part of the body's defense and repair systems.
- They **support homeostasis** by participating in regulation of **pH**, **fluid balance**, and **hormone deliveries**.

These functions make blood vessels much more than mere "pipes" — they are active, responsive components of cardiovascular health critical for survival and emergency medical response.

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10.10: Circulatory Pathways

The circulatory pathways form a connected network that ensures continuous blood flow through the pulmonary, systemic, and coronary circuits to deliver oxygen and nutrients throughout the body.

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

- Describe the overall organization of the pulmonary and systemic circuits and trace the general pathway of blood through each.
- Identify the major divisions of the aorta and explain how the names of arteries and veins change as they pass anatomical landmarks.
- Explain what an *anastomosis* is and describe the function of the Circle of Willis as an example of an arterial anastomosis.

Organization of the Circulatory Pathways

As you explore the vessels of the pulmonary and systemic circuits, you will notice that many arteries and veins share the same names. Those with identical names typically run side by side and are found on both the right and left sides of the body.

Some vessels, however, are unpaired or differ in branching patterns. For example, there are right and left femoral arteries and veins, but only one aorta in the midline of the body. Likewise, certain superficial veins, such as the great saphenous vein of the leg, have no arterial counterpart.

Another detail to keep in mind is that vessel names often change as they pass anatomical landmarks — much like a road that changes names at a city boundary. For instance, the left subclavian artery becomes the axillary artery as it enters the armpit (axilla) and then the brachial artery as it travels down the upper arm (brachium).

Finally, you will come across **anastomoses**, which are connections where two blood vessels that had separated join together again. These are especially common in veins, providing alternate routes for blood flow if one pathway becomes blocked. Some important arterial anastomoses also occur in the brain, ensuring continuous blood supply to this vital organ. A well-known example of an arterial anastomosis is the **Circle of Willis**, a ring-shaped network of arteries located at the base of the brain. It connects the major arteries supplying the brain — the internal carotid arteries (from the front) and the basilar artery (from the back) — forming a circular pathway. This arrangement allows blood to be rerouted if one part of the brain's blood supply becomes narrowed or blocked, helping to maintain consistent delivery of oxygen and nutrients.

In short, the Circle of Willis acts like a "traffic roundabout" for cerebral circulation, ensuring that blood can still reach all areas of the brain even if one route is compromised.

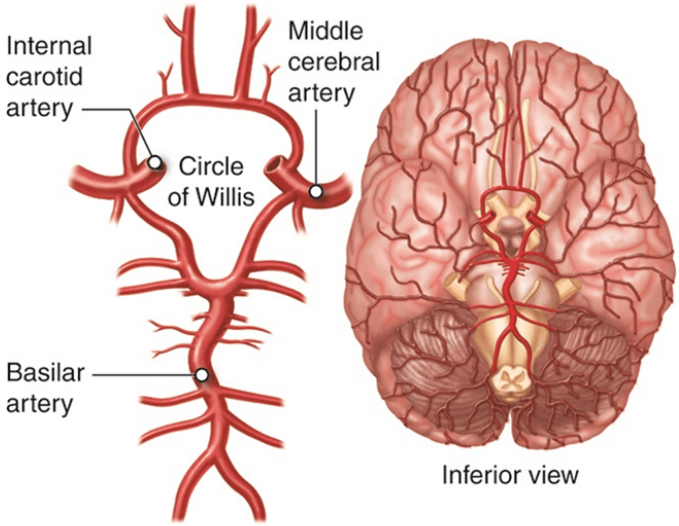


Figure 10.10.1: **Circle of Willis and Associated Arteries.** This circular network of arteries located at the base of the brain connects the internal carotid, the middle cerebral, and the basilar arteries. This arterial anastomosis provides multiple routes for blood to reach brain tissue, helping to maintain cerebral perfusion even if one vessel becomes blocked. The internal carotid arteries supply the anterior portion of the circle, while the basilar artery contributes posteriorly. Branches such as the middle cerebral arteries distribute blood to the cerebral hemispheres.

Overview of Systemic Circulation

Blood relatively high in oxygen concentration is returned from the pulmonary circuit to the left atrium via the four pulmonary veins. From the left atrium, blood moves into the left ventricle, which pumps blood into the aorta. The aorta and its branches — the systemic arteries — send blood to virtually every organ of the body.

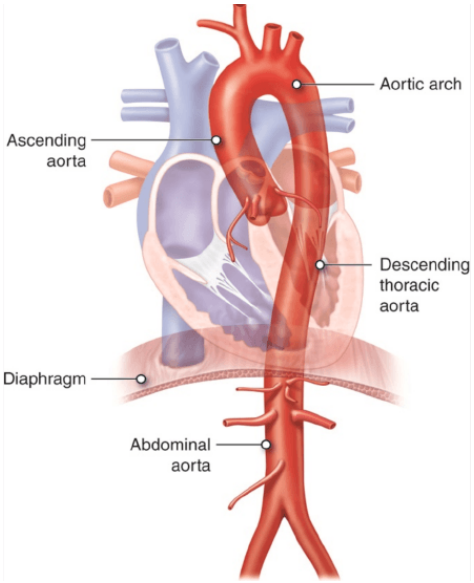


Figure 10.10.2: **Parts of Aorta in Relation to Heart and Diaphragm.** The ascending aorta, aortic arch, descending (thoracic) and abdominal aorta are shown. *(Image Credit: "OLI - Drawing Parts of aorta in relation to heart and diaphragm - English labels" by Open Learning Initiative, license: CC BY-NC-SA)*

The Aorta

The **aorta** is the largest artery in the body. It arises from the left ventricle and curves downward through the chest and abdomen before dividing into the two common iliac arteries at about the level of the fourth lumbar vertebra. The aorta has three main

regions: the **ascending aorta**, the **aortic arch**, and the **descending aorta**, which passes through the diaphragm and continues as the **abdominal aorta**. The aortic valve at its base prevents blood from flowing backward into the left ventricle during relaxation.

The **ascending aorta** extends upward for about 5 cm from the heart, then it curves to the left, forming the **aortic arch**. The arch then turns downward and becomes the **descending aorta**, which travels along the vertebral column. As it passes through the diaphragm at the **aortic hiatus**, it transitions into the **abdominal aorta**, which ultimately splits into the **right and left common iliac arteries**. Arteries branching from the aorta deliver oxygenated blood to nearly every organ and tissue of the body.

As you read about the circular pathways of blood flow, you may notice that some large arteries are referred to as *trunks*. The term *trunk* indicates a major vessel that branches into several smaller arteries. For example, the **celiac trunk** gives rise to the left gastric, common hepatic, and splenic arteries.

To help visualize the organization of the circulatory system, imagine taking a "Voyage of Discovery" like Lewis and Clark's 1804–1806 expedition. Picture yourself traveling by boat through a vast network of rivers and streams, charting each branch as it flows into smaller and smaller tributaries. In much the same way, you can trace the pathways of blood through the body's arterial and venous branches.

For this course, we will focus on only a few of the major routes of blood flow and name only the most important arteries and veins. Interestingy, circulation patterns can vary slightly from person to person. For example, a common variation in circulation patterns is found in the **Circle of Willis**. In many people, one or more of the communicating arteries may be smaller than usual or even absent. Despite these differences, blood flow to the brain is usually unaffected because the circle provides alternate routes for circulation if one part becomes narrowed or blocked.

Another frequent variation occurs in the **branches of the aortic arch**. While the typical pattern includes three branches — **the brachiocephalic trunk, left common carotid artery, and left subclavian artery** — some individuals have only two, because the left common carotid shares a common origin with the brachiocephalic trunk. These differences are normal and usually have no effect on health.

Table* 10.10.1*: Components of the Aorta

Vessel	Description
Aorta	Largest artery in the body, originating from the left ventricle and descending to the abdominal region, where it bifurcates into the common iliac arteries at the level of the fourth lumbar vertebra; arteries originating from the aorta distribute blood to virtually all tissues of the body
Ascending aorta	Initial portion of the aorta, rising superiorly from the left ventricle for a distance of approximately 5 cm
Aortic arch	Graceful arc to the left that connects the ascending aorta to the descending aorta; ends at the intervertebral disk between the fourth and fifth thoracic vertebrae
Descending aorta	Portion of the aorta that continues inferiorly past the end of the aortic arch; subdivided into the thoracic aorta and the abdominal aorta
Thoracic aorta	Portion of the descending aorta superior to the aortic hiatus
Abdominal aorta	Portion of the aorta inferior to the aortic hiatus and superior to the common iliac arteries

Aortic Arch Branches

There are three major branches of the aortic arch: the brachiocephalic artery, the left common carotid artery, and the left subclavian (literally "under the clavicle") artery. As you would expect based upon proximity to the heart, each of these vessels is classified as an elastic artery.

The **brachiocephalic artery (or trunk)** is located only on the right side of the body; there is no corresponding artery on the left. The brachiocephalic artery branches into the **right subclavian artery** and the **right common carotid artery**. The **left**

subclavian and **left common carotid arteries** arise independently from the aortic arch but otherwise follow a similar pattern and distribution to the corresponding arteries on the right side (see Figure 10.10.6). Each **subclavian artery** supplies blood to the arms, chest, shoulders, back, and central nervous system.

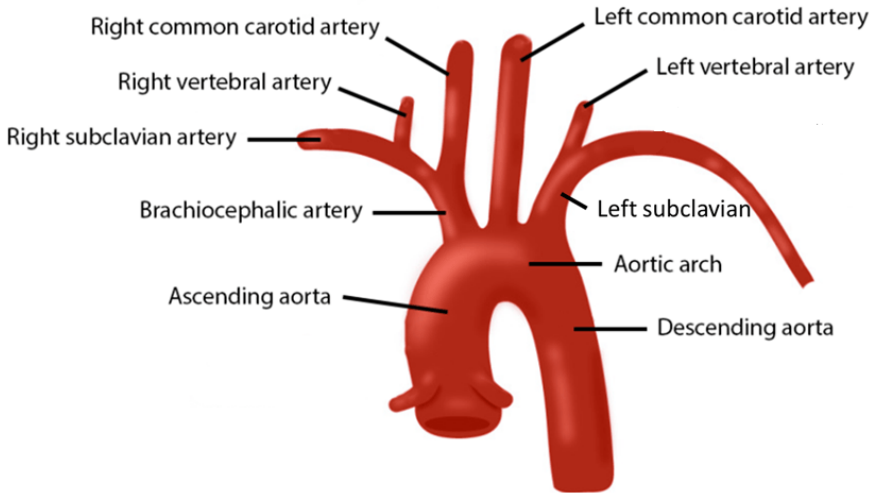


Figure 10.10.3: **Branches of the Aortic Arch.** The aortic arch gives rise to three large branches: the brachiocephalic artery (or trunk), the left common carotid artery, and the left subclavian artery. *(Image Credit: "Aortic Arch and Main Branches" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of "Palmer - Drawing Aortic arch - English labels" by Beckie Palmer, © StatPearls Publishing LLC, license: CC BY.)*

Major Systemic Blood Vessels

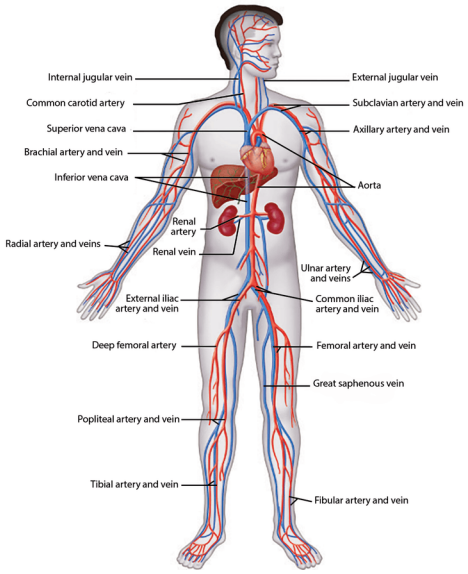


Figure 10.10.4: **Large Arteries and Veins.** The largest arteries and vessels in the body are depicted here. Branches of these vessels are showing in later images in this section. *(Image Credit: "C_M3_26.jpg" by Cenveo is licensed under CC BY 3.0, image from the OLI Repository, modifications by Jennifer Lange.)*

Pulmonary Circulation

Blood returning from the systemic circuit enters the **right atrium** through the **superior and inferior venae cavae** and the **coronary sinus**, which drains blood from the heart muscle itself. This blood is **low in oxygen** and **high in carbon dioxide**, since

oxygen has been used by body tissues and carbon dioxide has been picked up as a waste product.

From the right atrium, blood flows into the **right ventricle**, which pumps it into the **pulmonary circuit** — the pathway to and from the lungs.

The **pulmonary trunk** carries blood away from the right ventricle. At its base is the **pulmonary semilunar valve**, which prevents blood from flowing backward during relaxation. The trunk quickly divides into the **right and left pulmonary arteries**, which carry blood to each lung. Within the lungs, these arteries branch into smaller arterioles and **pulmonary capillaries** that surround the **alveoli**, where **gas exchange** occurs: carbon dioxide leaves the blood and oxygen enters.

The newly oxygenated blood then travels through **pulmonary venules** and larger **pulmonary veins**—two from each lung—that return it to the **left atrium**. The pulmonary circuit ends here, ready for the oxygen-rich blood to enter the systemic circuit.

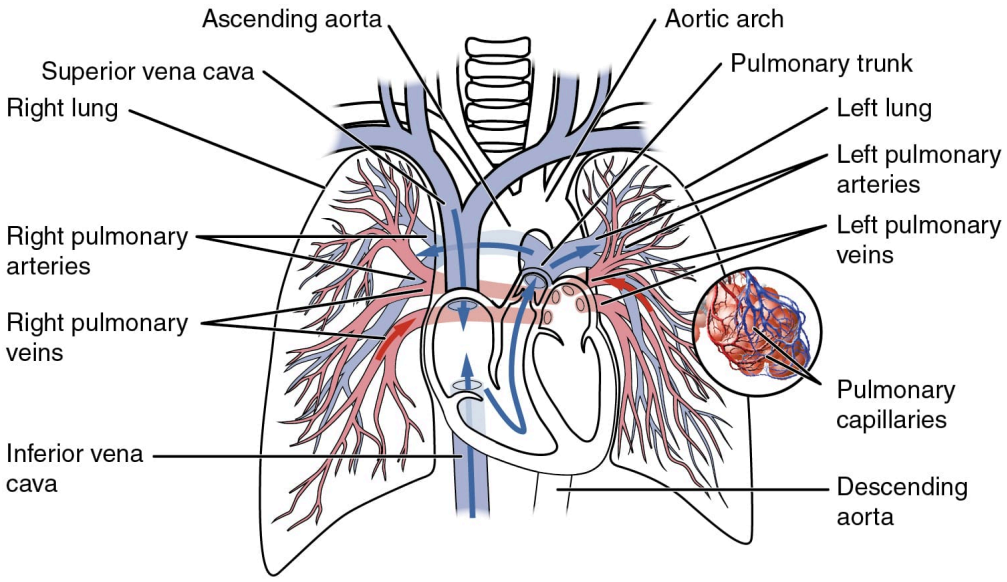


Figure 10.10.5: **Pulmonary Circuit.** Blood exiting from the right ventricle flows into the pulmonary trunk, which bifurcates into the two pulmonary arteries. These vessels branch to supply blood to the pulmonary capillaries, where gas exchange occurs within the lung alveoli. Blood returns via the pulmonary veins to the left atrium. (Image credit: "Pulmonary Circuit" by OpenStax is licensed under CC BY 3.0)

Table** 10.10.1**: Pulmonary Arteries and Veins

Vessel	Description
Pulmonary trunk	Single large vessel exiting the right ventricle that divides to form the right and left pulmonary arteries
Pulmonary arteries	Left and right vessels that form from the pulmonary trunk and lead to smaller arterioles and eventually to the pulmonary capillaries
Pulmonary veins	Two sets of paired vessels — one pair on each side—that are formed from the small venules, leading away from the pulmonary capillaries to flow into the left atrium

Coronary Circulation

The coronary arteries and veins encircle the heart like a crown, supplying the heart muscle with its own blood supply. The first branches of the ascending aorta are the right and left coronary arteries, which originate just above the aortic semilunar valve. These vessels deliver oxygen-rich blood to the myocardium so it can keep contracting effectively.

The **left anterior descending (LAD) artery** is the most commonly blocked vessel during a heart attack, followed by the **right coronary artery (RCA)** and the **left circumflex artery (LCX)**. The LAD is especially critical because it supplies blood to a large portion of the heart's main pumping chamber (the left ventricle). When this artery becomes blocked, the damage can be severe

and sometimes fatal, which is why it is often referred to as the “widowmaker.”

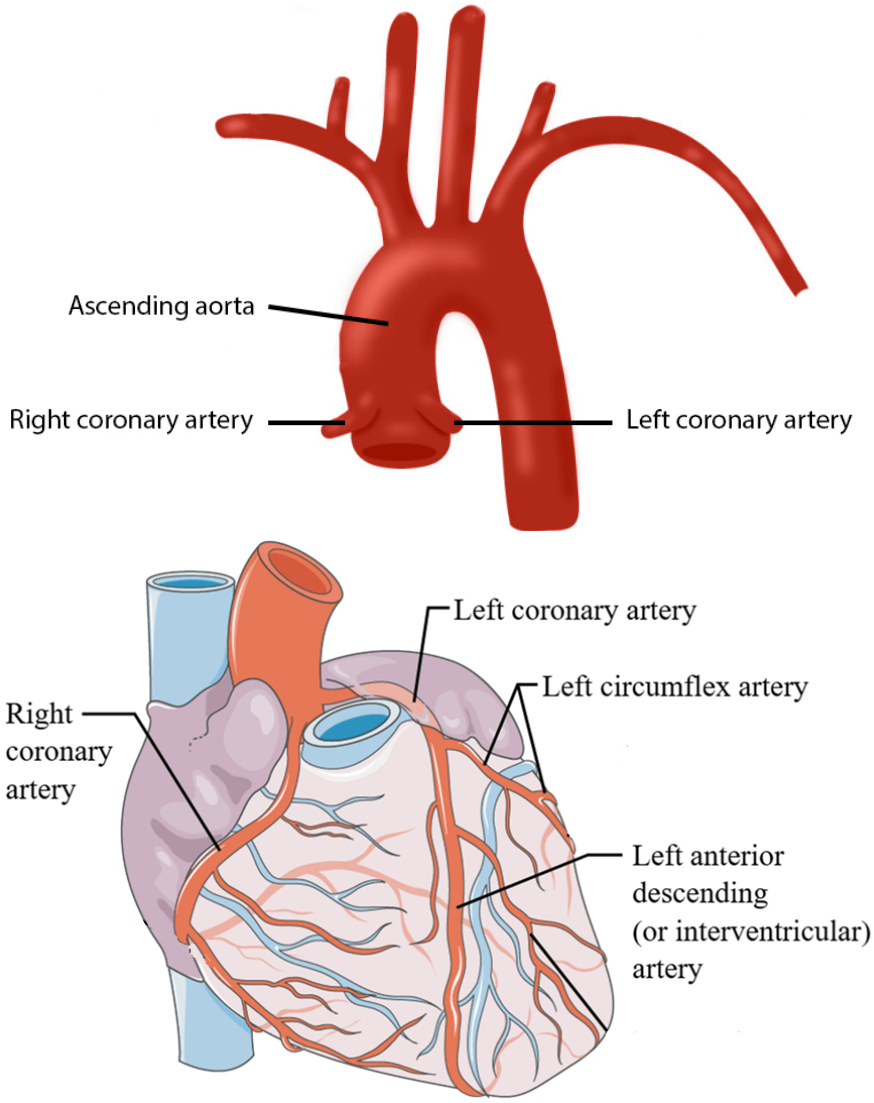


Figure 10.10.6: **Aorta and Coronary vessels.** *Image on the left:* The first two arteries to branch off the the aorta are the right and left coronary arteries. *(Image Credit: "Aorta and Coronary Arteries" by Jennifer Lange is licensed under CC BY-NC-SA 4.0*, modification of "*Palmer - Drawing Aortic arch - English labels" by Beckie Palmer, © StatPearls Publishing LLC, license: CC BY.) Image on the right:* Major vessels include the right and left coronary arteries, the anterior and posterior interventricular arteries, and the circumflex artery. *https://commons.wikimedia.org/wiki/F...d_arteries.svg*

The **left coronary artery** is short. It passes posterior to the pulmonary trunk and, upon emergence, splits into the **anterior interventricular artery** and the **circumflex artery**. The anterior interventricular artery travels toward the inferior margin of the heart in the anterior interventricular sulcus. The circumflex artery travels in the left atrioventricular sulcus to the posterior side of the heart. Along the way it gives off the **left marginal artery** to the lateral side of the left ventricle. The **great cardiac vein** travels first with the anterior interventricular artery and then with the circumflex artery. On the posterior surface it joins with other branches and becomes the **coronary sinus**.

Blood Collection

Venipuncture is the process of inserting a needle into a vein to draw blood or start an IV. It may sound routine, but it is one of the most valuable diagnostic tools in medicine — a quick snapshot of what is happening inside the body. Performed by trained professionals such as nurses or phlebotomists, venipuncture allows clinicians to assess how well the blood carries oxygen, how the immune system is responding, and whether the body's clotting mechanisms are functioning properly. It can also reveal important details about metabolism, hydration, and kidney health, making this simple procedure a key step in understanding a patient's overall condition.



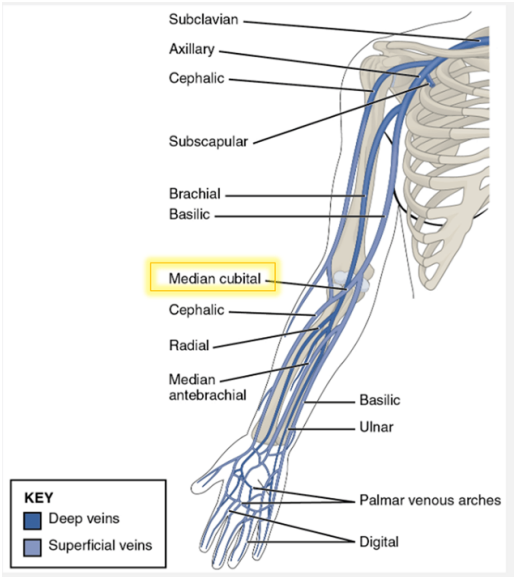


Figure 10.10.7: **Venipuncture for Blood Collection.** A healthcare professional performs *venipuncture* — the process of inserting a sterile needle into a vein, typically in the antecubital fossa (inner elbow)—to collect a blood sample for laboratory testing. The sample tubes fill as venous pressure drives blood into the collection system. *Image credit: "Venipuncture" by Infusion Nurses Society, CC BY-SA 4.0 via Wikimedia Commons.*

The most frequently used vein is the **median cubital vein**, located in the antecubital fossa (the bend of the elbow). This vein is preferred because it is typically large, close to the skin's surface, and less likely to move during puncture.

Check out these videos on Arteries, Veins, and Their Names.

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10.11: Portal Systems

Portal systems are special circulatory pathways in which blood flows through two capillary beds in sequence, allowing precise processing, regulation, and communication before returning to the heart.

Master this section and you'll be able to:

- Describe what a portal system is and how it differs from typical circulation.
- Identify the pathway and function of the hepatic portal system.
- Identify the pathway and function of the hypophyseal portal system.
- Summarize why portal systems are important for homeostasis.

Introduction to Portal Systems in the Human Body

In most circulatory pathways, blood flows from the heart to an artery, then into progressively smaller vessels until it reaches the capillaries of a target organ. After exchanging gases, nutrients, and waste products, the blood moves into veins and returns directly to the heart. **Portal systems are an important exception to this pattern.**

A **portal system** is a special circulatory pathway in which **blood travels through two separate capillary beds before returning to the heart**. These two capillary regions are connected by a unique vein known as **portal vein**. By passing through a second capillary network, the blood can undergo an additional round of filtration, modification, or hormone release before re-entering general circulation.

Portal systems are rare in the body, but where they occur, they perform functions that are essential for homeostasis, metabolism, growth, and endocrine regulation.

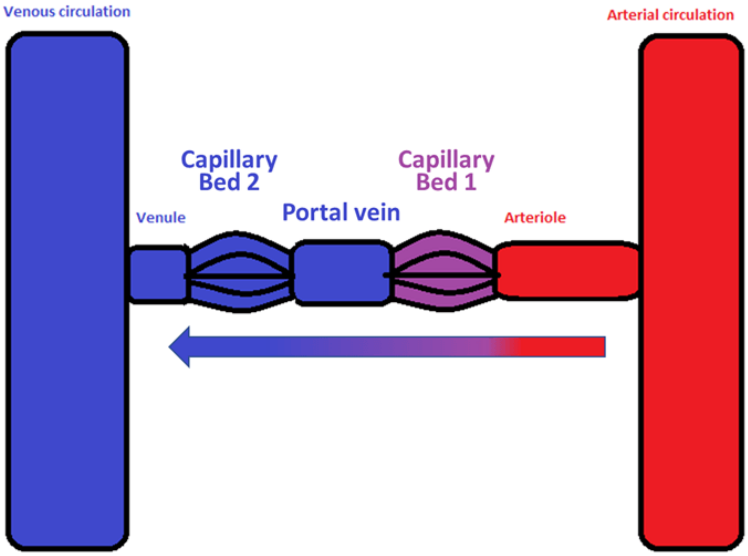


Figure 10.11.1: **Structure of a Portal System.** A portal system routes blood through **two sequential capillary beds** before returning it to the general venous circulation. Blood begins in the **arterial circulation** (right, red), flows through an **arteriole** into **Capillary Bed 1**, and then enters a **portal vein** instead of heading directly back to the heart. The portal vein delivers this blood to **Capillary Bed 2**, allowing a second opportunity for exchange. Only after passing through this second capillary network does the blood enter a **venule** and return to the **venous circulation** (left, blue). Portal systems allow substances picked up in the first capillary bed to be delivered at high concentration directly to the second bed without dilution in the general circulation.

Why Portal Systems Exist

Portal systems create a controlled route for substances to move directly from one region to another **without first being diluted in the systemic circulation**. This "shortcut" ensures that certain organs receive blood that is:

- **Rich in nutrients** (after digestion)
- **Rich in hormones** (before systemic dilution)
- **Ready for detoxification or processing**
- **Optimally concentrated for communication between organs**

The key idea is **direct delivery**. Instead of sending blood back to the heart and then out to the entire body, portal systems allow local responses that are **faster**, **more efficient**, and **more tightly regulated**.

Here is an analogy: Imagine a two-step security system at an airport. Passengers (blood components) first go through **one checkpoint** (first capillary bed). Then instead of boarding the plane immediately, they go through a **second checkpoint** (second capillary bed) for more specific screening or processing.

Portal systems work exactly like this: two checkpoints before returning to general circulation.

Two Major Portal Systems in the Human Body

1. Hepatic Portal System

The hepatic portal system is a special circulatory pathway that carries blood **from the digestive organs directly to the liver** before that blood reenters the main circulation. Veins from the stomach, intestines, pancreas, and spleen merge to form the hepatic portal vein, which delivers nutrient-rich blood to the liver so it can process nutrients, remove toxins, and filter out any bacteria absorbed from the gut.

Overall pathway:
Capillaries of digestive organs → **hepatic portal vein** → **liver sinusoids** → **hepatic veins** → inferior vena cava → heart.

Inside the liver, the incoming blood enters large, leaky capillaries called **sinusoids**, where liver cells rapidly absorb nutrients and detoxify substances. **Kupffer cells**, the liver's resident immune cells, remove bacteria and debris. The liver receives most of its blood (about 75 percent) from the hepatic portal vein, while the **hepatic artery** supplies oxygen-rich blood needed to support the liver's high metabolic activity.

After the liver finishes processing and cleaning the blood, it drains into the hepatic veins and then into the inferior vena cava on its way back to the heart.

Function:
To deliver nutrient-rich blood from the digestive tract to the liver for processing.

Why it matters:
The hepatic portal system ensures that the liver is the first organ to handle nutrients, toxins, drugs, and microbes absorbed during digestion. This allows the liver to regulate blood glucose, detoxify chemicals, metabolize medications, and filter out harmful organisms before the blood reaches the rest of the body.

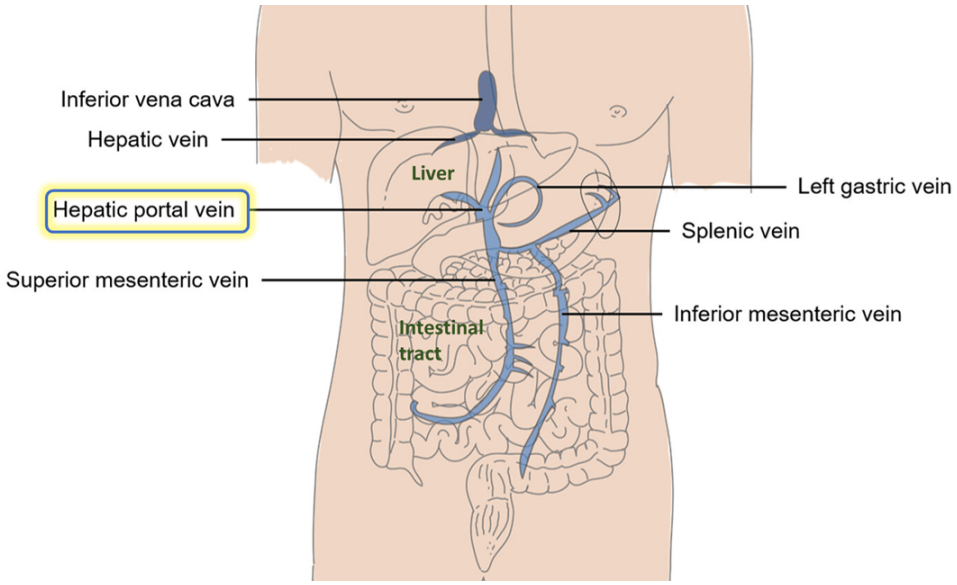


Figure 10.11.2: **Hepatic Portal System.** Major veins that drain the digestive organs (stomach, intestines, and spleen) merge to form the hepatic portal vein, which delivers nutrient-rich blood directly to the liver. There, nutrients and other absorbed substances are processed, stored, detoxified, or converted before the blood exits through the hepatic veins and enters the inferior vena cava.

2. Hypophyseal (Pituitary) Portal System

This portal system is part of the endocrine system and links the **hypothalamus** to the **anterior pituitary gland**.

Function:
To transport hypothalamic hormones directly to the anterior pituitary without dilution, allowing precise control of hormone release.

Pathway Overview:
Capillaries in the hypothalamus → **hypophyseal portal veins** → capillaries in the anterior pituitary → systemic veins → heart.

Why it matters:
This system allows the hypothalamus to precisely regulate anterior pituitary hormones (such as ACTH, TSH, LH, FSH, GH, and prolactin) using extremely small concentrations of releasing or inhibiting hormones.

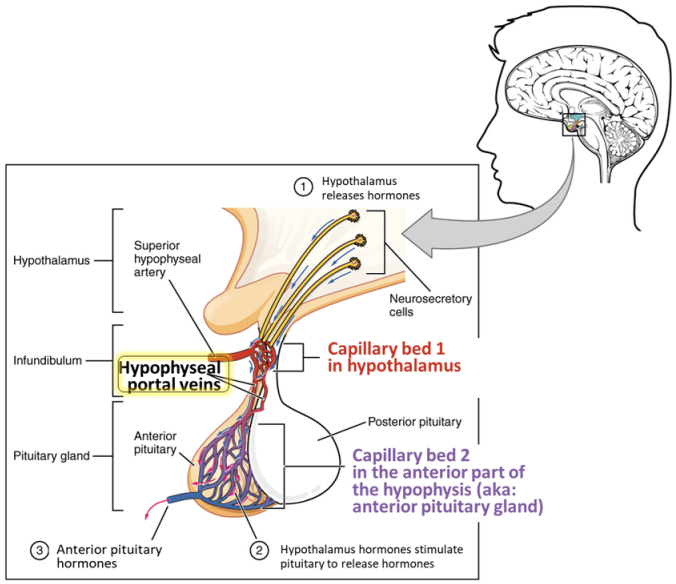


Figure 10.11.3: **Hypophyseal Portal System.** This portal system links the hypothalamus and anterior pituitary. Neurosecretory cells release regulatory hormones into the first capillary bed, and these travel through the hypophyseal portal veins directly to the second capillary bed in the anterior pituitary. There, they control the release of specific pituitary hormones. This arrangement provides rapid, targeted communication between the brain and endocrine system.

Physiological Importance of Portal Systems

Portal systems allow the body to:

- **Regulate metabolism** before nutrients enter circulation.
- **Detoxify harmful substances** efficiently.
- **Fine-tune hormonal communication** with pinpoint precision.
- **Maintain homeostasis** by modifying blood content locally.

Without portal systems, the body would lose a significant amount of control over endocrine signaling and nutrient handling.

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10.12: Vital Signs and Pulse

Vital signs provide quick, essential information about how well major body systems are functioning and help clinicians detect changes in a patient's health.

Master this section and you'll be able to:

- List and describe what each of the four basic vital signs measures.
- Identify normal adult vital sign ranges and recognize when values are abnormal.

Vital Sign



Vital signs are simple measurements that show how vital body systems are functioning. They help clinicians track a patient's current condition and monitor changes over time. The following are the four primary measurements:

- Body temperature
- Pulse (heart rate)
- Blood pressure
- Respiratory rate (breathing rate)
- Some settings also track oxygen saturation (SpO2), weight, pain, or blood glucose as additional "vital signs".

Vital signs are important because they help detect or monitor medical problems. In fact, abnormal vital signs can indicate illness, injury, or problems in a body system, sometimes before other symptoms appear. Clinicians use them for quick triage, ongoing assessment, and as part of every health evaluation.

Blood pressure will be explored in detail in the next section. For now, we will take a brief look at the other three main vital signs.

Body Temperature

Measures body heat and reflects core body functioning. Common routes of taking somebody's temperature include **oral**, **tympanic**, **axillary**, and **rectal**. Because temperature normally varies by location in the body, the route must always be documented. The method used depends on the patient's age, cognitive status, level of consciousness, and health condition.

Normal oral temperature is about 98.6°F (37°C), but slight variations are normal.

In most clinical settings, body temperature is measured and recorded in degrees Celsius (°C).

Arterial Pulse

Pulse is one of the key vital signs measured to assess heart and circulatory system health. Taking a pulse is a quick and important way to check how many times the heart beats per minute, as well as the rhythm and strength of those beats.

Pulse is the throbbing of arteries as blood is pushed through them each time the heart beats, creating a palpable rhythmic wave, usually felt at points where arteries run close to the skin. In a bit more technical terms: pulse represents the pressure wave that expands and recoils the artery when the heart contracts. It is palpated at many points throughout the body. Pulse is measured in **beats per minute (bpm)**. It determines if a person's heart is beating normally, too fast (**tachycardia**), or too slow (**bradycardia**).

The most common locations to accurately assess pulse as part of vital sign measurement include **radial**, **brachial**, **carotid**, popliteal, and apical pulse as shown in the figure below. In clinical practice, aspects like pulse rate, rhythm (regular or irregular), and strength (amplitude) are evaluated, as changes can point to various health conditions.

A normal resting adult heart rate is generally **60–100 bpm**, but normal ranges vary by age. Certain factors, such as pain, anxiety, fever, or crying in infants may temporarily raise the pulse. In clinical practice, aspects like pulse **rate**, **rhythm** (regular or irregular), and **strength** (amplitude) are evaluated, as changes can point to various health conditions.

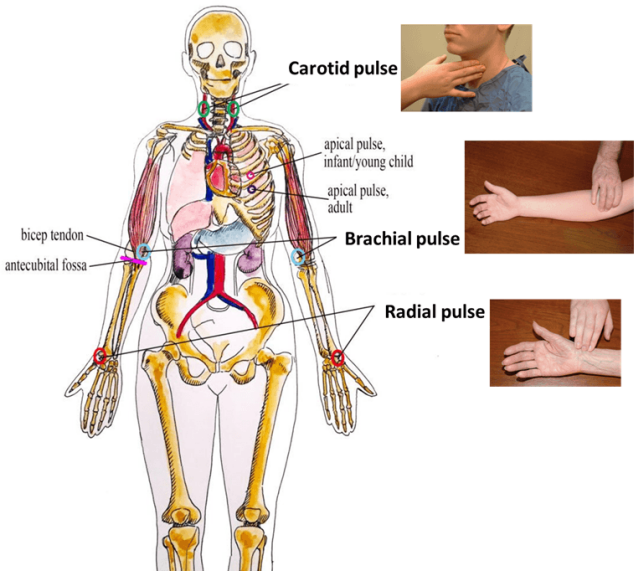


Figure 10.12.1: **Common Pulse Assessment Points.** There are several major locations where a pulse can be easily palpated during a physical assessment. These pulse points lie close to the surface of the body where arteries run over firm structures like bone or dense connective tissue. Examples include the carotid pulse in the neck, the apical pulse over the heart (with slightly different landmarks for adults versus infants), the brachial pulse in the antecubital fossa near the biceps tendon, and the radial pulse at the wrist. These sites are routinely used to assess heart rate, circulation, and overall cardiovascular status in clinical settings.

Respiratory Rate

Respiration refers to the movement of air into and out of the lungs, with **inspiration** bringing air in and **expiration** moving air out. One **respiratory cycle** consists of one inspiration and one expiration, and the **respiratory rate** is the number of cycles per minute. Assessing the respiratory rate reflects how well the lungs and respiratory system are working.

Normal respiratory rates vary by age — adults typically breathe **10–20 times per minute**, while infants may breathe **30–60 times per minute**. Rhythm should be regular and evenly spaced in children and adults who are awake, although newborns and young infants often breathe irregularly. When counting respirations, also consider factors such as sleep, pain, and crying, which can temporarily change the rate.

In addition to rate and rhythm, the **quality** of breathing is important. Normal breathing is quiet, relaxed, and effortless. Signs such as noisy breathing, nasal flaring, use of neck or chest muscles, or leaning forward in a tripod position suggest respiratory distress. If a patient shows any new signs of difficulty breathing during assessment, it is essential to notify the health care provider immediately or follow your agency's protocol.

Vital Signs Overview Summary Table

This table summarizes the four primary vital signs assessed during a routine clinical examination. Temperature reflects the body's core heat balance, pulse measures the number of heartbeats per minute, respiratory rate indicates breaths taken per minute, and blood pressure represents the force of blood pushing against arterial walls. Typical adult ranges are provided for reference and may vary slightly depending on individual health status.

Vital Sign	What It Measures	Typical Adult Range
Temperature	Core body heat	97.8–99.1°F (36.5–37.3°C)
Pulse	Heartbeats per minute	60–100 bpm
Respiratory Rate	Breaths per minute	12–16 breaths/min
Blood Pressure	Pressure of blood in arteries	~120/80 mmHg

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10.13: Understanding and Measuring Blood Pressure

Blood pressure without further specification usually refers to systemic arterial pressure measured at the upper arm. Understanding how it is produced, measured, and interpreted is key to assessing cardiovascular health.

Master this section and you'll be able to:

- Describe what systemic blood pressure represents and how systolic and diastolic pressures are defined.
- Explain how blood pressure changes as blood moves through different vessel types.
- Outline the basic steps of manual blood pressure measurement and identify Korotkoff sounds.
- Calculate pulse pressure from systolic and diastolic values and determine if it is normal, narrow, or wide.

What Is Systemic Blood Pressure?

Imagine your circulatory system as a giant, branching river network. Blood leaves the heart under high pressure, rushes through the large “main rivers” (arteries), slows down as it winds through tiny “streams” (arterioles and capillaries), and then gathers into the wider “return channels” (venules and veins) on its way back to the heart. Blood naturally **flows from high pressure to low pressure.** How smoothly that journey goes depends on several variables, including forces that push blood forward and forces that slow it down. Those slowing forces are called **resistance**, and you will explore them in this section.

What We Mean by “Blood Pressure”

All fluids push outward on the walls of their container — this is **hydrostatic pressure**. In the cardiovascular system, this outward push is what we call **blood pressure**. Although pressure exists everywhere in your vessels, the “blood pressure” that clinicians talk about refers specifically to **systemic arterial pressure**: the pressure in the major arteries that deliver blood to the body.

This pressure is measured in **millimeters of mercury (mmHg)** and is traditionally taken at the **brachial artery** in the upper arm. A reading such as *120/80 mmHg* gives a snapshot of how forcefully the heart is pumping and how well the arteries are handling that pressure.

Systolic vs. Diastolic Pressure

Systemic blood pressure is reported as two numbers:

- **Systolic pressure** (the first number) is the pressure when the left ventricle contracts and sends blood surging into the arteries.
- **Diastolic pressure** (the second number) is the pressure when the ventricle relaxes and the arteries recoil.

Together, they show how effectively blood is being delivered to the tissues.

Blood Pressure Patterns in the Systemic Circulation

As blood leaves the heart and enters the aorta and large arteries, it is under high pressure and shows strong, rhythmic **pulses** created by each heartbeat. These vessels are **elastic**, so they stretch with each surge of blood and then recoil, helping maintain pressure between beats. As blood continues into smaller muscular arteries and especially into the arterioles, pressure begins to drop. Arterioles provide the greatest resistance to flow because their diameter is small and can be adjusted by smooth muscle. This makes them the main regulators of how much pressure is delivered to downstream capillaries and therefore the tissues.

By the time blood reaches the **capillaries**, the pressure has fallen enough that the strong **pulsations disappear**. This lower, steady pressure is essential because capillaries are thin-walled and designed for **exchange**, not withstanding high force. Pressure continues to decline through the venules and veins, which serve mainly as low-pressure return vessels bringing blood back to the heart. Although venous pressure is very low, features such as valves and skeletal muscle contractions help keep blood moving forward. This gradual decline in pressure across the system ensures efficient flow while protecting delicate capillary networks.

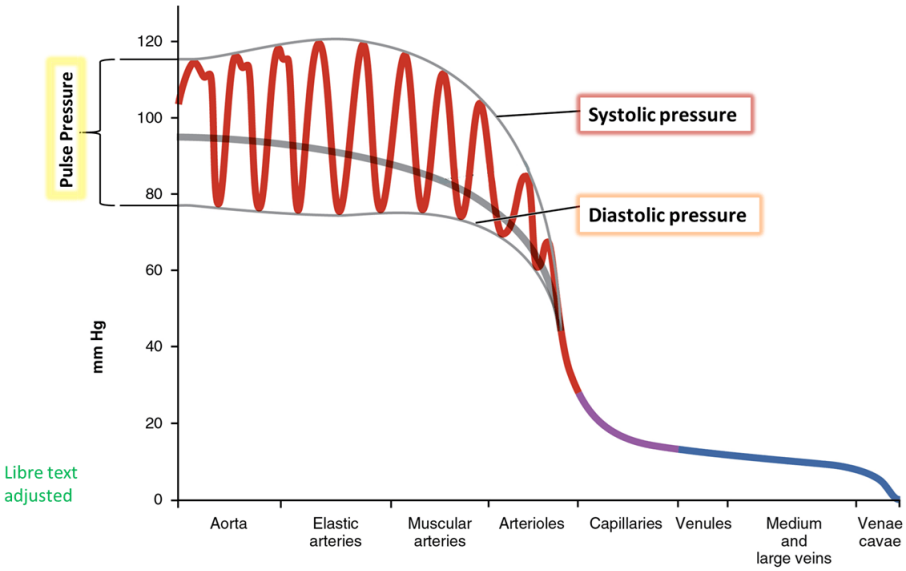


Figure 10.13.1: **Changes in Blood Pressure Across the Systemic Circulation.** Blood pressure is highest and most pulsatile in the aorta and major arteries, where each heartbeat produces distinct systolic peaks and diastolic troughs. As blood travels into smaller vessels, especially the arterioles, pressure drops sharply and the pulse pressure narrows. By the time blood reaches the capillaries and then the veins, the pulsatile pattern has nearly disappeared and pressures are much lower. This gradual decline supports forward blood flow while allowing efficient exchange of gases, nutrients, and wastes in the capillary beds.

How Blood Pressure Is Measured

To measure blood pressure manually, a clinician uses a **stethoscope and a sphygmomanometer** (blood pressure cuff). The cuff is wrapped around the upper arm and inflated until it briefly stops blood flow through the brachial artery. As the cuff slowly deflates, the clinician listens for **Korotkoff sounds** — the tapping noises first described by Dr. Nikolai Korotkoff.

- The **first** Korotkoff sound marks the **systolic** pressure.
- The **last** sound heard before silence marks the **diastolic** pressure.

To ensure accuracy, the cuff is usually inflated to about 30 mmHg above the point where the radial pulse disappears, and then deflated at a slow, steady rate of 2–3 mmHg per second.

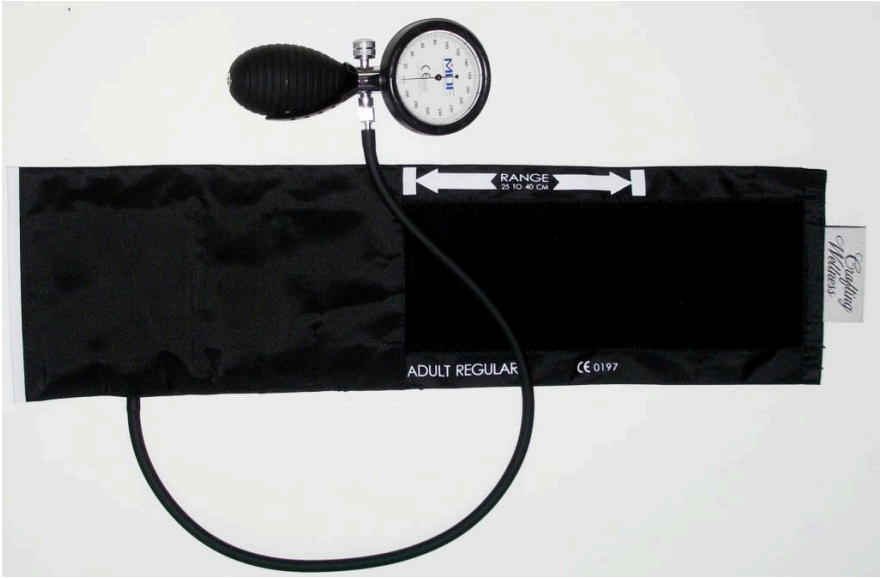


Figure 10.13.2: **Manual Blood Pressure Cuff (Sphygmomanometer).**
This standard adult-size manual blood pressure cuff is wrapped around a patient's upper arm during blood pressure measurement. The inflatable cuff is connected by tubing to a hand bulb used to pump air into the cuff and to an analog pressure gauge (manometer) that displays pressure in millimeters of mercury (mm Hg). When the cuff is inflated, it temporarily stops blood flow through the brachial artery, allowing clinicians to determine systolic and diastolic pressures as the cuff slowly deflates.

Why BP Numbers Matter

Normal adult blood pressure is **below 120/80 mmHg**. Persistent readings of **130/80 mmHg or higher** are classified as **hypertension**, which signals that the heart and vessels are under extra strain. Before diagnosing hypertension, health care providers take multiple readings on more than one occasion to ensure that the average truly reflects the patient's baseline.

Blood Pressure Categories Based on Systolic and Diastolic Values

Blood Pressure Category	Systolic mm Hg (upper #)	Diastolic mm Hg (lower #)
Normal	< 120	< 80
Elevated	120 - 129	< 80
Stage 1	130-139	80-89
Stage 2	At least 140	At least 90
Hypertensive Crisis	> 180	> 120

Interactive Element

In this short instructional video, a nurse demonstrates how to take an accurate manual blood pressure using a sphygmomanometer and stethoscope. The video walks you through each step of the technique, from gathering supplies and positioning the patient to locating the brachial artery and checking for the auscultatory gap, a temporary "silent" period

that can cause incorrect readings if missed. You learn how to estimate the systolic pressure by palpation, properly inflate and deflate the cuff, and identify the systolic and diastolic values by listening for the first and last Korotkoff sounds. The demonstration concludes with cuff removal, equipment cleaning, and documentation of the final blood pressure reading.

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Pulse Pressure (PP)

Pulse pressure (PP) is the **difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP)** — *see Figure* 10.13.1. A normal resting pulse pressure is **about 30 to 40 mm Hg** in most healthy adults, typically at least one quarter of the systolic value.

Pulse pressures consistently below 25 percent of the systolic value are considered **narrow** (or low). Narrow pulse pressures often reflect a **low stroke volume**, which can occur in conditions such as congestive heart failure, aortic valve stenosis, or significant blood loss after trauma.

Pulse pressure/approaching or exceeding **100 mm Hg** at rest are considered **wide** (or high). A wide PP can appear in healthy individuals after strenuous exercise, when an ordinary resting pulse pressure of 30 to 40 mm Hg may rise temporarily to about 100 mm Hg. However, a persistently elevated resting pulse pressure at or above 100 mm Hg may indicate increased **arterial resistance and can be associated with several cardiovascular disorders**. Chronic high pulse pressure places stress on the heart, brain, and kidneys, and usually requires medical evaluation and management.

Normal Range for PP is 40–60 mmHg. **Formula for calculating pulse pressure: PP = SBP - DBP**

Examples:

- If a person's blood pressure is 120 over 80 mm Hg, the pulse pressure is 40 mm Hg and therefore normal.
- If the person has a BP of 160/75 mm Hg, the puls pressure would be 160 - 75 = 85 mmHg which means this person has a wide (or high) PP.

Why Pulse Pressure Matters

Pulse pressure is more than just a math problem between systolic and diastolic pressure; it is a meaningful window into cardiovascular health. A wide pulse pressure often means the arteries are becoming stiff, which raises the risk for heart disease, heart attack, and stroke, especially in older adults or people with diabetes. It may also point to specific conditions such as aortic regurgitation, arteriosclerosis, severe anemia, or hyperthyroidism.

In contrast, a narrow pulse pressure can signal that the heart is struggling to pump effectively, as seen in shock or congestive heart failure. Because pulse pressure reflects both how forcefully the heart beats and how well the arteries can stretch, it sometimes predicts future cardiovascular problems even better than systolic or diastolic pressure alone. For clinicians, tracking pulse pressure helps guide decisions about treatment, lifestyle changes, and how aggressively to manage cardiovascular risk.

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10.14: Hypertension

Blood pressure disorders such as hypertension and hypotension affect how well blood moves through the vessels, and understanding them helps explain both long-term health risks and immediate problems with perfusion.

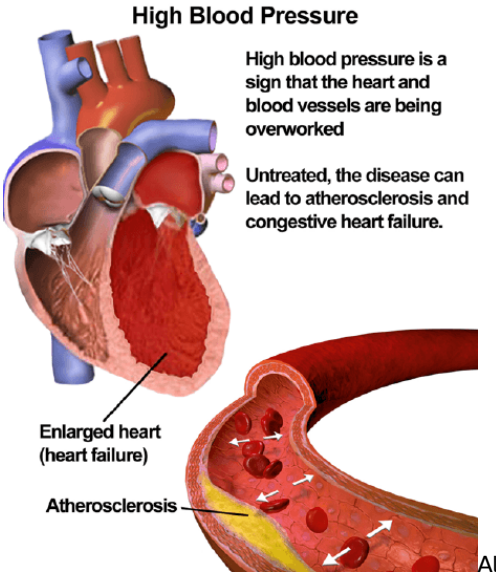
Master this section and you'll be able to:

- Distinguish normal, hypertensive, and hypotensive ranges for blood pressure and pulse pressure.
- Explain key causes and health effects of chronic hypertension and hypotension.
- Differentiate primary and secondary hypertension and identify factors that cause inaccurate readings.

Hypertension (high blood pressure) is a chronic condition in which pressure inside the systemic arteries remains elevated over time. When arterial pressure is consistently high, the heart must work harder than normal to push blood through the vessels. You have learned in the previous section that blood pressure is described using two numbers: the systolic pressure, which reflects the force when the ventricles contract, and the diastolic pressure, which reflects the force when the heart relaxes between beats.

Hypertension: A Silent but Serious Condition

Hypertension (high blood pressure) is often called a "silent disorder" because most people do not feel any symptoms, even when their pressure is dangerously high. Hypertension is often called a **"silent killer"** because most people do not feel any symptoms, even if their pressure is dangerously high. This makes it easy for patients to underestimate the seriousness of the condition or stop following their treatment plan. Often, elevated arterial pressure is an important warning sign of other health problems, and it can cause long-term harm if left untreated.



All blood pressure places some mechanical stress on arterial walls, but **higher pressures create far more strain**. Over time, this extra stress:

- Increases the workload on the heart
- Promotes the growth of atherosclerotic plaques (atheromas) inside artery walls
- Leads to thickening and enlargement of the heart muscle, which eventually weakens its function

Today we understand that **both systolic pressure and pulse pressure** (the difference between systolic and diastolic values) are important predictors of cardiovascular risk. While diastolic pressure used to receive most attention, high systolic pressure and wide pulse pressure are now known to be strong indicators of arterial stiffness and disease. In fact, lowering an excessively high

diastolic pressure too much may widen the pulse pressure and increase risk. When systolic pressure rises above 140 mmHg but diastolic pressure remains below 90 mmHg, the condition is called **isolated systolic hypertension**, which is especially common in older adults and still carries significant health concerns.

If hypertension continues untreated, the long-term strain on vessels and the heart can lead to serious, potentially life-threatening complications, such as:

- Heart attack
- Stroke
- Aneurysm (ballooning of a weakened blood vessel wall)
- Peripheral arterial disease (blocked vessels in the limbs)
- Chronic kidney disease
- Heart failure

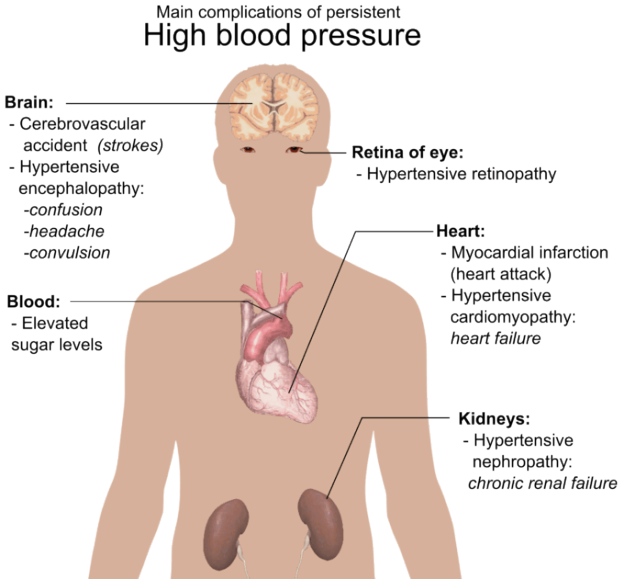


Figure 10.14.1: **High Blood Pressure Complications**: Long-term, uncontrolled hypertension can damage multiple organ systems. In the brain, high pressure can lead to strokes, and the eyes may develop hypertensive retinopathy, which can impair vision. The heart is especially vulnerable, with risks including myocardial infarction (heart attack) and hypertensive cardiomyopathy that may progress to heart failure. Chronic renal failure can also develop due to hypertensive nephropathy.

A normal resting blood pressure typically falls between 100–120 mmHg systolic and 60–80 mmHg diastolic. Hypertension is diagnosed when blood pressure remains at or above 140/90 mmHg on repeated measurements. Chronically elevated pressure can gradually damage vessel walls throughout the body, contribute to arterial disease, strain the heart, and even lead to neurological problems through a stroke.

Primary (or Essential) Hypertension

Hypertension is grouped into two main types: **primary (essential) hypertension** and **secondary hypertension**. Primary hypertension makes up about 90 to 95 percent of all cases. In these individuals, blood pressure is high even though there is no single, identifiable medical cause. Most people with primary hypertension have normal cardiac output, but their small arteries and arterioles offer more resistance than normal. This increased resistance is usually due to the gradual narrowing of these vessels, and in some cases a reduced number of capillaries may also contribute.

Secondary Hypertension

Secondary hypertension accounts for the remaining 5 to 10 percent of cases and develops when another health condition raises blood pressure. **Kidney disease** is the most common cause of secondary hypertension. Other causes include certain endocrine disorders, such hyperthyroidism, hypothyroidism. Secondary hypertension can also result from **obesity**, sleep apnea, and **pregnancy**, amongst other conditions.

If high blood pressure is not controlled over time, it can **damage blood vessels and organs throughout the body**. Chronic hypertension is a major risk factor for heart attack, heart failure, stroke, aneurysms, peripheral arterial disease, and chronic kidney disease. Even moderate, long-term elevation of blood pressure can shorten life expectancy. Healthy lifestyle changes can support blood pressure control and reduce health risks, but many individuals also require medication to keep blood pressure within a safe range.

Not every high BP reading means the patient truly has hypertension. Common errors in measurement and natural fluctuations in blood pressure can result in readings that erroneously suggest hypertension. Blood pressure can appear elevated because of:

- **Errors in technique** (cuff too small, cuff placed incorrectly, arm not at heart level)
- **Operator error**
- **Client anxiety ("white coat effect")**
- **Situational factors** such as pain, anxiety, stress, or recent activity, caffeine, smoking, etc.

It is important to distinguish between elevated blood pressure and a diagnosis of hypertension. Elevated blood pressure refers to an isolated reading, whereby the client has an elevated finding. Hypertension is clinical diagnosis whereby the client has met the criteria for chronic elevated blood pressure.

Hypotension: How Low Blood Pressure Differs From High Blood Pressure

When we talk about blood pressure problems, **hypertension (high blood pressure)** usually gets the most attention. That is because hypertension is extremely common and can silently damage the blood vessels, heart, kidneys, brain, over many years without causing symptoms.

Hypotension, on the other hand, refers to **blood pressure that is too low**, usually defined as less than **90/60 mmHg**. Hypotension is less common than hypertension and often gets less attention, but it can still be important because **blood pressure must be high enough to deliver oxygen-rich blood to vital organs** such as the brain, heart, and kidneys.

Causes and Concerns of Hypotension

Hypotension can occur for many reasons, including:

- **Dehydration**
- **Bleeding or blood loss**
- **Heart problems** that reduce the amount of blood the heart pumps
- **Side effects of medications**, such as those used to treat high blood pressure or depression

When blood pressure is too low, the body may not be able to maintain adequate **perfusion**. Perfusion refers to the **delivery of oxygen-rich blood to the tissues and organs of the body**. In other words, it is how well blood is flowing through the capillaries to supply cells with the oxygen and nutrients they need. Inadequate perfusion can lead to symptoms such as dizziness, weakness, blurry vision, or even fainting. In severe cases, very low blood pressure can become life-threatening because organs are not receiving enough oxygen.

Orthostatic (Postural) Hypotension

A specific type of low blood pressure is **orthostatic hypotension**, which happens when someone moves from lying down or sitting to standing.
Clinically, it is defined as a **drop of at least 20 mmHg systolic or 10 mmHg diastolic within three minutes of standing**.

Here is why it happens:

- When a person stands, gravity pulls blood toward the legs.
- This briefly reduces the amount of blood returning to the heart.
- Blood pressure drops for a moment.
- Normally, the nervous system quickly corrects this drop by tightening blood vessels and increasing heart rate.

Most people barely notice this temporary change.
However, some individuals do **not** compensate well. They may experience:

- Light-headedness
- Dizziness
- Fainting

This is an important **safety concern**, especially in older adults, because fainting can lead to serious falls and injuries.

Comparison of Hyper- and Hypotension.

Feature	Hypertension (High BP)	Hypotension (Low BP)
Frequency	Very common	Less common
Symptoms	Often none (“silent”)	Often dizziness, fainting
Main concern	Long-term organ damage (heart, brain, kidneys)	Not enough blood flow to organs right now
Serious risks	Heart attack, stroke, kidney failure	Falls, injury, shock (especially in older people and people who have been bedridden for extended time periods.
Why it matters	Chronic strain on vessels and heart	Immediate lack of perfusion

In Short:

- **Hypertension is dangerous because it causes long-term damage silently.**
- **Hypotension is dangerous when it reduces blood flow to organs or causes fainting and falls.**

Both conditions matter, but **hypertension is the bigger public-health threat**, while **hypotension is more about immediate safety and perfusion**.

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10.15: Atherosclerosis

Arteriosclerosis and atherosclerosis describe hardened, narrowed arteries that can progress silently and lead to serious cardiovascular disease.

Master this section and you'll be able to:

- Differentiate arteriosclerosis from atherosclerosis based on causes and effects on arteries.
- Describe how atherosclerotic plaque develops and leads to conditions like angina, heart attack, and stroke.
- Identify key modifiable risk factors and strategies that slow arterial hardening.

Arteriosclerosis and Atherosclerosis: How Hardened Arteries Differ

You may have seen the terms *arteriosclerosis* and *atherosclerosis* and wondered if they mean the same thing.

Arteriosclerosis

Arteriosclerosis is the **general term** for "hardening of the arteries," referring to any condition in which artery walls become thickened, stiff, or less elastic. This hardening often increases with age as vessels naturally become less elastic and more rigid. This alone can cause arteriosclerosis, even if plaque is not involved. Arteriosclerosis can happen faster if a person has conditions such as:

- **High Blood Pressure (Hypertension):** The pressure damages artery walls, causing them to thicken and stiffen over time, especially in small arteries.
- **Diabetes:** High blood sugar damages blood vessel walls, leading to hardening, especially in smaller arteries.
- **Autoimmune Diseases:** Conditions like lupus or rheumatoid arthritis cause ongoing inflammation which can harm artery walls and make them stiffer.

Atherosclerosis

Atherosclerosis is **one specific type of arteriosclerosis.** It develops when **fatty deposits, or plaques,** accumulate inside the arterial wall. These plaques contain cholesterol, fats, immune cells, and connective tissue that gradually narrow the vessel and restrict blood flow. The term comes from the Greek *athero*, meaning "gruel," because a cut plaque reveals a thick, yellow, cholesterol-rich material, and *sclerosis*, meaning "hard."

In short, arteriosclerosis is the umbrella term for hardened arteries, while atherosclerosis is the most common form caused by plaque buildup. All atherosclerosis is arteriosclerosis, but not all arteriosclerosis is atherosclerosis.

Arteriosclerosis vs. Atherosclerosis

Feature	Arteriosclerosis	Atherosclerosis
Definition	General hardening and stiffening of arterial walls	Specific type of arteriosclerosis caused by plaque buildup inside arteries
Cause	Aging, loss of elasticity, or various vessel changes	Accumulation of cholesterol, fats, immune cells, and connective tissue forming plaques
Location of Change	Thickening or stiffening of the arterial wall	**Plaque** forms within the inner lining (intima) of the artery

Feature	Arteriosclerosis	Atherosclerosis
Effect on Blood Flow	May reduce elasticity and increase resistance	Narrows the vessel lumen and restricts blood flow
Relationship	Broad category	Most common form within that category

For the rest of this section we will focus on Atherosclerosis.

Atherosclerosis: When the Arterial Highway Starts to Narrow

Imagine your blood vessels as smooth, flexible highways built for easy blood flow. Over time, however, those highways can begin to narrow and stiffen as sticky, fatty material slowly collects on the inner walls. This long-term process, called **atherosclerosis**, forms **plaques** made of fats, cholesterol, immune cells, and connective tissue. As plaques enlarge, they reduce the open space inside the artery and make the vessel less elastic, forcing the heart to work harder to move blood forward.

Atherosclerosis progresses silently for years and is a major cause of peripheral artery disease. As plaque buildup continues, the arterial lining thickens, scars, and loses elasticity. The condition becomes dangerous when a plaque ruptures and a blood clot (**thrombus**) forms, which can block the artery at that spot. A clot can also break loose and travel as an **embolus** until it gets stuck in a smaller vessel, cutting off oxygen to tissues and causing many heart attacks and strokes.

Understanding how this process develops helps you connect daily choices with long-term cardiovascular health.

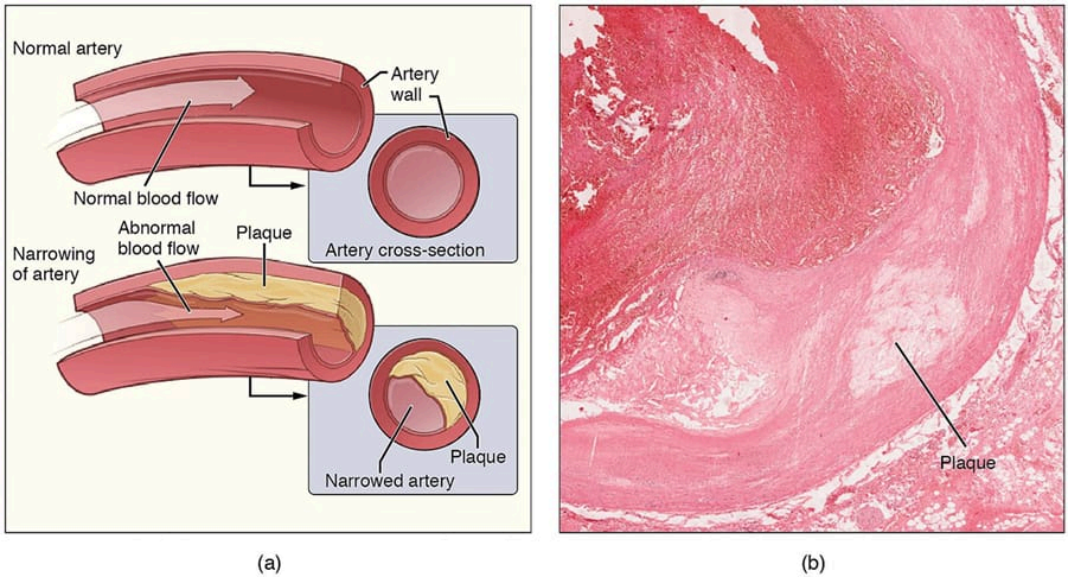


Figure 10.15.1: **Atherosclerotic Plaque Formation in Arteries.** (a) A healthy artery shows a wide, open lumen that supports smooth blood flow, while an atherosclerotic artery contains a fatty plaque that narrows the passage and disrupts flow. (b) A histological section of an artery highlights the pale plaque material embedded in the vessel wall, illustrating how plaque buildup thickens and stiffens the artery.

As you know, arteries deliver oxygen-rich blood to every organ, so the effects of atherosclerosis depend on **which arteries are narrowed or blocked**. When it affects the coronary arteries, it becomes **coronary artery disease**, which can lead to **angina** or a **heart attack**. When it affects arteries supplying the brain, it becomes **cerebrovascular disease**, which can lead to a **stroke**.

Coronary Arteries and Angina

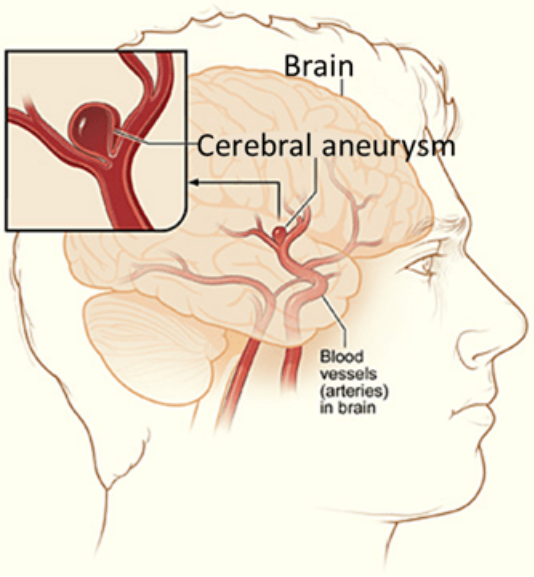
If the heart muscle does not receive enough oxygen during activity, a person may feel **angina pectoris**, a pressure or discomfort that can appear as chest pain, nausea, numbness, or even jaw pain. Exercise increases the heart's need for oxygen, but narrowed

arteries cannot keep up. Rest usually relieves the symptoms.

Atherosclerotic plaques can suddenly rupture or completely block flow. When a coronary artery becomes fully blocked, part of the heart muscle loses oxygen and begins to die. This is a **heart attack**, and severe damage can stop the heart from contracting altogether.

Brain Arteries and Stroke

Blockage of an artery supplying the brain causes an **ischemic stroke**. Ischemic means **lacking adequate blood flow**. When a tissue becomes ischemic, it is not receiving enough oxygen and nutrients because its blood supply has been reduced or blocked. Without enough oxygen, cells cannot make energy normally, and the tissue begins to malfunction. If ischemia lasts too long, the affected cells can die.



A **hemorrhagic stroke** occurs when a weakened artery wall (often from high blood pressure) forms an **aneurysm** that ruptures. An aneurysm is a **bulging or ballooning** of a weakened section of an artery. Over time, pressure from the blood flowing through the vessel causes the weakened wall to stretch outward, much like a worn spot on a garden hose. Most aneurysms form silently with no symptoms. The danger is that the stretched wall can **rupture**, leading to sudden, life-threatening internal bleeding, or it can form a **clot** that blocks blood flow downstream.

In both cases, oxygen delivery to brain tissue stops, leading to symptoms such as sudden weakness or numbness, difficulty speaking, vision loss, a sudden severe headache, dizziness, or collapse. Rapid medical care is critical.

A Long, Quiet Disease

Atherosclerosis develops slowly over decades. Arteries can narrow to one-quarter of their original diameter before symptoms appear, and for some people, the first sign is a catastrophic event. Despite this, the age-adjusted U.S. death rate from heart disease has dropped dramatically since the 1950s, thanks to lower smoking rates, dietary changes, and better treatment of hypertension and heart disease.

Artery Care 101: Practical Ways to Reduce Plaque and Stiffness

Although aging naturally stiffens arteries, many of the factors that accelerate arteriosclerosis and atherosclerosis can be changed. The overall goal is to protect the endothelium, slow plaque formation, and keep vessels flexible so blood can move freely. It is never too early to start.

- **Maintain Healthy Blood Pressure.** Keeping systemic arterial pressure within a normal range reduces mechanical stress on vessel walls. Regular monitoring, managing sodium intake, staying active, and following treatment plans all help prevent hypertension, one of the strongest drivers of arterial damage.
- **Improve Lipid Profile.** Lowering LDL cholesterol and raising HDL slows plaque formation. Emphasize: limiting saturated and trans fats; choose unsaturated fats (olive oil, nuts, fish); increase fiber (vegetables, fruits, whole grains); have your blood checked regularly.
- **Engage in Regular Physical Activity.** Aerobic activity (walking, swimming, cycling) improves endothelial function, decreases LDL, and increases vessel elasticity. Even short, regular bouts of activity help counteract plaque progression.
- **Avoid Smoking and Secondhand Smoke.** Tobacco damages the endothelium, encourages plaque formation, stiffens arteries, and accelerates all types of cardiovascular disease. Avoiding smoking is one of the most effective ways to prevent atherosclerosis.
- **Maintain Healthy Body Weight.** Excess adiposity increases inflammation, raises LDL, and contributes to hypertension and diabetes. Gradual, sustainable weight management improves cardiovascular health and reduces plaque progression.
- **Control Blood Glucose.** Chronically high blood glucose damages blood vessels and accelerates atherosclerosis. Students with diabetes or prediabetes should monitor glucose, follow medical guidance, and maintain consistent physical activity.
- **Manage Stress.** Chronic stress can raise blood pressure and promote harmful behaviors. Relaxation techniques, sleep hygiene, and social support help regulate sympathetic drive and reduce vascular strain.

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10.16: Capillary Exchange

Capillary exchange is the process by which gases, nutrients, wastes, and fluids move between the bloodstream and tissues, using specialized mechanisms that keep every cell supplied.

Master this section and you'll be able to:

- Identify and briefly explain the three mechanisms of capillary exchange: diffusion, transcytosis, and bulk flow.
- Explain how hydrostatic and osmotic pressures determine whether bulk flow leads to filtration or reabsorption.
- Describe the role of the lymphatic system in returning excess fluid to the bloodstream and how its failure leads to edema.

Capillaries are the smallest blood vessels in the body and the sites where all exchange between the bloodstream and tissues occurs. Most capillaries are less than 1 millimeter long and so narrow that red blood cells must pass through in single file and may even need to bend as they move along. Because capillaries weave densely among body cells, no cell is ever far from its supply line.

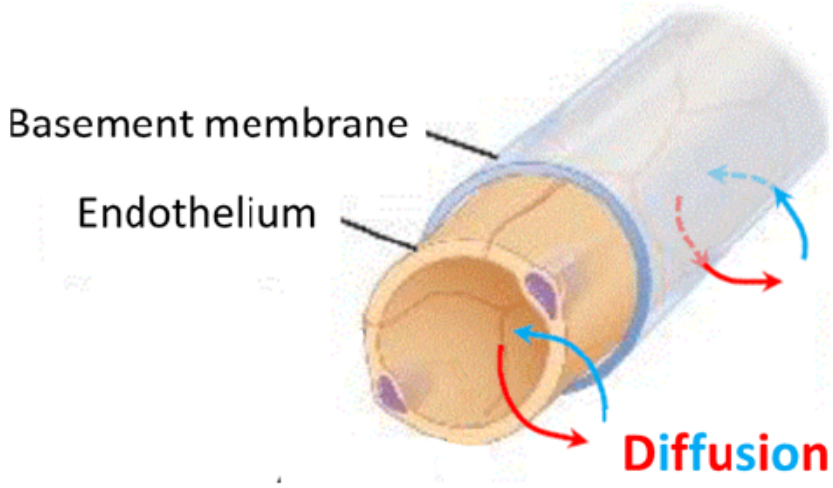
How Materials Move Across Capillary Walls

A main job of the cardiovascular system is to deliver gases, nutrients, and other substances to the body's cells and carry away wastes. **Capillary exchange** is the term for the movement of substances between the blood and tissues. Three mechanisms support this exchange: diffusion, transcytosis, and bulk flow.

Diffusion is the most common mechanism of capillary exchange. **Small**, **lipid-soluble molecules** such as oxygen, carbon dioxide, and lipids **diffuse directly** through the endothelial cell membranes. **Water-soluble** small substances — like glucose, amino acids, and ions (sodium, potassium, calcium, chloride) — use specific channel proteins to cross by facilitated diffusion. (Module 2, pages 2.10–2.11). Some of these molecules can also move through the small spaces between endothelial cells called intercellular clefts. Fenestrated capillaries contain pores that allow medium-sized molecules to pass, and sinusoid capillaries have large gaps that permit even plasma proteins to move through.

Some large proteins and other macromolecules travel across the endothelial cells by **transcytosis**. In this process, they are packaged into **vesicles** on one side of the cell (**endocytosis**), transported across the interior, and released on the opposite side (**exocytosis**).

Finally, water and many dissolved substances move together across the capillary wall by **bulk flow**, a pressure-driven process. Bulk flow is especially important for regulating the distribution of fluids between the blood and interstitial spaces. Water follows its own concentration gradient by osmosis or is pushed and pulled across the wall by hydrostatic and osmotic pressures.

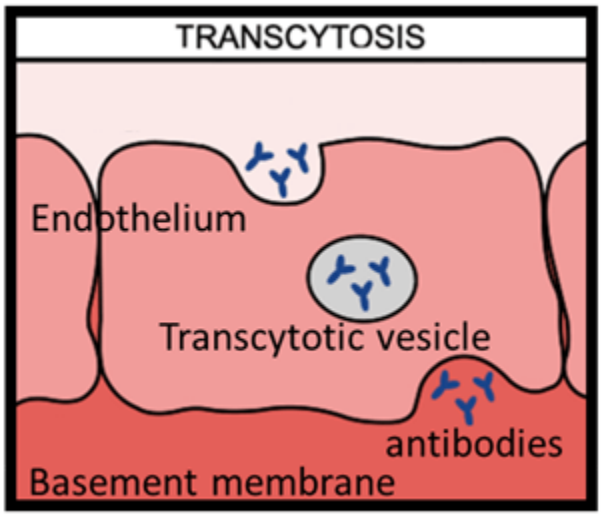


1) Diffusion

Capillaries are designed for efficient exchange. Each capillary has a very thin wall made of a single layer of endothelial cells resting on a delicate basement membrane *(see image on the right)*. Because this barrier is so thin, small molecules can move easily across it by simple or facilitated diffusion. **Diffusion always moves substances from areas of higher concentration to lower concentration.** As a result, materials that are more concentrated in the blood (such as oxygen and glucose) diffuse outward into the tissues, while substances produced by nearby cells (such as carbon dioxide and other wastes) diffuse into the blood.

Diffusion is the primary mechanism of capillary exchange and accounts for the movement of most small molecules between blood and tissues. The direction and rate of this movement depend on the concentration gradients between the blood and interstitial fluid.

2) Transcytosis



Transcytosis, or **vesicular transport**, is the second mechanism that facilitates capillary exchange, along with diffusion and bulk flow.

Some large, water-insoluble molecules cannot use other transport methods, so they must move through the endothelial cells inside vesicles. Often, these molecules first attach to **specific receptors** on the endothelial cell surface, which triggers **receptor-mediated endocytosis**: the cell forms a small vesicle around the molecule and brings it inside. The vesicle then travels across the cell and releases the molecule on the opposite side. This allows important **macromolecules** to move from the blood into the tissues, or vice versa, even though they are too large to pass through pores or channels. Vesicles can merge with others, mix their

contents, or be directed toward specific tissues as needed.

Although transcytosis is a normal and useful way for large molecules to cross a capillary wall, it can unfortunately also be used by harmful microbes. Some pathogens "hijack" this vesicle-transport system to move through epithelial barriers that would normally protect the body. Examples are:

- *Cronobacter sakazakii* is a bacterium that can contaminate powdered infant formula and cause severe infections in newborns, including sepsis and meningitis. It is dangerous because it can cross the intestinal wall and even the blood-brain barrier.
- *Listeria monocytogenes* is a bacterium found in foods like soft cheeses and deli meats. It can cause listeriosis, an illness that is especially serious for pregnant individuals, newborns, older adults, and immunocompromised people. Listeria is unusual because it can cross several body barriers, including the intestinal lining and the placenta.

Pharmaceutical researchers are exploring how to use transcytosis to carry medicines across the blood-brain barrier. Because this barrier blocks most drugs from entering the brain, using the body's own transport system may help deliver treatments — especially large molecules like antibodies — to the brain more effectively.

3) Bulk Flow: Filtration and Reabsorption

Bulk flow is the **pressure-driven movement** of water and the **small, lipid-insoluble solutes** carried with it across the capillary wall. How much bulk flow occurs depends on the type of capillary and how porous it is. **Continuous** capillaries have very tight walls and allow only limited bulk flow. **Fenestrated** capillaries contain small pores that permit more flow. **Discontinuous** (sinusoid) capillaries have large gaps and allow the greatest amount of bulk flow.

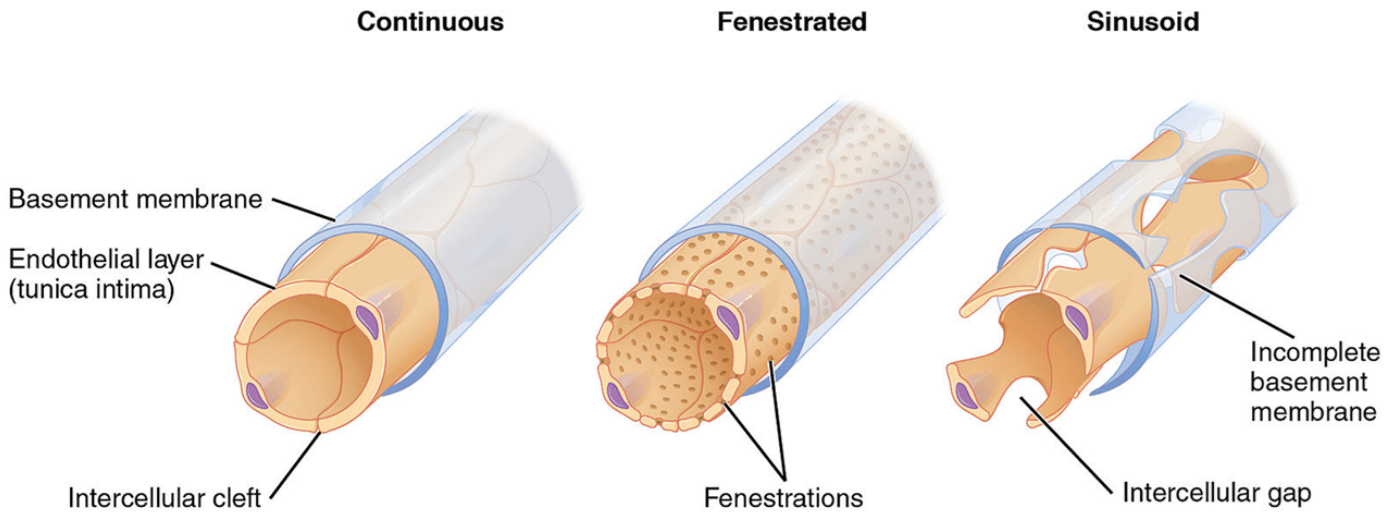


Figure 10.16.1: **Three Structural Types of Capillaries.**
This figure compares the three main capillary types found in the human body. **Continuous capillaries** (left) have a solid endothelial lining with small intercellular clefts and an intact basement membrane, allowing only small molecules like gases and nutrients to pass through. **Fenestrated capillaries** (middle) contain pores called fenestrations that increase permeability, making them ideal for organs that require rapid exchange such as the kidneys, intestines, and endocrine glands. **Sinusoidal capillaries** (right) have large intercellular gaps and an incomplete basement membrane, creating wide openings that let whole cells and large proteins move through, as seen in the liver, spleen, and bone marrow.

Bulk flow depends on **two opposing pressures:**

1. **Hydrostatic pressure.** This is essentially the blood pressure, the **"pushing" force** created by the fluid inside the capillary. This pressure tends to push water and small solutes out into the surrounding tissues.
2. **Osmotic** (also called oncotic) **pressure**. This pressure is the **"pulling" force** created mostly by **plasma proteins** that cannot leave the the capillaries and attract water back toward the bloodstream.

Bulk flow can therefore move fluid **out of the bloodstream into the tissues** or **from the tissues back into the bloodstream**,

depending on which pressure is stronger.

When fluid moves out of the capillary and into the surrounding tissue, the process is called **filtration**. This happens when the fluid pressure inside the capillary is higher than the pressure in the surrounding tissue.

When fluid moves from the tissue back into the capillary, the process is called **reabsorption**. This happens when the "pulling" force of proteins in the blood is stronger than the pressure in the tissues.

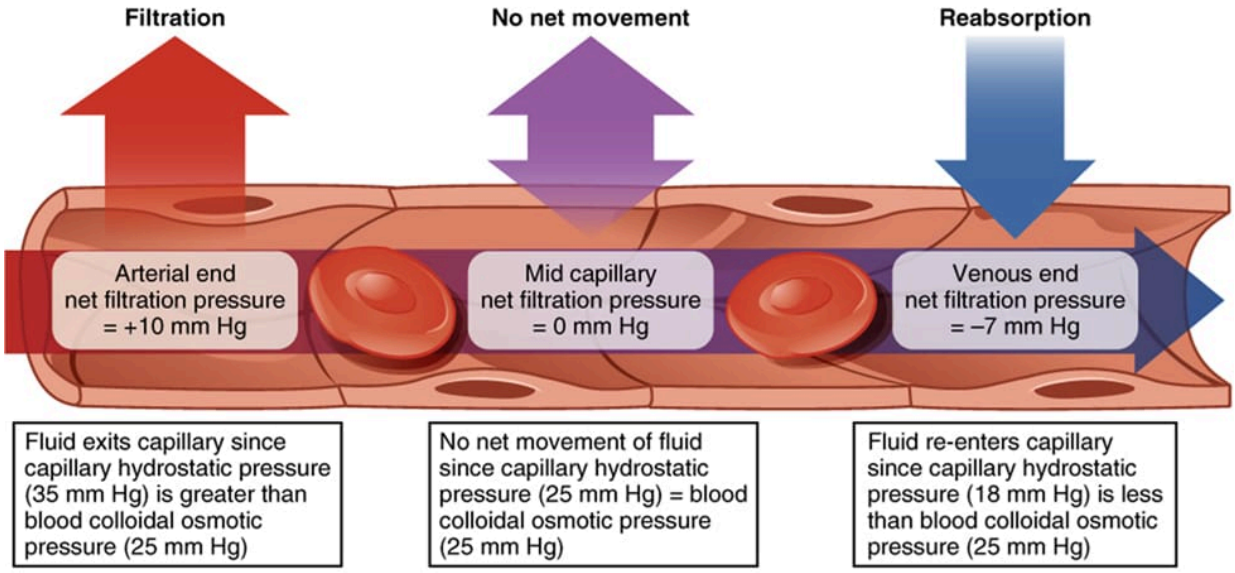


Figure 10.16.2: **Filtration and Reabsorption Across a Capillary Bed.** This diagram illustrates how fluid movement across a capillary wall changes from the arterial end to the venous end. At the arterial end, higher capillary hydrostatic pressure pushes fluid out of the blood and into the surrounding tissues, producing net filtration. In the mid-capillary region, hydrostatic and osmotic pressures are balanced and there is no net fluid movement. At the venous end, hydrostatic pressure has fallen below blood colloid osmotic pressure, so fluid is drawn back into the capillary, resulting in net reabsorption.

The image above reflects the classical teaching of filtration and reabsorption. Newer research shows that capillaries do not reabsorb as much fluid at their venous end as older diagrams suggested. Instead, many capillaries tend to push fluid outward along most of their length, and the extra fluid is carried back to the bloodstream by the **lymphatic system.** Reabsorption does still happen, but mainly in special situations, such as after blood loss, or in certain organs like parts of the intestine and kidney.

In summary, bulk flow depends on two types of pressure:

- **Hydrostatic pressure**, which pushes fluid outward.
- **Osmotic pressure**, which pulls fluid inward.

The balance between these pressures determines whether filtration or reabsorption occurs.

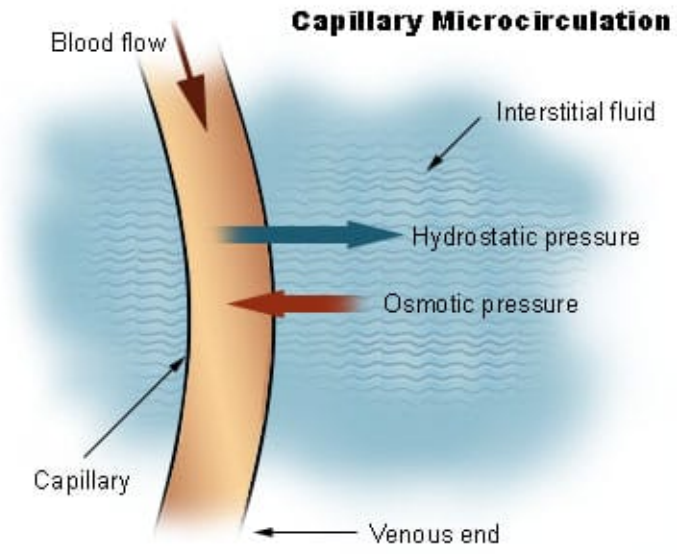


Figure 10.16.3: **Capillary Dynamics**. Two opposing forces move fluid across a capillary wall. **Hydrostatic pressure** pushes fluid out of the capillary and into the interstitial space, while **osmotic pressure** pulls fluid back toward the capillary. The balance of these pressures determines whether fluid is filtered out or reabsorbed as blood flows from the arterial to the venous end of the capillary bed.

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Watch this great video about **Capillaries and Capillary Exchange** by **ThePenguinProf**

Lymphatic System

Capillary beds do not work alone! To help manage the fluid that leaves the capillaries, the body relies on a second circulation system, the **lymphatic system**.

Lymph vessels are thin, low-pressure tubes that run alongside blood capillaries and act as a drainage system for the body. In most capillary beds, more fluid is pushed out of the blood than is pulled back in, so a small amount of excess fluid collects in the surrounding tissues. Instead of letting this extra fluid build up and cause swelling, lymph vessels pick it up and return it to the bloodstream through a network of vessels and nodes. In other words, lymph vessels help keep capillary beds in balance by preventing fluid from accumulating in the tissues and by maintaining normal blood volume.

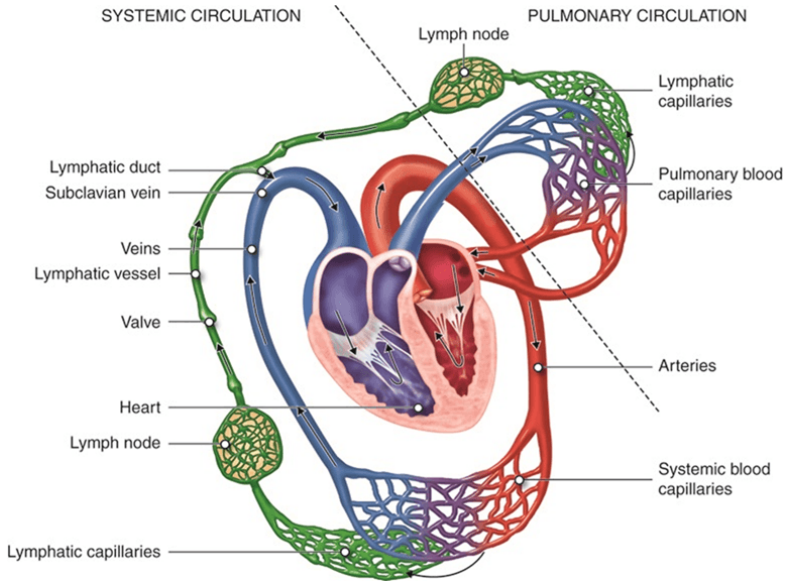


Figure 10.16.4: **Overview of Blood and Lymph Circulation.** Lymphatic capillaries are found wherever blood capillaries are located except in the central nervous system and bone marrow. Some fluid that left the blood capillaries enters nearby lymphatic capillaries (green), becoming lymph. Lymph flows through lymphatic vessels and lymph nodes, where it is filtered, before rejoining the bloodstream at the subclavian veins.

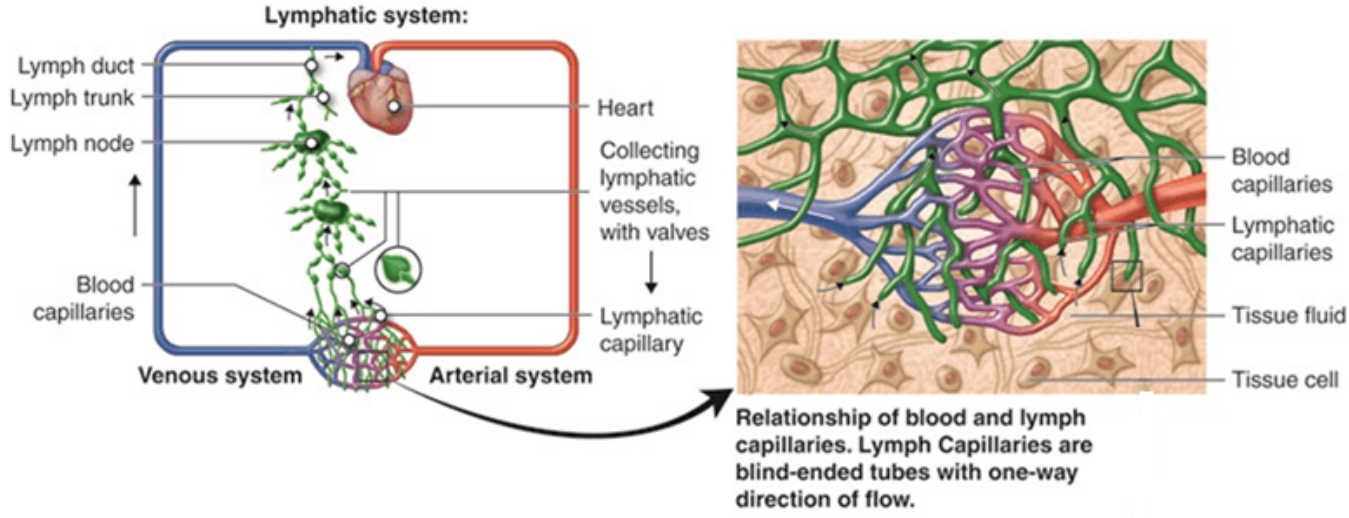


Figure 10.16.5: **Relationship of blood and lymph.** Lymphatic capillaries sit near blood capillaries and pick up the excess fluid that filters out of the bloodstream. These tiny vessels merge into larger lymphatic vessels, which resemble small veins and contain one-way valves to keep lymph moving forward. As nearby skeletal muscles contract, they squeeze the vessels and help push lymph along its one-way path toward the chest. Eventually, all lymph drains into either the subclavian or jugular veins.

When the lymphatic system is damaged or blocked by surgery, injury, infection, or genetic conditions, lymph fluid cannot drain efficiently. As fluid builds up in the tissue spaces, swelling develops, a condition known as **lymphedema**.

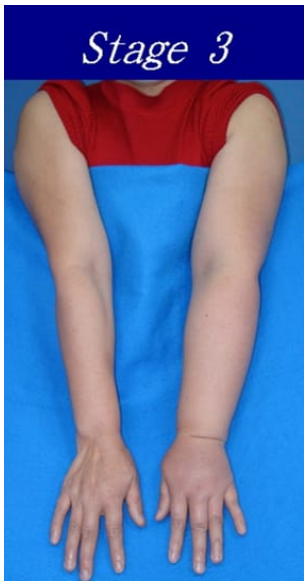


Figure 10.16.6: **Lymphedema of the Arm.** In this case of stage 3 lymphedema, you can see the marked swelling of the left arm. Breast cancer treatment — such as removal of lymph nodes or radiation therapy — is the most frequent cause of this type of lymphedema in the United States.

Vein problems can create a similar issue. Conditions such as chronic venous insufficiency, varicose veins, or deep vein thrombosis increase pressure inside the veins and push extra fluid out into the surrounding tissues. When this excess fluid exceeds the lymphatic system's ability to remove it, **edema** forms.

Watch this Video

Watch this video to explore the lymphatic system.

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11: RESPIRATORY SYSTEMS

11.1: Respiratory System Introduction

11.2: Anatomical Regions of the Respiratory Tract

11.3: Functional Anatomy of the Respiratory Tract

11.4: A Closer Look at the Air We Breathe

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11.14: Cystic Fibrosis

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11.1: Respiratory System Introduction

The respiratory system brings oxygen into the body, removes carbon dioxide, and works with the circulatory system to maintain gas exchange and stable blood pH.

Master this section and you'll be able to:

- List the main reasons for breathing

Introduction to the Respiratory System: Why We Breathe

Breathing is the physical movement of air into and out of the lungs. Although breathing and respiration are often used interchangeably, **respiration** also refers to *cellular respiration*, the process inside cells that uses oxygen to release energy from glucose and produces carbon dioxide and water as waste.

Cells depend on a constant supply of oxygen for normal function, and lack of oxygen can quickly lead to serious problems. The respiratory system ensures that oxygen enters the body and carbon dioxide is removed. Gas exchange takes place in the alveoli of the lungs, where oxygen and carbon dioxide move between the air and the bloodstream by **simple diffusion**. Each gas naturally moves from an area where it is more concentrated to an area where it is less concentrated, and this process requires no energy.

The respiratory and circulatory systems work together closely. Once oxygen enters the blood, the circulatory system transports it to the tissues while carrying carbon dioxide back to the lungs to be exhaled.

Breathing also helps keep the blood **pH** within a safe range of about **7.35 to 7.45**. Carbon dioxide dissolved in the blood forms hydrogen ions (H^+), so more carbon dioxide makes the blood more acidic and lowers the pH. Too much acidity leads to acidosis of the blood. One type, **respiratory acidosis**, can occur during hypoventilation, when a person is not breathing enough to remove carbon dioxide. Carbon dioxide then builds up, increasing hydrogen ions. Other forms of acidosis, such as metabolic acidosis, can occur for reasons unrelated to breathing. Typical symptoms of acidosis can include headache, confusion, a rapid heart rate, and muscle weakness.

Respiratory alkalosis is the opposite problem. If a person breathes too much and removes carbon dioxide too quickly, the blood loses hydrogen ions, raising the pH and making the blood too alkaline. This can happen with **hyperventilation**.

Normally, negative feedback mechanisms adjust breathing rate to keep pH stable. However, these controls may fail in people with chronic respiratory diseases such as emphysema or bronchitis, or when certain drugs interfere with the response, which can lead to persistent acidosis or alkalosis.

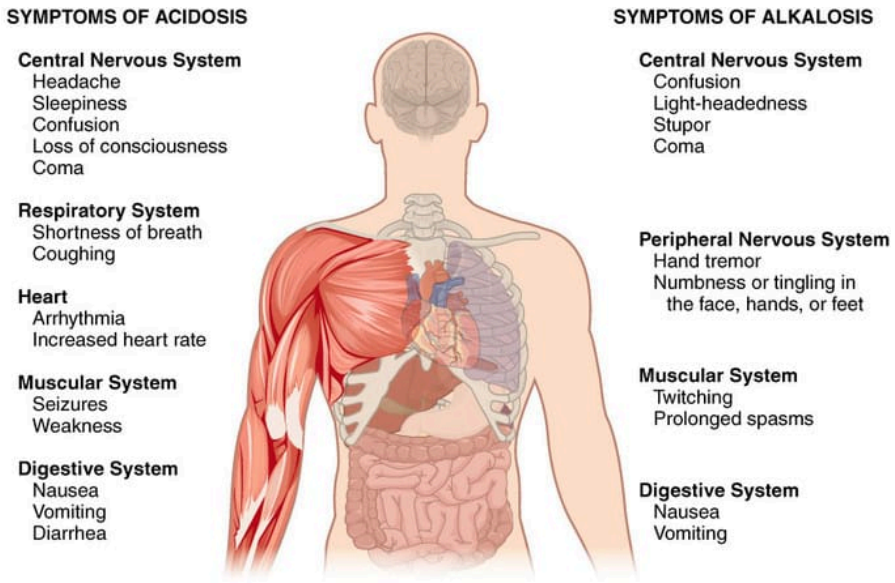


Figure 11.1.1: **Some Symptoms of Acidosis and Alkalosis**: One of the primary reasons for breathing is to regulate blood pH so that respiratory acidosis and alkalosis don't occur.

The respiratory system can be divided in **two different ways**, depending on what you want to emphasize: the **anatomical parts** or the **functional roles.** Let's start in the next section by looking at some of the anatomical parts.

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11.2: Anatomical Regions of the Respiratory Tract

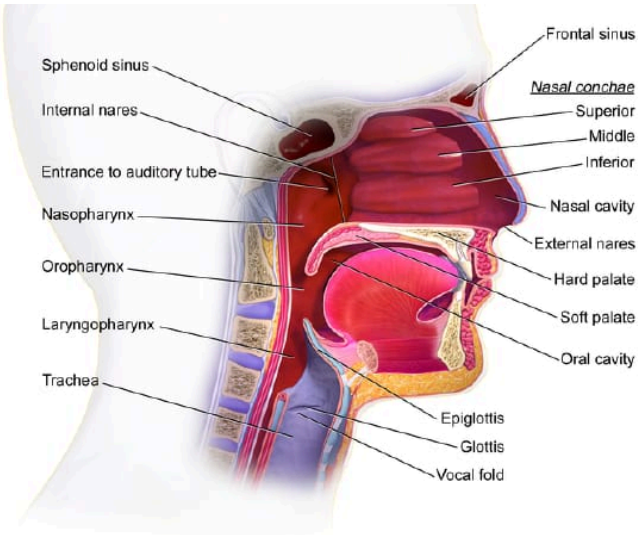
The respiratory system is organized into upper and lower regions, each containing specialized structures that guide, condition, and ultimately exchange the air we breathe.

Master this section and you'll be able to:

- Describe the major structures of the upper and lower respiratory systems and explain how air moves from the nose to the alveoli.
- Outline the role these structures have in the functioning of the respiratory system
- Describe how the pleural membranes support lung movement within the thoracic cavity.

In anatomy, the respiratory system is often divided into **upper** and **lower** regions:

- The **upper respiratory system** comprises the nose, nasal cavity, pharynx, and the paranasal sinuses.
- The **lower respiratory system** starts at the larynx and includes the trachea, bronchi, bronchioles, and alveoli.



The Upper Respiratory System

Anatomy of the Upper Respiratory System (URS)

The upper respiratory system includes the structures that **bring air into the body, warm it, moisten it, and clean it, help us speak, and trap particles** before the air moves down toward the lungs.

Nose and Nasal Cavity

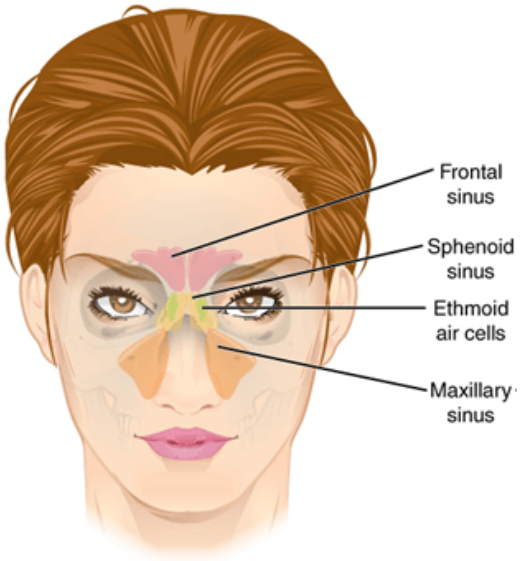
Air enters the body through the **nares**, or nostrils, which open into the **nasal cavity**, the open space inside the nose.The nasal cavity is lined with hairs and a mucous membrane that trap dust, pollen, and microorganisms. Mucus produced here keeps the surface moist and helps remove debris by moving it toward the throat. Inside the nasal cavity are the **nasal conchae**, which are curved ridges along the side walls of the nasal cavity. As air moves through the nasal cavity, the conchae make the air **swirl** instead of flowing straight through.

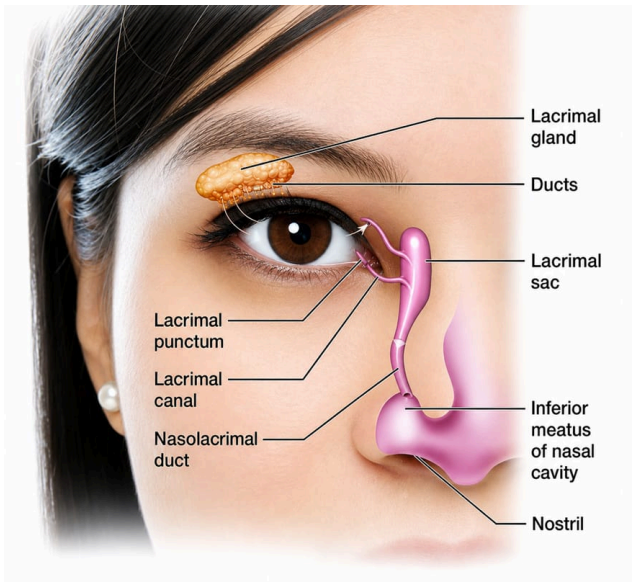
This swirling gives the nasal cavity more time to:

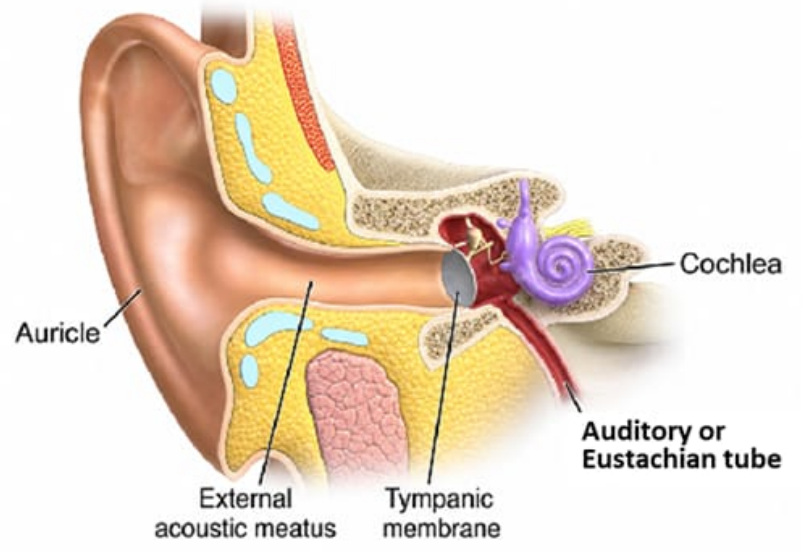
- **Warm** the air
- **Moisten** the air
- **Filter** dust and particles from the air

The nasal cavity also connects to several nearby spaces:

- **Paranasal sinuses**: small paired cavities in the skull that open into the nasal cavity. Shown in the image on the right are the right sphenoid sinus and the right frontal sinus.
- **Nasolacrimal ducts (tear ducts)**: drain tears from the eyes into the nasal cavity. This connection explains why your nose becomes runny when you cry: excess tears drain into the nose, mix with mucus, and increase the fluid in the nasal passages. See image on the left.
- **Eustachian tube (auditory tube)**: connects the middle ear to the nasopharynx and help equalize pressure.
- Because these areas connect with the nasal cavity, microorganisms can move between them, explaining why colds may lead to sinus or ear infections.







Pharynx (Throat)

The **pharynx**, often called the **throat**, is a muscular passageway behind the nose, mouth, and larynx. It is part of both the **respiratory system** and the **digestive system** because both **air** and **food/liquid** pass through it.

Air entering through the nose moves through the upper portion of the pharynx, while air that enters through the mouth joins a little lower down. All air passes through the oropharynx and laryngopharynx before entering the larynx and trachea.

Because the pharynx handles both breathing and swallowing, its lining helps protect the tissues from friction and irritation. Several tonsils are located at the back and along the sides of the throat; these are part of the immune system and help trap and destroy pathogens that enter through the nose or mouth.

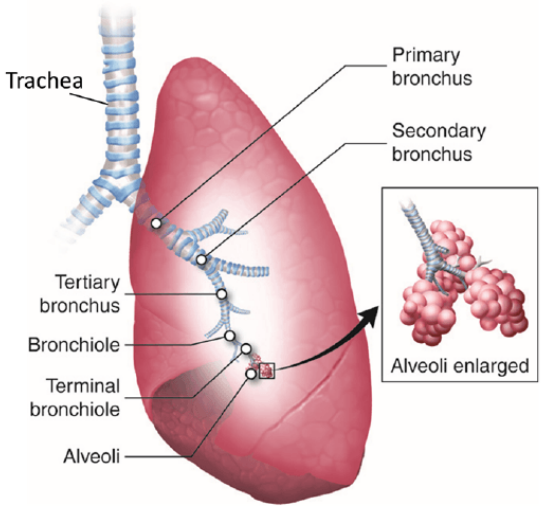
Anatomy of the Lower Respiratory System (LRS)

The lower respiratory system includes all the structures found **below the pharynx**: the **larynx, trachea, bronchi, bronchioles, and the lungs**, including their internal passageways.

Larynx: The Voice Box and Airway Guard

The larynx, also called **voice box**, is located just below the pharynx and above the trachea. It is part of the **respiratory system only** because only air should pass through it. It is made mostly of cartilage and contains the **vocal cords**, which vibrate as air passes over them to produce sound.

The larynx also helps protect the lower respiratory tract. During swallowing, the **epiglottis** folds down over the opening of the larynx, helping keep food and liquid out of the trachea and lower airways. The epiglottis is also anatomically considered part of the larynx. It is a leaf-shaped flap of elastic cartilage attached to the entrance (inlet) of the larynx, specifically connected to the thyroid cartilage and hyoid bone. While it sits just above the laryngeal opening and closely interacts with the pharynx during swallowing, its structural attachments and role firmly place it within the laryngeal framework.



The Lower Respiratory System

Trachea

The trachea, or windpipe, extends from the larynx into the thoracic cavity. It is a flexible tube supported by **16–20 C-shaped rings of hyaline cartilage**, which prevent collapse and help keep the airway open. The open ends of the rings face the esophagus and are connected by the trachealis muscle, allowing slight expansion of the esophagus during swallowing. The trachea conducts air downward until it divides into the primary bronchi.

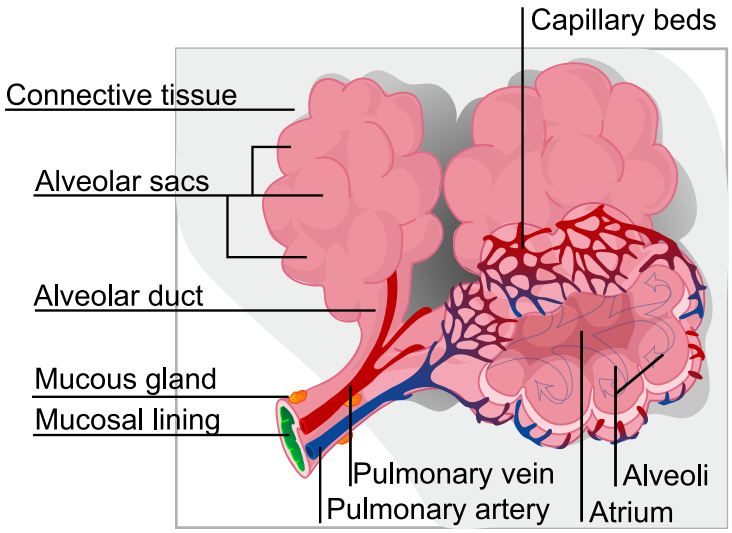
Bronchi

Just before entering the lungs, the trachea splits into the **right and left primary bronchi**, each entering a lung. Inside the lungs, each primary bronchus branches into **secondary bronchi** (one for each lobe: three in the right lung and two in the left). The secondary bronchi divide into **tertiary bronchi**, which supply smaller regions within each lobe. The bronchi form a branching network supported by plates of hyaline cartilage that become smaller and less regular as the airways become narrower.

Bronchioles

Tertiary bronchi continue branching into smaller tubes called **bronchioles**. These airways are less than 1 mm in diameter and differ from bronchi because they contain **no cartilage**. Instead, their walls contain smooth muscle that can change the diameter of the airway. Bronchioles continue branching until they reach the **terminal bronchioles**, which represent the final and smallest passageways of the conducting system.

Alveoli



The tiny alveoli, finally, are thin-walled air sacs at the very end of the bronchioles. They are the primary sites of gas exchange in the lungs. Each alveolus is surrounded by a dense network of capillaries, allowing oxygen to diffuse into the blood and carbon dioxide to diffuse out. Their walls are made of **simple squamous epithelium** to keep the diffusion distance extremely small, and they are **coated with surfactant to prevent collapse**. In fact, the alveoli are highly elastic, so they can stretch as they are filled with air during inhalation. They then spring back during exhalation in order to expel the carbon-dioxide-rich air.

The human lungs contain an average of about 480 million alveoli, though estimates may differ due to individual variability in lung size and methodology used for counting. This vast number of alveoli collectively provides an enormous surface area for gas exchange within the lungs and therefore makes efficient gas exchange possible.

These air sacs are at the end points of the respiratory tract.

Now that you have followed the pathway of air all the way from the nose, through the branching bronchi and bronchioles, and finally into the tiny alveoli where gas exchange takes place, it is time to step back and look at the larger structures that house all of these passageways. The lungs are not just collections of tubes and air sacs; they are large, complex organs with distinct shapes, lobes, and protective coverings that support all of the microscopic work happening inside. Let's introduce the lungs so you can see how all of the smaller structures fit into the bigger picture.

Gross Anatomy of the Lungs

The lungs are paired, cone-shaped organs that occupy most of the thoracic cavity. The **right lung has three lobes** and the **left lung has two lobes** to accommodate the position of the heart. Each lung is surrounded by a double-layered serous membrane called the **pleura**, which produces lubricating fluid to reduce friction as the lungs expand and recoil during breathing. Inside each lung, the branching passageways end in clusters of alveoli, where gas exchange occurs.

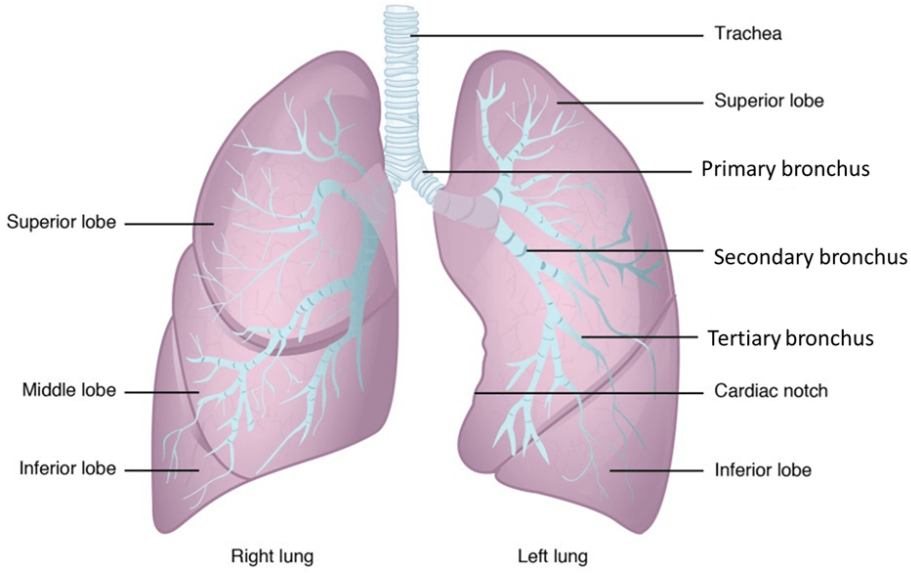


Figure 11.2.1**: Gross Anatomy of the Lungs.** The trachea divides into right and left main (primary) bronchi, which enter each lung and then branch into secondary and segmental tertiary bronchi. The right lung has three lobes — superior, middle, and inferior — while the left lung has two lobes, superior and inferior, with a noticeable indentation called the cardiac notch that accommodates the heart. The branching bronchial tree delivers air to smaller and smaller passages as it moves toward the gas-exchange surfaces deeper in the lungs.

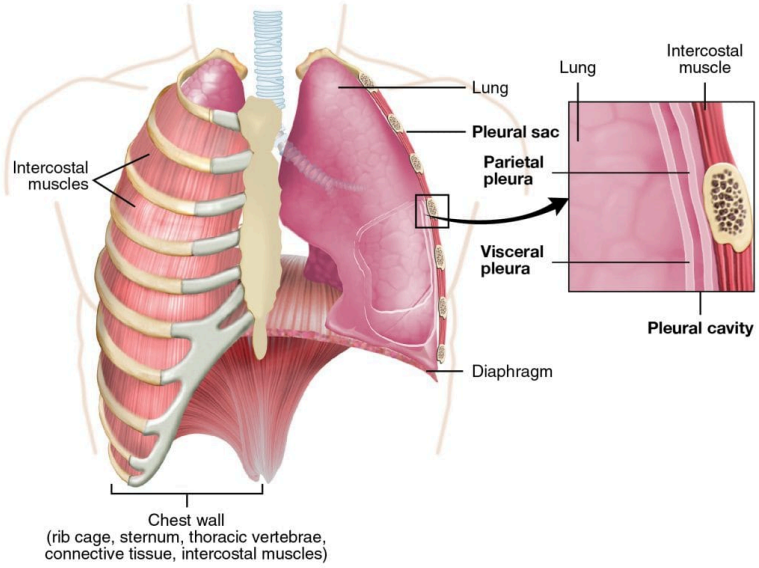


Figure 11.2.2**: The Pleura Surrounding the Lungs.** The **pleural sac** is a thin, double-layered membrane that encloses each lung. The **visceral pleura** is the inner layer that lies directly on the lung surface, while the **parietal pleura** is the outer layer that lines the inner surface of the chest wall and diaphragm. The small space between them, the **pleural cavity**, contains a thin film of fluid that reduces friction and allows the lungs to move smoothly against the chest wall during breathing.

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11.3: Functional Anatomy of the Respiratory Tract

Functional anatomy of the respiratory system focuses on what each region does during breathing, highlighting how air is moved, conditioned, and ultimately exchanged for gases in the lungs.

Master this section and you'll be able to:

- Distinguish the conducting zone from the respiratory zone based on their structures and functions.
- Explain the role of the turbinate bones.
- Compare the respiratory membrane with the respiratory epithelium.
- Describe the roles of type I alveolar cells, type II alveolar cells, and alveolar macrophages.

In the previous section you examined the **anatomical** divisions of the respiratory system. However, the system can also be divided **functionally**, depending on which aspect you want to emphasize. The anatomical approach focuses on where structures are located in the body. The functional approach highlights **what each region does** during breathing and gas exchange.

Functionally, the respiratory system is divided into

- **Conducting Zone**
  Including the **nose, nasal cavity, pharynx, larynx, trachea, bronchi, and most bronchioles**. These passageways move air to and from the lungs while filtering, warming, and humidifying it. No gas exchange occurs here.

- **Respiratory Zone**
  Including the **respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli.** These thin-walled structures are the sites of gas exchange, where oxygen enters the blood and carbon dioxide leaves it.

Structures appear in both anatomical and functional classifications, but they are grouped differently depending on the perspective. For example: Anatomically, the **bronchi** are part of the lower respiratory tract, but functionally they belong to the **conducting zone**. Seeing the system from both perspectives provides a clearer understanding of how breathing works from structure to function.

The major organs of the respiratory system function primarily to provide oxygen to body tissues for cellular respiration, remove the waste product carbon dioxide, and help to maintain acid-base balance. Portions of the respiratory system are also used for non-vital functions, such as sensing odors and speech production.

Conducting Zone

The major functions of the conducting zone are to provide a route for incoming and outgoing air, remove debris and pathogens from the incoming air, and warm and humidify the incoming air. Several structures within the conducting zone perform other functions as well. The epithelium of the nasal passages, for example, is essential to sensing odors, and the larynx is our voice box.

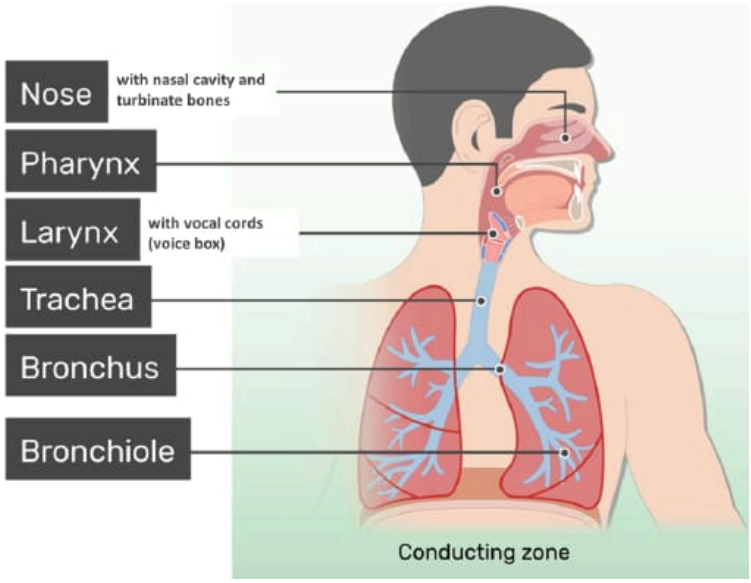
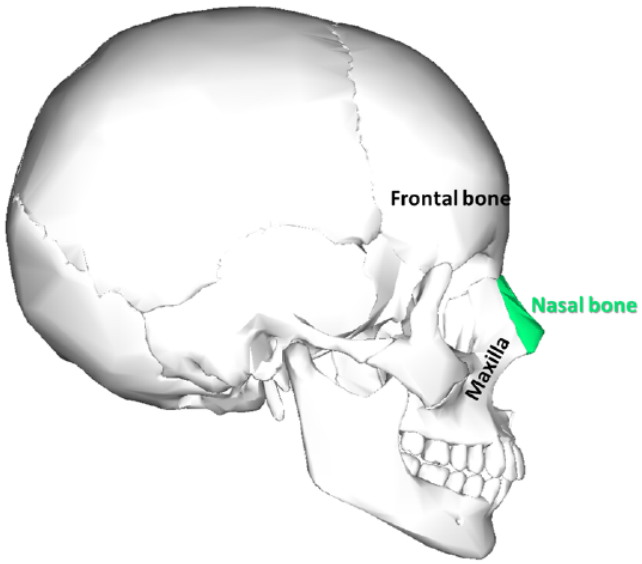


Figure 11.3.1: **Structures of the Conducting Zone.** Air enters through the nose and nasal cavity, travels through the pharynx and the larynx (which contains the vocal cords), then passes down the trachea. From there, it continues into the primary bronchi and through increasingly smaller bronchioles. These structures warm, filter, and humidify incoming air and provide a clear route to the gas-exchange surfaces deeper in the lungs.

The Nose and its Adjacent Structures

Air enters and leaves the respiratory system mainly through the nose. To understand its structure, it helps to divide the nose into two regions: the **external nose** and the **nasal cavity** (internal nose).



The upper part of the external nose is **bone**, but most of the visible, protruding portion is made of **hyaline cartilage**. This is why a skull appears “noseless” in the front: the cartilage does not remain after death.

Two small paired bones, the **nasal bones**, form the bridge of the nose. They connect superiorly to the **frontal bone** and laterally to the **maxillary bones**.

The openings into the nose, the **external nares** (nostrils), are framed medially by the **alar cartilages** and **lateral cartilages**. The

outer (lateral) parts of the external nares have no cartilage, which makes that region more flexible. These openings lead directly into the right and left nasal cavities.

Inside the nose, the space is divided into right and left sections by the **nasal septum**.

Along each lateral wall of the nasal cavity three curved bony shelves called the **turbinate bones** (or nasal conchae) stick out into the nasal cavity. Because of their curled, uneven surfaces, they force the air you breathe in to **swirl and tumble** rather than flow straight through. The **turbulence** caused by this swirling motion is helpful because it:

- **Slows the airflow**
  When air moves more slowly, it spends more time in contact with the warm, moist mucous membranes. This gives the nose more time to **warm and humidify** the air before it enters the lungs.

- **Increases particle capture**
  As air swirls, dust, pathogens, and other particles are more likely to collide with the mucus lining instead of slipping straight through. This improves **filtration** and keeps harmful debris from reaching the lower respiratory tract.

- **Enhances smell**
  Turbulence helps direct some air up toward the olfactory region, improving the ability to **detect odors**.

Several surrounding bones contain air-filled spaces called **paranasal sinuses**. These hollow cavities open into the nasal cavity and add further surface area. They also influence the **resonance** of your voice, which is why your voice sounds different when your nose is plugged or when you are congested.

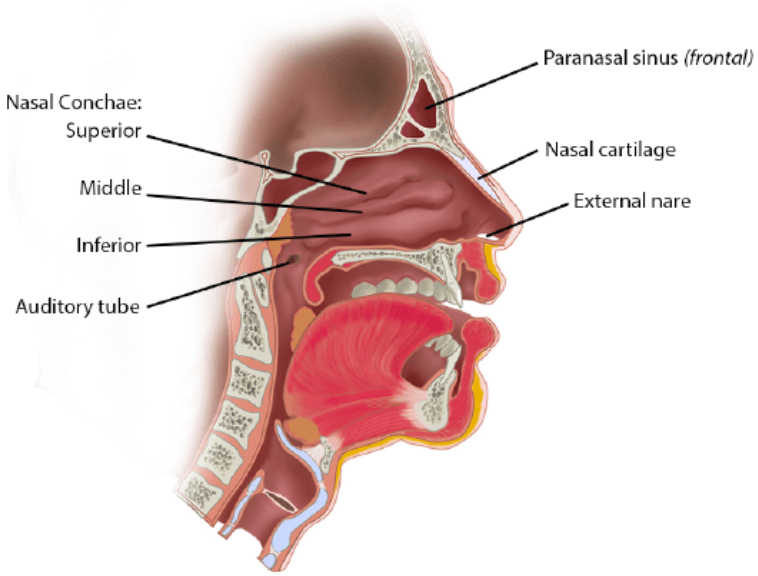


Figure 11.3.2: **Nasal Passages - Sagittal Section.** Air passes through the external naris and enters the nasal cavity, which has raised nasal conchae protruding into the space. *(Image credit: "Nasal Cavities" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of "Slagter - Drawing Head and neck: sagittal section - no labels" by Ron Slagter.)*

Respiratory Epithelium

The nasal cavity, turbinate bones, and paranasal sinuses are lined by a **mucous membrane called the respiratory epithelium.** This lining is made of **ciliated pseudostratified columnar epithelium** *(see figure below)*. **Goblet cells** within this epithelium produce **mucus**, which traps dust and other particles. The **cilia** beat in a coordinated, upward wave that moves the mucus and trapped debris toward the throat, where it can be swallowed and removed from the respiratory system. Cold air slows the movement of the cilia, which allows mucus to build up and contributes to a runny nose in cold weather.

A small region at the top of the nasal cavity contains specialized **olfactory epithelium** for detecting odors.

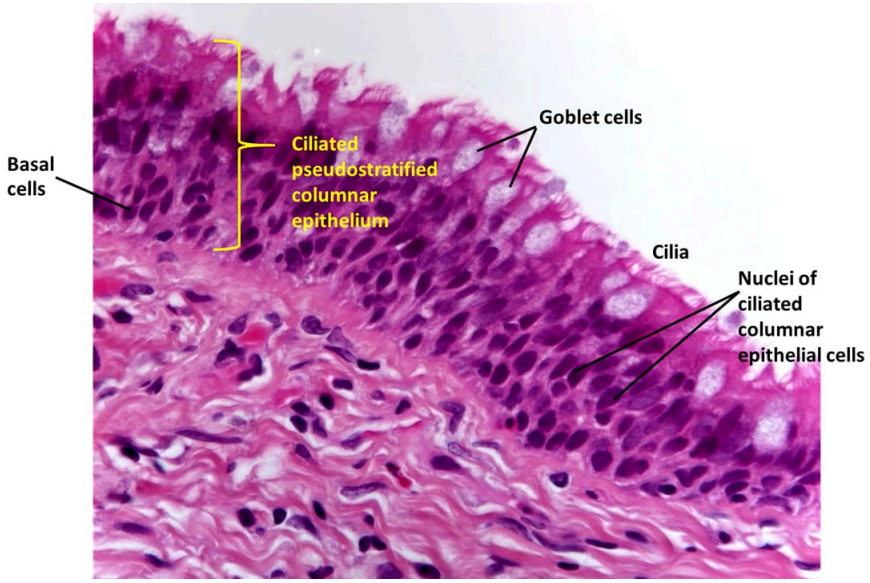


Figure 11.3.3: **Pseudostratified Ciliated Columnar Epithelium of the Respiratory Tract.** The respiratory epithelium that lines the conducting zone is made up of tall, column-shaped epithelial cells. They appear "pseudostratified" because their nuclei sit at different heights, but every cell touches the basement membrane. Note the cilia along the apical surface, which beat to move mucus toward the throat, and the pale, mucus-filled goblet cells scattered among the epithelium. Beneath the epithelium lies loose connective tissue containing fibroblasts and extracellular fibers that support and anchor the epithelium.

Pharynx and Larynx

After air passes through the nasal cavity, it enters the **pharynx**, a muscular tube shared by both the respiratory and digestive systems. The pharynx helps guide air toward the lungs and food toward the esophagus. Its lining is continuous with the nasal cavity and helps protect the tissues as air or food moves through.

Below the pharynx is the **larynx**, or voice box, a short passageway made mostly of cartilage. The larynx connects the pharynx to the trachea and has two important jobs:

1. **Keeping food out of the airway**. During swallowing, the **epiglottis** folds down to cover the opening of the larynx so food goes into the **esophagus** instead of the lungs.

2. **Producing sound**. Inside the larynx are the vocal cords, which vibrate as air moves past them.

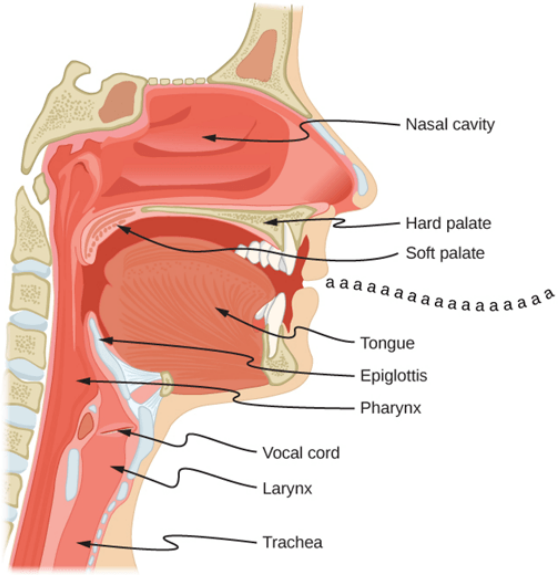


Figure 11.3.4: **Pharynx and Larynx.** These are the two key structures that guide air as it moves from the mouth and nasal cavity toward the lungs. The **pharynx** is a muscular tube that serves as a shared passageway for both air and food, directing inhaled air downward toward the **larynx**. The **larynx**, located just below the pharynx, contains the **epiglottis**, which helps keep food out of the airway, and the **vocal cords**, which vibrate to produce sound. Together, the pharynx and larynx form the main corridor for airflow into the trachea and play important roles in breathing, swallowing, and speech. (Image credit: OpenStax, CC BY 4.0. File: /mnt/data/cf561e23-be90-4bd0-9329-1f8e8f18c250.png)

Trachea

The trachea, or windpipe, is the airway that carries air from the larynx down toward the lungs. Its inner lining is still the ciliated pseudostratified columnar epithelium with the goblet cells. The cilia move mucus and trapped debris upward toward the throat, helping keep the airway clean.

Beneath the lining is connective tissue with small glands that add more mucus and fluid to keep the airway moist. Around the trachea are 16–20 C-shaped **rings of hyaline cartilage.** These rings keep the trachea open so it does not collapse, with the open part of each “C” facing the esophagus in the back.

The open ends of the rings are connected by the **trachealis muscle**, a band of smooth muscle and elastic tissue. This flexible area allows the trachea to widen and stretch slightly as you breathe and gives the esophagus room to expand when you swallow. When the trachealis muscle contracts, it helps push air out more forcefully during coughing.

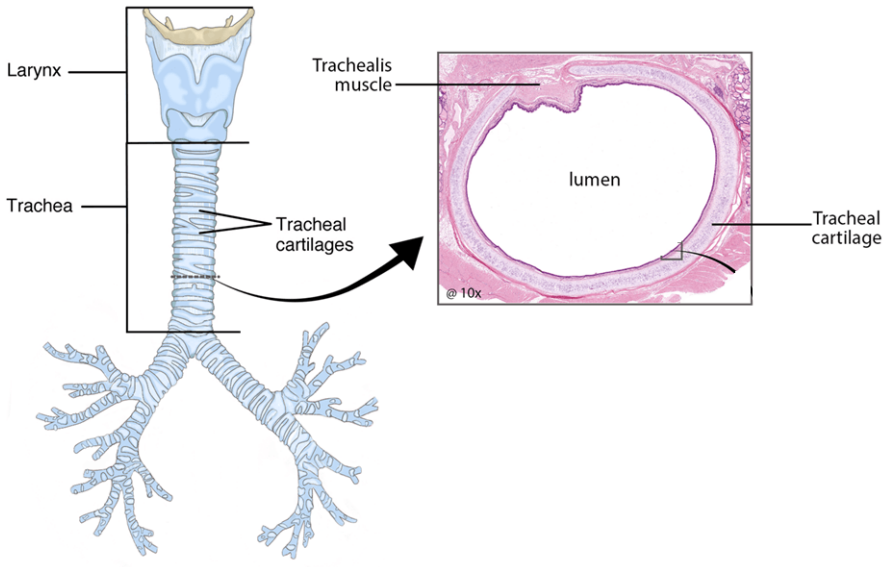


Figure 11.3.5: **Tracheal Anatomy and Histology.** The inside of the trachea is still lined with ciliated pseudostratified columnar epithelium that includes mucus-producing goblet cells, all sitting on a layer of connective tissue. Below this is the submucosa, which contains seromucous glands. Deeper in the wall are the C-shaped rings of hyaline cartilage, open at the back. The open ends are connected by the trachealis muscle and connective tissue. *(Image credit: "Trachea" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of illustration by Open Stax College, slide @ 10x provided by Virginia Commonwealth University and slide @ 400x provided by the Regents of the University of Michigan Medical School © 2022.)*

Bronchial Tree

The trachea splits into the right and left **primary bronchi** at the **carina**, a ridge that can trigger a strong cough if something enters the airway. The bronchi are also still lined with ciliated respiratory epithelium and goblet cells and are also supported by cartilage rings like the trachea.

Each primary bronchus branches into **secondary bronchi**, and each secondary bronchus divides again into **tertiary bronchi**, carrying air deeper into smaller and smaller regions of the lungs.

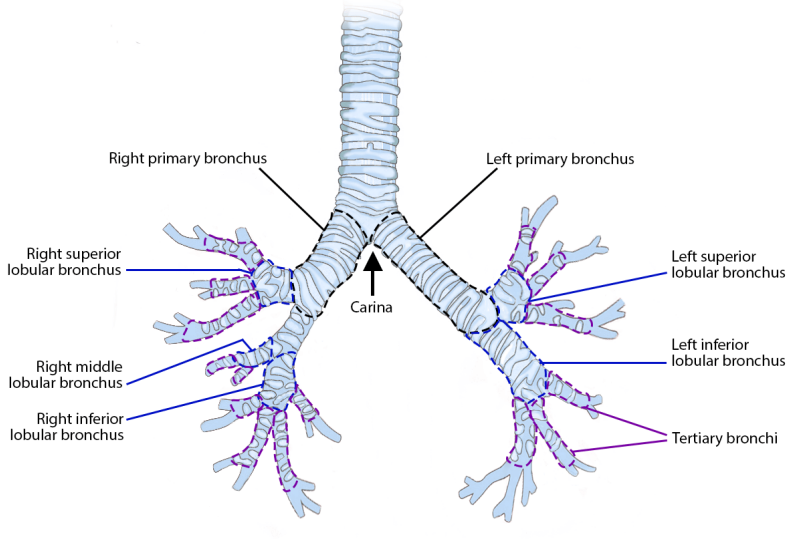


Figure 11.3.6: **Bronchi.** The trachea branches at the carina into the right and left primary bronchi that deliver air to each lung. The primary bronchi branch into the secondary bronchi that deliver air to the lobes of each lung. The secondary bronchi branch into the tertiary bronchi that deliver air into the bronchopulmonary segments of each lobe. *(Image credit: "Bronchi" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; contains modification of original by OpenStax College.)*

All of the branching airways inside the lungs together form the **bronchial tree**, named because the branching pattern looks like an upside-down tree. Like the rest of the conducting zone, these airways mainly provide a passageway for air to move in and out of the lungs. Their lining traps debris in mucus, and the cilia move that mucus upward toward the throat to be swallowed.

The **primary, secondary, and tertiary bronchi** all contain **hyaline cartilage**, which keeps the airways open. The amount of cartilage decreases as the bronchi get smaller. Smooth muscle in their walls can **bronchoconstrict** (narrow the airway) or **bronchodilate** (widen it), and this ability increases in the smaller bronchi.

Tertiary bronchi continue branching into smaller and smaller tubes until they become **bronchioles**, which are less than 1 mm wide. Bronchioles eventually lead to **terminal bronchioles**, the last part of the conducting zone. As the passages get smaller, the epithelial lining becomes thinner and gradually loses cilia and goblet cells. Bronchioles do not have cartilage, but they contain a thick layer of smooth muscle that allows strong control over airway diameter and airflow.

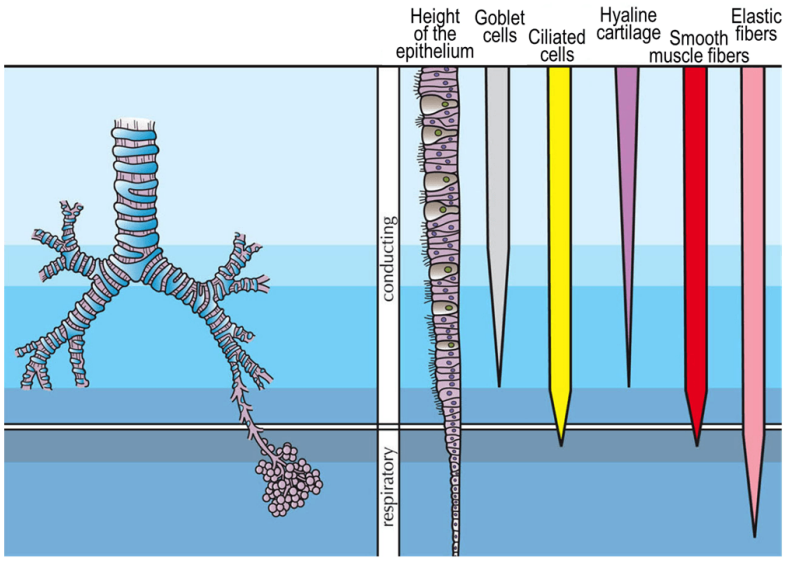


Figure 11.3.7: **Structural Changes from Conducting to Respiratory Zones.** Airway structure shifts as passages narrow: the epithelium becomes shorter, goblet and ciliated cells diminish, cartilage disappears, smooth muscle increases, and elastic fibers become more abundant as the airways transition from conducting tubes to the gas-exchange regions of the lungs.

Respiratory Zone

The respiratory zone is the area where actual gas exchange takes place.

Once a terminal bronchiole reaches the end of the conducting zone, it becomes a **respiratory bronchiole**, which marks the start of the respiratory zone. Respiratory bronchioles branch into **alveolar ducts**, and these ducts open into clusters called **alveolar sacs**, where oxygen and carbon dioxide are exchanged.

Respiratory bronchioles look very similar to terminal bronchioles, but their lining is different:

- **Terminal bronchioles** have **simple columnar epithelium**.
- **Respiratory bronchioles** have a thinner **simple cuboidal epithelium**, which helps reduce the barrier between air and blood.

As stated above, the terminal bronchioles mark the end of the air-moving pathways and the starting point of the gas-exchange region. As bronchioles get smaller, their walls become thinner, the epithelium changes from ciliated pseudostratified columnar to simple columnar and then simple cuboidal, and both cilia and mucus-producing goblet cells gradually disappear. The bronchioles also lack cartilage, unlike the bronchi, and instead contain smooth muscle that can widen or narrow to regulate airflow.

Beyond the terminal bronchioles lie the respiratory bronchioles, the first structures of the respiratory zone where tiny alveoli begin to appear in the walls and gas exchange can finally start.

Alveolar Ducts and Alveoli

The respiratory bronchioles divide into **alveolar ducts**, which are small passageways formed by the walls of the many alveoli that line them. Each alveolar duct opens into a cluster of alveoli called an **alveolar sac**. The lungs contain an estimated **480 million alveoli**, creating a huge surface area for gas exchange. Neighboring alveoli are connected by **alveolar pores**, which help equalize air pressure throughout the lung.

Each alveolar sac is wrapped in a dense **capillary bed** (see figure below). Deoxygenated blood arrives through arterioles from the pulmonary artery, and oxygenated blood leaves through venules that drain to the pulmonary vein.

An individual **alveolus** is about **200 µm** in diameter and has elastic walls. These walls stretch like a small balloon during

inhalation to increase surface area, then recoil during exhalation to help push air out.

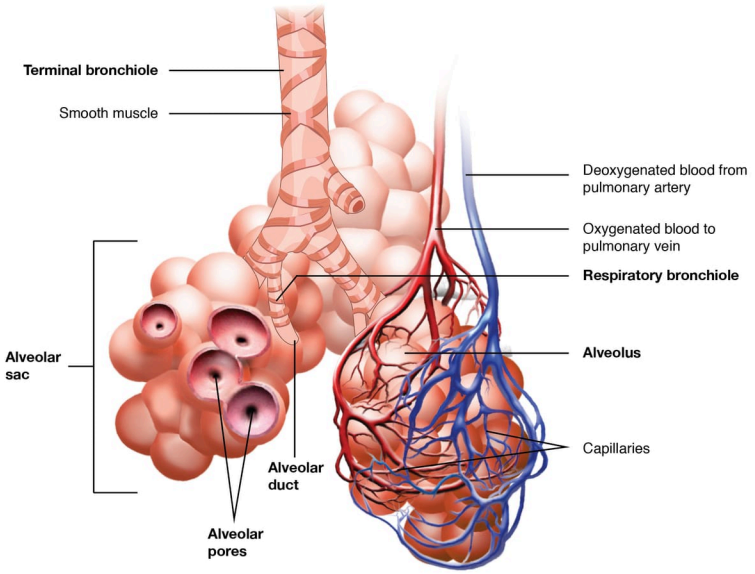


Figure 11.3.8: **Respiratory Zone.** Each respiratory bronchiole branches to a few alveolar ducts that connect to alveoli in the respiratory zone. *(Image credit: "Respiratory Zone Structures" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of The Respiratory Zone by OpenStax. "Respiratory Zone Histology" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022 under CC BY-NC-SA 3.0.)*

Alveolar Cell Types

The walls of the alveoli are made of simple squamous epithelium and include three main cell types.

Type I alveolar cells
These very thin, **squamous cells** make up about 97% of the alveolar surface area. Their extreme thinness makes gas exchange fast and efficient.

Type II alveolar cells
These cells sit between the type I cells and secrete **surfactant**, a substance that reduces surface tension so the alveoli do not collapse. They also help repair the alveolar wall when it is damaged.

Alveolar macrophages
These are **immune cells** that crawl along the inside surface of the alveoli to remove dust, debris, and pathogens that reach the deep lungs.

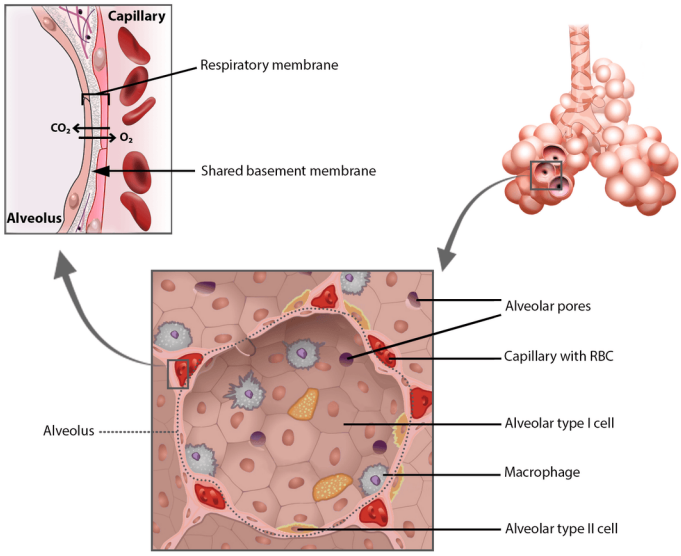


Figure 11.3.9: **Respiratory Membrane.** The alveolus is responsible for gas exchange with the blood in capillaries. Their areas of closest contact are is called the respiratory membrane, which is made of two layers of simple squamous epithelium with a shared basement membrane. *(Image credit: "Respiratory Membrane" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of The Respiratory Zone by OpenStax; includes Red blood cells by Jessica Polka.)* **Muscles of Breathing**

The Respiratory Membrane

The thin layer formed by type I alveolar cells sits on an elastic basement membrane. The capillaries touching each alveolus also have simple squamous walls, and their endothelial cells share the same basement membrane. Together, the alveolar wall, basement membrane, and capillary wall form the **respiratory membrane**, which is only about **0.5 micrometers thick**.

Because this membrane is so thin, oxygen can diffuse easily from the air into the blood, and carbon dioxide can diffuse out of the blood into the alveolus to be exhaled.

🤓 **Remember the Look-alikes That Are Nothing Alike:**

- The **respiratory epithelium** is the lining tissue that covers most of the conducting zone (nose, nasal cavity, trachea, bronchi). It is mostly **ciliated pseudostratified columnar epithelium** with goblet cells, which filters, warms, and humidifies the air and moves mucus toward the throat.
- The **respiratory membrane** is the thin barrier in the alveoli where gas exchange occurs. It is made of **simple squamous epithelium** (type I alveolar cells) fused with a basement membrane and the simple squamous endothelium of the capillaries, allowing oxygen and carbon dioxide to diffuse efficiently.

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11.4: A Closer Look at the Air We Breathe

Air entering the lungs differs from the air leaving them, and those differences provide important clues about how gas exchange and lung function work

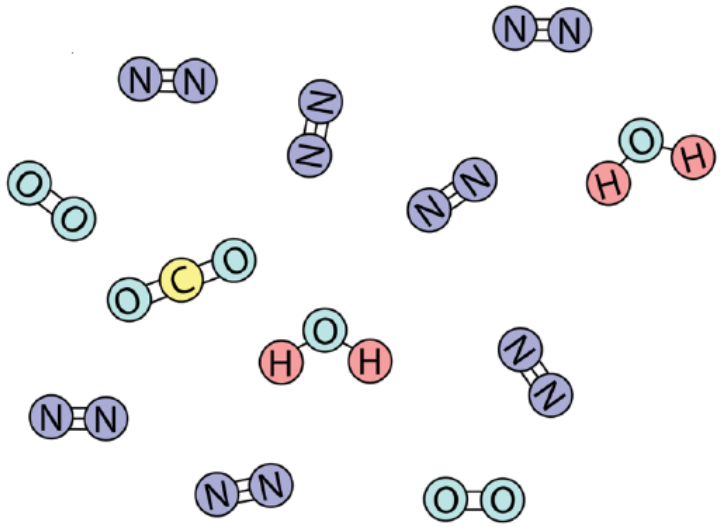
Master this section and you'll be able to:

- Distinguish the major differences between inhaled and exhaled air and explain what these differences reveal about gas exchange in the lungs.
- Identify common clinical tools used to measure oxygen and carbon dioxide in exhaled air and explain what each tool tells us about ventilation and metabolic activity.

In the previous section you examined the **anatomical** divisions of the respiratory system. However, the system can also be divided **functionally**, depending on which aspect you want to emphasize. The anatomical approach focuses on where structures are located in the body. The functional approach highlights **what each region does** during breathing and gas exchange.

Functionally, the respiratory system is divided into

Composition of Inhaled and Exhaled Air



When studying the respiratory system, it's essential to understand the differences between inhaled (inspired) and exhaled (expired) air. Inhaled air, which comes directly from the atmosphere, typically contains about **21% oxygen (O_2), 0.04% carbon dioxide (CO_2), and roughly 78% nitrogen (N)**, with trace amounts of other gases and a variable amount of water vapor depending on humidity. This composition aligns closely with the Earth's atmospheric air, as the human respiratory system does not filter out specific gases during inhalation.

Once air enters the lungs, gas exchange occurs in the alveoli. Oxygen moves from the alveoli into the bloodstream, while CO_2 and water vapor — waste products of cellular respiration — move from the blood into the alveoli to be exhaled. As a result, **exhaled air contains less oxygen (around 16 -17%)**, much more **CO_2** (about 4 - 4.4%), and is saturated with water vapor. Nitrogen content remains essentially unchanged at around 78%, as it is not metabolized by the body.

This difference in gas composition is vital for understanding how the lungs maintain efficient oxygen delivery to tissues and remove metabolic waste. The increased water vapor in exhaled air also helps humidify the respiratory passages and protect delicate tissues from drying out. Understanding these differences helps you see why simple tests for carbon dioxide, like lime water turning cloudy, reveal the presence of exhaled breath, and how your lungs work as both gas exchangers and natural

humidifiers for your body.

Key Differences of Inhaled and Exhaled Air

Gas	Inhaled Air (%)	Exhaled Air (%)
Oxygen	21	16 – 17
Carbon dioxide	0.04	4 – 4.4
Nitrogen	78	78
Water vapor	variable (low)	saturated (high)

Measuring Oxygen and Carbon Dioxide in Exhaled Air

Clinicians can measure the gases in exhaled air to understand how well someone is **ventilating**, meaning how effectively they move air in and out of their lungs and whether their "air exchange system" is working as it should. Oxygen and carbon dioxide can be measured with several simple but clinically important tools:

• **Capnography** measures the amount of CO_2 at the end of each breath, giving a quick, real-time picture of how well someone is ventilating. The word root "capno" comes from the Greek *kapnos*, meaning smoke, and was adopted in medicine to refer to carbon dioxide.

• **Color-changing CO_2 detectors** help confirm that a breathing tube has been placed correctly in the trachea rather than mistakenly in the esophagus. If the tube is in the right place, exhaled CO_2 will cause the device to change color.

• **Oxygen analyzers** measure how much oxygen remains in the exhaled air. The less oxygen that comes back out, the more the body has absorbed. This information helps clinicians and exercise specialists estimate how hard the body is working, evaluate lung and heart function, and identify medical conditions that reduce oxygen use.

• **Indirect calorimetry** measures both oxygen use and CO_2 production. From those two numbers, it can calculate how much energy the body is burning at that moment, which is the metabolic rate.

Connection: Air Pollution and Your Respiratory System

Air pollution changes the air you breathe by adding particles and chemicals such as smoke, dust, ozone, and exhaust gases. When these pollutants enter the respiratory tract, they irritate the lining of the airways, increase mucus production, and can narrow the bronchi and bronchioles. These changes make it harder for air to reach the alveoli and can reduce how much oxygen moves into the blood. People with asthma, allergies, or other respiratory conditions feel these effects more strongly because their airways are already sensitive and more likely to react.

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11.5: Overview of Respiratory Physiology

Air entering the lungs differs from the air leaving them, and those differences provide important clues about how gas exchange and lung function work

Master this section and you'll be able to:

- Identify the four major processes of respiratory physiology and explain how each contrigutes to oxygen

The major organs of the respiratory system work together to achieve three essential goals: supplying oxygen to body tissues for cellular respiration, removing carbon dioxide produced by those tissues, and helping maintain the body's acid–base balance. The system also supports several non-vital but important roles, such as detecting odors with olfactory receptors and producing vocal sounds for speech and communication.

Respiratory physiology focuses on how air is moved into and out of the lungs, how gases are exchanged between the lungs and the blood, and how oxygen is transported to cells that depend on it for energy. Each step of the process is tightly coordinated to maintain homeostasis, ensuring that cells receive enough oxygen for ATP production and that excess carbon dioxide — an acid-producing waste — is efficiently removed.

Pulmonary Ventilation

Pulmonary ventilation, or breathing, is the physical movement of air into and out of the lungs. As air passes through the conducting zone — the nose, pharynx, larynx, trachea, and bronchi — it is filtered, warmed, and humidified, protecting the delicate alveolar surfaces. The mechanics of breathing depend on pressure changes within the thoracic cavity. When the diaphragm and external intercostal muscles contract, the thoracic cavity expands, lung volume increases, and intrapulmonary pressure falls below atmospheric pressure, causing air to flow in (inhalation). When these muscles relax, elastic recoil of the lungs and chest wall reduces lung volume, pressure rises, and air flows out (exhalation). These alternating pressure changes sustain a continuous flow of air that reaches the respiratory zone where gas exchange occurs.

External Respiration

External respiration refers to gas exchange that occurs in the lungs between alveolar air and pulmonary capillary blood. At the alveolar membrane (only two cell layers thick) oxygen diffuses from alveoli into the blood because the partial pressure of oxygen is higher in alveolar air than in the deoxygenated blood arriving from the pulmonary arteries. Carbon dioxide moves in the opposite direction, diffusing from the blood into the alveoli where its partial pressure is lower. This exchange follows simple diffusion principles and depends on both gas solubility and the thinness and surface area of the respiratory membrane.

Transport of Gases in the Blood

Once oxygen enters the bloodstream, it must be transported efficiently to tissues throughout the body. About 98.5 percent of oxygen binds reversibly to hemoglobin within red blood cells, forming oxyhemoglobin. The remaining oxygen dissolves directly in plasma. Hemoglobin's affinity for oxygen changes depending on local factors such as temperature, pH, and carbon dioxide concentration — allowing it to release oxygen where cells need it most. Carbon dioxide, the byproduct of cellular metabolism, travels in three forms: roughly 70 percent as bicarbonate ions (HCO_3^-) in plasma, about 23 percent bound to hemoglobin as carbaminohemoglobin — different attachment site than O_2, — and around 7 percent dissolved directly in plasma.

Internal Respiration

Internal respiration occurs at the systemic capillaries between the blood and body tissues. Oxygen diffuses out of the blood and into cells, while carbon dioxide diffuses out of cells and into the blood. This gas movement continues to follow partial pressure gradients: oxygen moves from areas of higher to lower concentration, ensuring that active tissues receive what they need for

cellular respiration. The carbon dioxide produced as a metabolic waste is carried back to the lungs for exhalation, maintaining both energy balance and acid–base stability.

Together, these four interconnected processes — pulmonary ventilation, external respiration, gas transport, and internal respiration — illustrate how structure and function work seamlessly to sustain life. They explain why the composition of inspired air differs from expired air, how breathing rate can change with exercise or disease, and how clinical measurements such as blood gases reflect respiratory health. Overall, respiratory physiology demonstrates how the respiratory system not only supports gas exchange but also plays a key role in maintaining homeostasis across the entire body.

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11.6: Mechanics of Breathing — Pulmonary Ventilation

Breathing begins with a simple physical principle: air moves into and out of the lungs only when the body creates a pressure difference that draws it inward or pushes it outward.

Master this section and you'll be able to:

- Describe how changes in thoracic volume create pressure differences that drive airflow into and out of the lungs.
- Identify the primary muscles involved in quiet inspiration and quiet expiration.
- Summarize how pleural membranes, pleural fluid, and negative intrapleural pressure keep the lungs attached to the thoracic wall.

To move air into the lungs, the body must create a pressure difference: the pressure inside the lungs has to fall below atmospheric pressure so that air flows inward down its pressure gradient. This drop in pressure occurs when lung volume increases, because expanding the space inside the lungs spreads the gas molecules farther apart and lowers their pressure.

In other words, the essence of breathing in is **reducing intrapulmonary pressure** so that atmospheric pressure can push air into the airways until the two pressures equalize. To understand how this pressure drop is created, we need to look at two related ideas: how the respiratory muscles expand the thoracic cavity, and how the lungs and thoracic wall interact to produce the actual change in lung volume.

Ley's begin with the respiratory muscles and how their contractions enlarge the thorax.,

Changing Thoracic Volume

Because the lungs are attached to the inner surface of the thoracic wall through the **pleura**, they cannot change their volume on their own. Any change in lung volume happens only when the thoracic cavity itself expands or recoils, and the lungs simply follow those movements.

Mechanism of Inhalation (Inspiration)

The muscle that generates the greatest change in thoracic volume (and thereby the greatest contribution to breathing) is the diaphragm (figure 2.1). Separating the thoracic and abdominal cavities, this sheetlike muscle forms a dome shape in the relaxed state that encroaches into the thorax. This sheet is formed of three sections, the anterior portion originating at the ribs and sternum, and the posterior portion originating on the vertebrae. These are connected by the central portion that is comprised of a tendon sheet.

Inhalation begins with the **contraction of the diaphragm** and is **assisted by the external intercostal muscles**. Under normal resting conditions, a typical human **respiratory rate** ranges from about **12 to 18 breaths per minute**. When breathing becomes more forceful, such as during vigorous inhalation above roughly 35 breaths per minute or in situations approaching respiratory failure, additional accessory muscles are recruited. These include the sternocleidomastoid, platysma, and scalene muscles of the neck, as well as muscles of the chest and back such as the pectorals and latissimus dorsi.



During quiet breathing, the **diaphragm** is the **primary muscle** driving inhalation. When it contracts, it flattens and moves downward, expanding the thoracic cavity. At the same time, the **external intercostal muscles** lift and

widen the rib cage. Together, these actions increase thoracic volume and lower the pressure inside the lungs below atmospheric pressure. It is similar to pulling open an accordion — expanding the space inside creates lower pressure, and air naturally flows in to fill that space.

Because air naturally moves from higher pressure to lower pressure, this drop in intrapulmonary pressure draws air into the conducting zone — through the trachea, bronchi, and bronchioles — where it is filtered, warmed, and humidified on its way to the lungs.

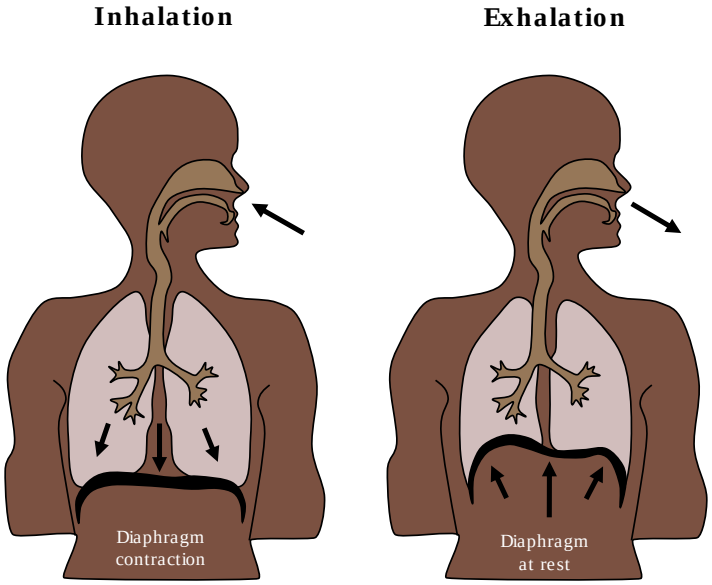


Figure 11.6.1: **Mechanics of Breathing.** During inspiration, the diaphragm contracts and moves downward, increasing thoracic volume and drawing air into the lungs. During expiration, the diaphragm relaxes and rises, decreasing thoracic volume and pushing air out.

Mechanism of Exhalation (Expiration)

Expiration is **usually a passive process** that follows the end of inhalation. When the diaphragm relaxes, it moves upward toward its dome shape, and the external intercostal muscles release their pull on the rib cage. Because the lungs contain abundant elastic fibers, they naturally recoil toward their smaller resting size once the stretching force of inspiration is gone. This **elastic recoil** creates a rise in intrapulmonary pressure, pushing air out of the lungs.

The lungs recoil effectively because of elastin within the lung tissue and the presence of surfactant, which reduces the surface tension of the thin layer of water lining the alveoli. Without surfactant, the surface tension would be so strong that the alveoli would collapse at the end of each breath, making the next inhalation extremely difficult. With adequate surfactant, the lungs return smoothly to their resting size as air flows out.

Although quiet expiration is passive, expiration can become an active, forceful process when breathing demands increase. In **forced exhalation**, the **internal intercostal muscles pull the rib cage downward and inward**, reducing thoracic volume. At the same time, the abdominal muscles contract to push the abdominal organs upward against the diaphragm, accelerating the expulsion of air. These muscle actions help clear the lungs more completely during activities such as vigorous exercise, coughing, or respiratory distress.

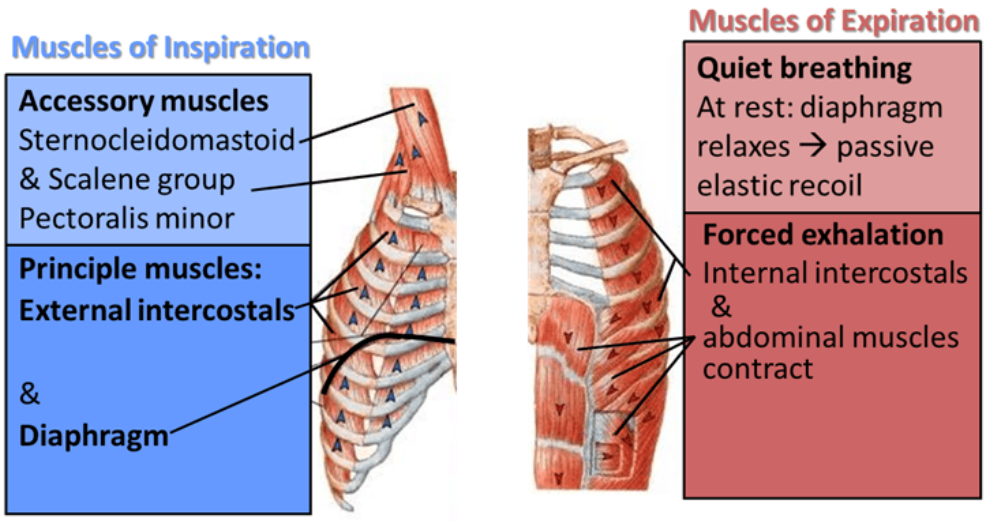


Figure 11.6.2: **Muscles Involved in Breathing.** During inspiration, the diaphragm and external intercostal muscles enlarge the thoracic cavity, while accessory muscles in the neck and upper chest assist during deeper or labored breaths. During expiration at rest, the diaphragm simply relaxes and the elastic tissues of the lungs return to their smaller size. During forced exhalation, the internal intercostals and abdominal muscles actively contract to push air out more quickly.

How the Lungs Move with the Chest Wall

As you know, the lungs cannot move on their own because they have no muscles, so they depend completely on the movements of the thoracic wall. When the thoracic wall changes its volume, the lungs come along for the ride.

The Pleural Membranes and Their Fluid

The inside of the thoracic cavity is lined by the **parietal pleura** and the outer surface of each lung is wrapped by the **visceral pleura**. The extremely thin space between these two membranes is the **pleural cavity**, which contains only about 5 to 10 mL of pleural fluid. This tiny fluid layer creates **surface tension**, and that tension holds the two pleural layers tightly together.

A simple analogy is how a contact lens sticks smoothly to the eye because of the thin film of tears between the two surfaces. It stays in place yet moves when the eye moves. This is similar to how pleural fluid keeps the lungs following the chest wall. The surface tension keeps the lungs adhered to the chest wall so that when the thoracic wall expands or recoils, the lungs move with it.

Intrapleural Pressure

To understand why the pleural membranes matter so much, we also need to consider **intrapleural pressure**, the pressure inside the pleural space. Even at rest the elastic tissues in the lungs are slightly stretched. This stretching means the lungs naturally want to recoil inward. The chest wall is built the opposite way. Its tissues and shape tend to push outward.

These two opposing forces would normally pull away from each other. The surface tension in the pleural fluid prevents that separation, and the constant pull in opposite directions creates a pressure in the pleural space that is slightly below atmospheric pressure. This **negative intrapleural pressure** is the reason the lungs stay expanded and follow every movement of the chest wall.

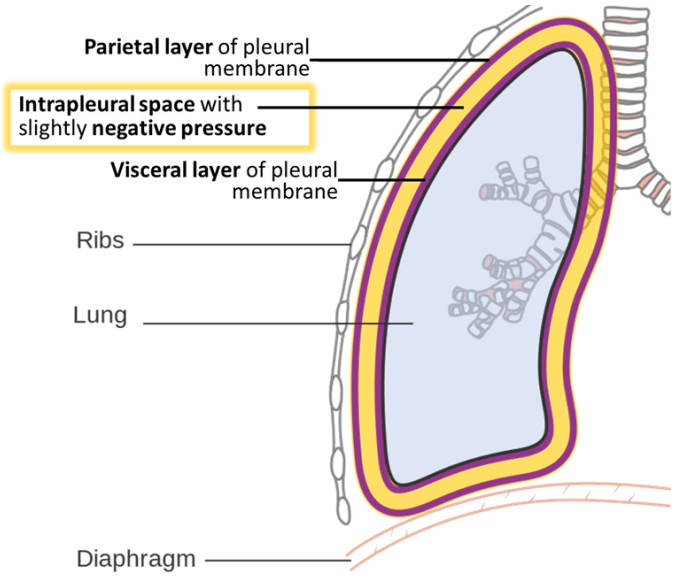


Figure 11.6.3: **The Pleura and the Lung.** A double-layered pleural membrane surrounds each lung, with the parietal pleura tightly attached to the inner surface of the thoracic wall and the visceral pleura covering the lung itself. A thin film of fluid in the pleural space, and the sllightly negative pressure causes the two layers to cling together, so when the ribs and diaphragm move, the lungs follow. This adhesion is what allows the lungs to expand and recoil with every breath.

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11.7: Pulmoany Function Tests — Spirometry

Spirometry is a pulmonary function test that measures how effectively air moves into and out of the lungs, helping clinicians determine whether a person has an obstructive or restrictive pulmonary disease.

Master this section and you'll be able to:

- Describe the purpose of pulmonary function testing and explain how these tests assess respiratory volumes and capacities.
- Explain how changes in diffusion and pulmonary surface area influence breathing rate and depth.
- Summarize how central and peripheral chemoreceptors regulate respiratory rate in response to carbon dioxide, pH, and oxygen levels.
- Distinguish between obstructive and restrictive lung diseases.

Introduction

Pulmonary function tests measure how well the lungs move air and exchange gases, giving clinicians a clearer picture of respiratory health. They are performed to understand the cause of shortness of breath, to track lung function over time, and to evaluate how well treatments are working. These tests quantify airflow, lung volumes, and gas exchange to show what the lungs can do and how efficiently they do it.

Because oxygen uptake and carbon dioxide removal must remain balanced between the tissues and the lungs, any disruption in diffusion across the respiratory membrane can alter normal breathing patterns. Diffusion depends in part on pulmonary surface area, which can shrink with disease, injury, or even changes in body position. When surface area decreases, gas exchange becomes less efficient and the rate and depth of breathing usually rise to compensate. Pulmonary function tests help reveal these changes by measuring how much air the lungs can move and how effectively gases are exchanged.

Spirometry is one of the simplest ways to assess lung performance. It measures airflow during breathing and is widely used because it can reveal changes in lung volume and airway resistance.

Respiratory Controls and Breathing Rate

The breathing rate is continually adjusted to match the body's metabolic needs. These adjustments are directed by **respiratory control centers in the medulla oblongata and pons**, which regulate the depth and rate of breathing to keep blood gases, especially carbon dioxide, within homeostatic limits. The normal respiratory rate is about 12 to 18 breaths per minute.

Most respiratory control is driven by carbon dioxide. When CO_2 levels rise, they combine with water to form carbonic acid, lowering blood pH. Medullary chemoreceptors detect this drop in pH and increase the breathing rate. Faster breathing removes more CO_2, raising blood pH back toward normal. When balance is restored, ventilation returns to baseline.

Peripheral chemoreceptors in the carotid bodies and aortic bodies provide additional input. They detect changes in CO_2, pH, and, to a lesser degree, oxygen. When CO_2 rises or oxygen becomes unusually low, they stimulate an increase in ventilation. When CO_2 falls, the respiratory center slows the breathing rate.

Obstructive and Restrictive Pulmonary Disease

• Restrictive Lung Disease: The Problem Is Expansion

In restrictive lung diseases, the lungs cannot expand fully. Their compliance is reduced because the tissue becomes stiff, scarred, inflamed, or filled with fluid. Even with strong inspiratory muscle effort, the lungs do not open much, so total lung volumes drop.

Think of it as trying to inflate a stiff backpack. The lungs never open very far.

Common causes include **pulmonary fibrosis, pneumonia, and pulmonary edema,** and **obesity-related reduction in lung expansion.**

- ## Obstructive Lung Disease: The Problem Is Airflow Out

Obstructive lung diseases narrow or block the airways. The lungs may expand well, but exhalation becomes slow and incomplete because air cannot move out easily. This leads to air trapping and larger-than-normal lung volumes.

Think of it as trying to exhale through a narrow straw. Filling is not the issue, but emptying is slow and difficult.

Examples include **asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), and emphysema.**



Spirometry as a Diagnostic Tool for Obstructive or Restrictive Disease

Spirometry measures how much air a person can inhale and exhale and how quickly that air can be expelled. It is one of the most common clinical assessments because it can reveal **obstructive patterns**, where airflow is limited, and **restrictive patterns**, where lung expansion is reduced.

A spirometry test is performed by breathing forcefully through a mouthpiece connected to a handheld flow sensor. A nose clip ensures that all air moves through the mouthpiece. *(See image on the right).*
Sensors measure airflow and send the data to a computer. The resulting graph shows the volume of air exhaled over time and allows clinicians to calculate specific lung volumes and capacities. These measurements provide essential information about how well the lungs are functioning.

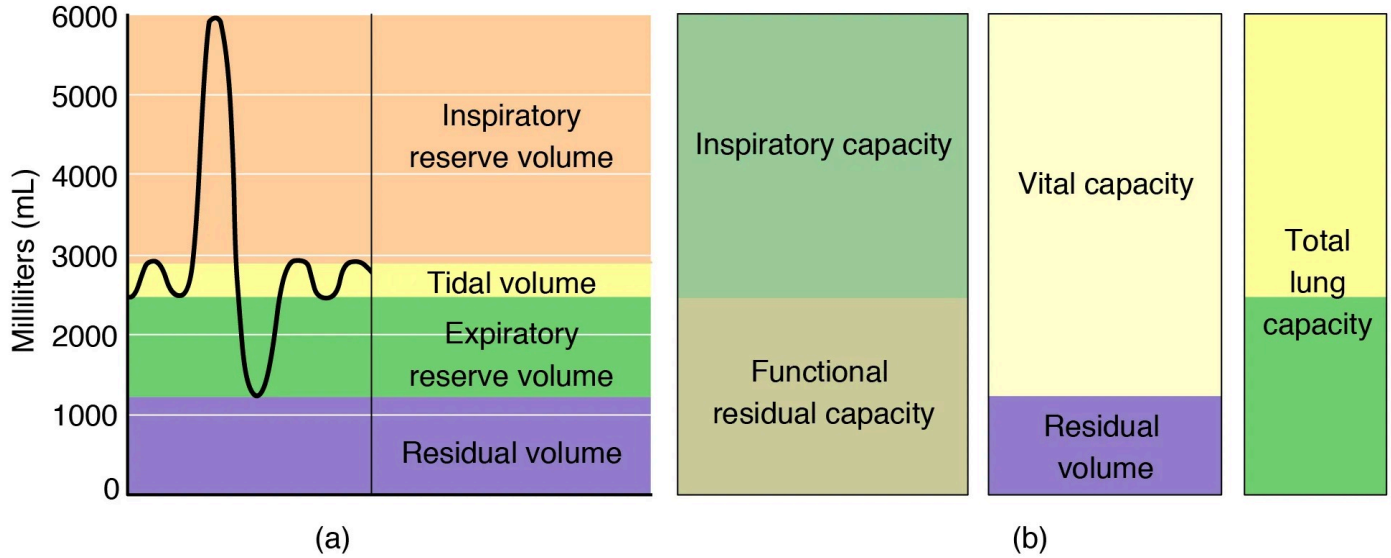


Figure 11.7.1: **Spirogram and Specific Lung Volumes.** These measurements are obtained using a spirometer, which records airflow and volume changes during breathing.

Respiratory Volumes

Respiratory volume refers to the different amounts of air moved by, or contained within, the lungs at specific points in the breathing cycle. Four major respiratory volumes are typically measured:

- **Tidal volume (TV):** The amount of air that enters or leaves the lungs during quiet, unforced breathing. In most adults this is roughly **500 milliliters.**
- **Inspiratory reserve volume (IRV):** The additional air that can be drawn into the lungs with a deep, forceful inspiration beyond the tidal inhale.
- **Expiratory reserve volume (ERV):** The extra amount of air that can be forcefully exhaled after a normal tidal exhalation, up to about 1200 milliliters in men.
- **Residual volume (RV):** The air that remains in the lungs after a maximal exhalation. This leftover air prevents alveolar collapse and makes the next breath easier to initiate.

These volumes vary with factors such as age, sex, body size, and respiratory health. Measuring them can provide important insight into how well the lungs are functioning.

Respiratory Capacities

Respiratory capacities describe how different lung volumes combine to show how much air the lungs can hold or move at a given time. Each capacity is made from two or more of the basic respiratory volumes.

- **Total Lung Capacity (TLC)**

  TLC is the sum of *all* lung volumes (TV + IRV + ERV + RV). It represents the total amount of air in the lungs after a forceful inhalation. On average, TLC is about 6000 mL in men and about 4200 mL in women.

- **Vital Capacity (VC)**

  VC is the total amount of air that can be moved into or out of the lungs. It equals TV + IRV + ERV — all of the movable volumes, but not residual volume. For most adults, VC ranges from about 4000 to 5000 mL.

- **Inspiratory Capacity (IC)**

  IC is the maximum amount of air that can be inhaled after a normal tidal exhalation. It combines tidal volume and inspiratory reserve volume (TV + IRV).

Two of the Most Frequently Assessed Spirometry Values

1. Forced Vital Capacity (FVC)

FVC is the total amount of air a person can forcefully exhale after taking the deepest possible breath in. It assesses overall lung volume and helps identify both obstructive and restrictive patterns.

FVC is usually reduced in restrictive disorders — such as pulmonary fibrosis, neuromuscular disorders, or obesity-related restriction — because the lungs cannot fully expand. It may be normal or only slightly reduced in obstructive conditions.

2. Forced Expiratory Volume in 1 Second (FEV_1)

FEV_1 is the amount of air exhaled in the first second of a forced exhalation. It is especially useful for assessing **airway resistance.** A low FEV_1 often indicates an obstructive problem, such as such as asthma, COPD, chronic bronchitis, emphysema, or cystic fibrosis.

Comparison of Restrictive and Obstructive Lung Diseases Based on Spirometry Findings.

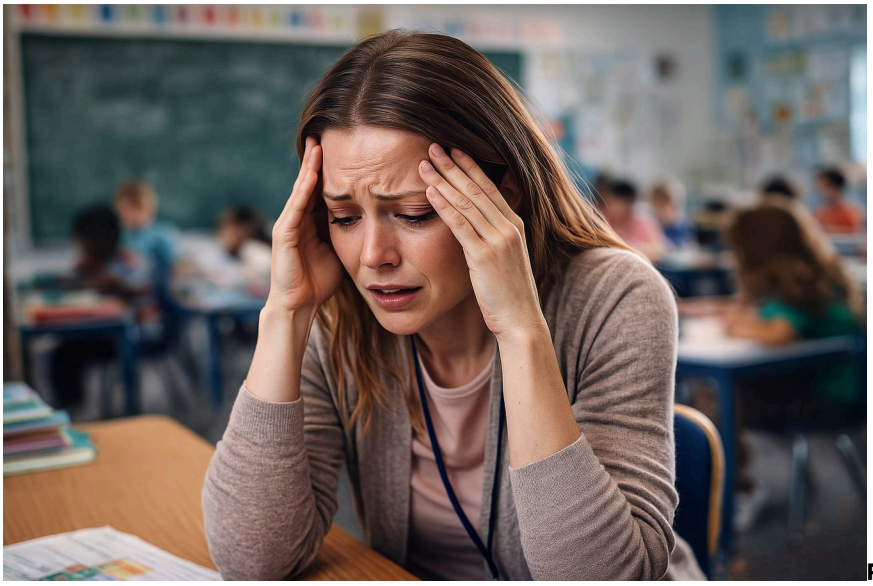
Disease Type	FEV_1 %	FVC	What the Disease Means
Restrictive	80 percent or higher	Low	The **lungs cannot expand** well because the tissue is stiff, fibrotic, inflamed, or fluid-filled. Total lung volumes are reduced because the lungs never fully open.
Obstructive	Lower than 80 percent	Normal or low	The **airways are narrowed or blocked**, making it hard to exhale air. Air becomes trapped, and exhalation is slow and incomplete. Lung expansion may be normal or increased.

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11.8: Normal and Altered Breathing Patterns

Case Study: “Something Is Off With My Breathing”



Patient: *Maya R.*, 32-year-old elementary school teacher
Chief Complaint: “I feel like I cannot catch my breath, and now my fingers feel tingly.”

Background

Maya is normally healthy, physically active, and has no history of respiratory disease. Earlier in the day she returned from recess duty where she jogged lightly with her students. After returning indoors, she began to feel “lightheaded” and noticed her breathing becoming fast and shallow.

When she arrives at the campus health center, her vital signs are:

- Respiratory rate: **32 breaths per minute**
- Tidal volume estimate: **well below normal, shallow breathing**
- Pulse: **110 beats per minute**
- SpO_2: **98 percent**

She reports tingling around her mouth and fingertips and says, “It is weird because I feel short of breath even though I am breathing so fast. I keep trying to take deeper breaths, but I cannot.”

History and Context

Maya explains that this episode began after she received an email notifying her that one of her students had been seriously injured in an accident off-campus. She felt a sudden rush of anxiety, followed by rapid breathing.

She denies:

- Chest pain
- Recent illness or fever
- Long-distance travel
- Coughing or wheezing
- Use of sedatives, opioids, or alcohol

She has recently been training for a local 5K race and states she “never has trouble breathing when running.”

Physical Examination

- No signs of airway obstruction
- Clear lung sounds
- No abnormal posturing or use of accessory muscles
- Breathing pattern: **very rapid and shallow**
- No cyanosis
- Normal neurological exam

Clinician’s Observations

The clinician notes a mismatch between how fast Maya is breathing and her actual metabolic demand at rest. Despite rapid breathing, her oxygen saturation is normal.

In-Visit Change

After guided breathing exercises (slow, paced breathing), Maya’s symptoms improve within minutes. Her respiratory rate decreases to **16 breaths per minute**, and the tingling fades.

Questions

1. Based on Maya's respiratory rate and breathing depth, which term best describes Maya’s breathing pattern/ventilation type on arrival at the health center?
   Explain why.

2. No blood pH was determined. Can you guess though what her blood pH likely looks like and why? How does this explain the tingling sensation in her mouth and fingertips?

3. How does hyperventilation differ from hypoventilation with regard to:

   - CO_2 levels
   - pH changes
   - Possible causes
   - Expected breathing patterns

4. What breathing pattern should Maya display given her sitting in the class room? Provide expected respiratory rate and tidal volume.

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11.9: External Respiration

External respiration describes the exchange of gasses between the external environment and the bloodstream in the alveoli.

Master this section and you'll be able to:

- Describe what external respiration means.
- Explain how oxygen and carbon dioxide diffuse down their partial pressure gradients during gas exchange.
- Identify the structural components of the respiratory membrane and describe why its thinness is essential for diffusion.
- Describe how alveolar surface area, membrane thickness, and gas solubility influence external respiration.
- Summarize how ventilation–perfusion matching maintains efficient gas exchange in the lungs.

Gas Exchange

Gas exchange takes place at two locations in the body:

1. **in the lungs**, where oxygen is taken up and carbon dioxide is released at the respiratory membrane, and
2. **in the tissues**, where oxygen is delivered and carbon dioxide is collected.

External respiration refers to gas exchange with the external environment in the alveoli of the lungs, whereas **internal respiration** refers to gas exchange with the internal environment at the tissues. Both processes rely on simple diffusion rather than energy-dependent transport. Oxygen and carbon dioxide move passively down their pressure gradients across membranes. Several features of lung anatomy maximize this diffusion, including the high permeability of the respiratory membrane, the extremely thin layers separating air from blood, and the large overall surface area of the alveoli.

External Respiration: Gas Exchange in the Lungs

External respiration refers to the exchange of gases between the alveoli and the pulmonary capillaries. Deoxygenated blood arrives from the heart through the pulmonary artery, branches repeatedly, and eventually forms a dense meshwork of pulmonary capillaries. These capillaries lie directly against the alveoli, creating the respiratory membrane—an extremely thin barrier where gases diffuse between air and blood.

As blood moves through this capillary network, oxygen (O_2) diffuses from the alveolar air into the blood, while carbon dioxide (CO_2) diffuses from the blood into the alveoli to be exhaled. A small amount of oxygen dissolves directly into the plasma, but most binds to hemoglobin in red blood cells. Oxygenated hemoglobin turns the blood bright red, and this oxygen-rich blood returns to the heart via the pulmonary veins. Carbon dioxide is released in dissolved form, from hemoglobin, or after being chemically converted in the plasma.

External respiration includes both the movement of air into and out of the lungs (ventilation) and the diffusion of gases across the respiratory membrane. Diffusion occurs because each gas moves down its own partial pressure gradient. In the alveoli, the partial pressure of oxygen (PO_2) averages about 104 mmHg, while incoming pulmonary capillary blood has a PO_2 of about 40 mmHg. This steep 64-mmHg gradient drives oxygen rapidly into the blood.

The partial pressure gradient for CO_2 is much smaller (about 45 mmHg in the blood and 40 mmHg in the alveoli). However, because CO_2 is roughly twenty times more soluble than oxygen in blood and alveolar fluid, it still diffuses very rapidly, and nearly equal amounts of O_2 and CO_2 cross the membrane despite the unequal gradients.

Four major anatomical and physiological features make external respiration efficient:

- a very large alveolar surface area,
- a very thin respiratory membrane

- a strong partial pressure gradients for O_2 and CO_2, and
- a close matching of airflow (ventilation) and blood flow (perfusion).

Let's look a bit closer at each of these:

1) Alveolar Surface Area & Thickness of the Respiratory Membrane

Combining all ~300 million alveoli in the lungs creates an enormous surface area for gas exchange, about the size of a tennis court. Each alveolus is wrapped in a dense capillary bed, providing countless sites where gases can diffuse. Diseases that destroy alveolar walls, such as emphysema, reduce surface area and impair gas exchange.

Diffusion is most effective across very short distances. The respiratory membrane is therefore very thin — only about 0.5 micrometers thick — allowing efficient movement of O_2 into the blood and CO_2 into the alveoli.

Structurally, the membrane is composed of three layers:

- The simple squamous epithelium of the alveolus (type I alveolar cells).
- A shared basement membrane.
- The simple squamous endothelial lining of the pulmonary capillary.

In many areas, the alveolar and capillary basement membranes fuse, eliminating extra space and making the membrane even thinner. Because gases must dissolve before crossing, the entire surface is covered with a thin fluid matrix.

Because it is so thin, the respiratory membrane is also vulnerable to disease. Any condition that thickens, inflames, or fills this membrane with excess fluid slows the diffusion of gases. Disorders such as pneumonia or pulmonary edema increase the distance gases must travel and impair gas exchange by reducing the amount of oxygen that enters the blood with each breath. Shortness of breath becomes very noticeable under these conditions.

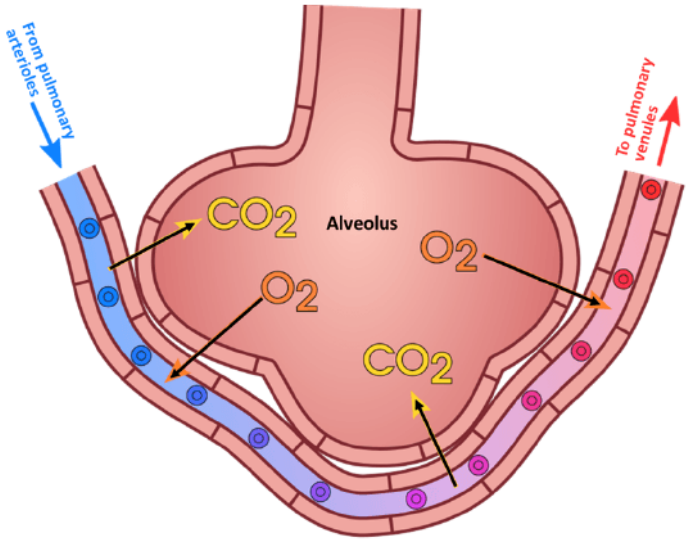


Figure 11.9.1: **Capillary Gas Exchange at the Alveolus.** Oxygen and carbon dioxide diffuse across the thin respiratory membrane between an alveolus and nearby pulmonary capillaries. CO_2 moves from the blood into the alveolus, while O_2 moves from the alveolus into the blood, allowing deoxygenated blood from the pulmonary arterioles to leave oxygenated through the pulmonary venules.

2) Partial Pressure Gradients

Partial pressure gradients drive both the loading of oxygen into the blood and the unloading of carbon dioxide from the blood. These processes occur simultaneously in each alveolus.

Oxygen Gradient

Oxygen has a steep partial pressure gradient of about 60–64 mmHg (104 mmHg in alveolar air vs. ~40 mmHg in deoxygenated blood). Because of this, oxygen diffuses rapidly into the capillary. Equilibrium is reached within the first one-third of the capillary's length, well before the blood exits the alveolus. Blood leaving the capillary has a PO_2 of about 100 mmHg.

Carbon Dioxide Gradient

CO_2 has a much smaller gradient of about 5 mmHg (45 mmHg in deoxygenated blood vs. 40 mmHg in alveolar air). Because it has a much higher solubility than oxygen it diffuses more rapidly even with a small pressure difference. Equilibrium for CO_2 is also reached quickly, within about half the capillary length. Blood leaving the capillary has a PCO_2 of about 40 mmHg.

3) Ventilation – Perfusion Matching

For external respiration to be efficient, airflow to the alveoli (ventilation) must closely match the blood flow reaching them (perfusion). Severe mismatches indicate significant lung disease, but the body normally makes constant adjustments to keep ventilation and perfusion balanced.

Perfusion Adjusts to Partial Pressure of Oxygen Inside the Alveoli (PAO_2)

When ventilation decreases in a region of the lung — such as during an asthma attack where airways constrict — alveolar PO_2 falls. In response, the small arteries supplying that area constrict, reducing blood flow. This prevents blood from arriving in an area with too little oxygen, limiting the mismatch known as a shunt. In contrast, breathing oxygen-enriched air increases alveolar PO_2, causing vasodilation and greater perfusion.

Ventilation Adjusts to Partial Pressure of Carbon Dioxide Inside the Alveoli ($PACO_2$)

Airflow adjusts based on changes in alveolar CO_2 ($PACO_2$). If airflow is high relative to blood flow, $PACO_2$ decreases, and the bronchioles constrict to reduce ventilation. If airflow is low, $PACO_2$ increases, and bronchioles dilate to bring in more fresh air. These local reflexes help balance ventilation and perfusion moment to moment.

Watch this video:

This animation gives you a great overview of many of the structures and functions of the human respiratory system that you have covered so far. Enjoy!

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

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11.10: Transport of Gases

The blood uses hemoglobin and simple chemical reactions to move oxygen and carbon dioxide between the lungs and the tissues.

Master this section and you'll be able to:

- Describe the principles of oxygen transport
- Describe the structure of hemoglobin
- Describe the principles of carbon dioxide transport

Oxygen Transport in the Blood

Oxygen does not dissolve well in liquids, so only about 1.5 percent of the total oxygen in the bloodstream is transported dissolved in the plasma. The remaining oxygen is carried by a specialized transport system inside erythrocytes (or RBCs).

You have already learned that erythrocytes contain **hemoglobin**, a metalloprotein that binds and transports oxygen. The **heme portion** of hemoglobin contains **iron**, and this iron is the site that attaches to oxygen. Each hemoglobin molecule contains four heme groups, so one hemoglobin molecule can carry up to four oxygen molecules.

When oxygen diffuses across the respiratory membrane from the alveolus into the pulmonary capillary, it continues into the red blood cell and binds to hemoglobin. This reversible reaction produces **oxyhemoglobin (HbO2).** Oxyhemoglobin has a bright red color, which gives oxygenated blood its characteristic appearance.:

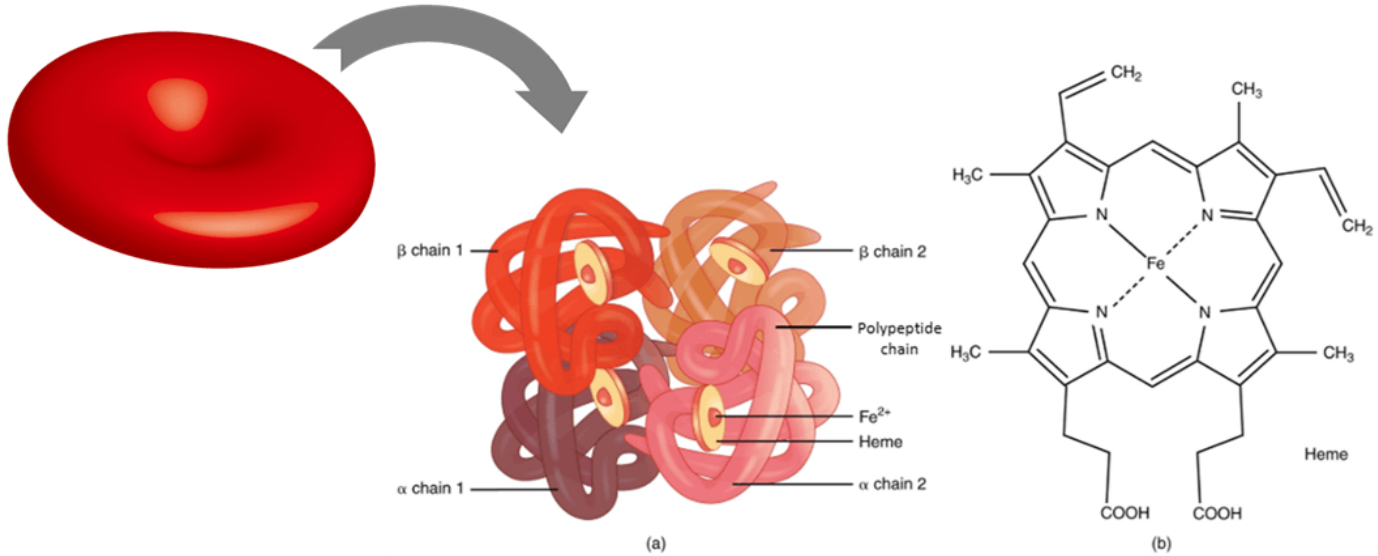


Figure 11.10.1: **RBC with Hemoglobin and Heme Group.** (a) Hemoglobin consists of **four polypeptide chains** (two α and two β), each containing a **heme group** with a central **Fe^{2+} ion** that binds oxygen. (b) The Fe ion in the center of the heme group is what actually grabs onto oxygen and then lets it go again when the body needs it, allowing RBCs to transport oxygen throughout the body.

Function of Hemoglobin

Hemoglobin is a protein made of four parts, each with a heme group that contains an iron atom. Each iron atom can bind one oxygen molecule, so a single hemoglobin can carry up to four oxygen molecules.

When the first oxygen molecule attaches, hemoglobin slightly changes shape. This makes it easier for the next oxygen to bind. Each new oxygen increases hemoglobin's ability to pick up the next one. The same idea works in reverse at the tissues. Once the first oxygen is released, the next ones come off more easily. This process helps hemoglobin load oxygen quickly in the lungs and

unload it where the tissues need it.

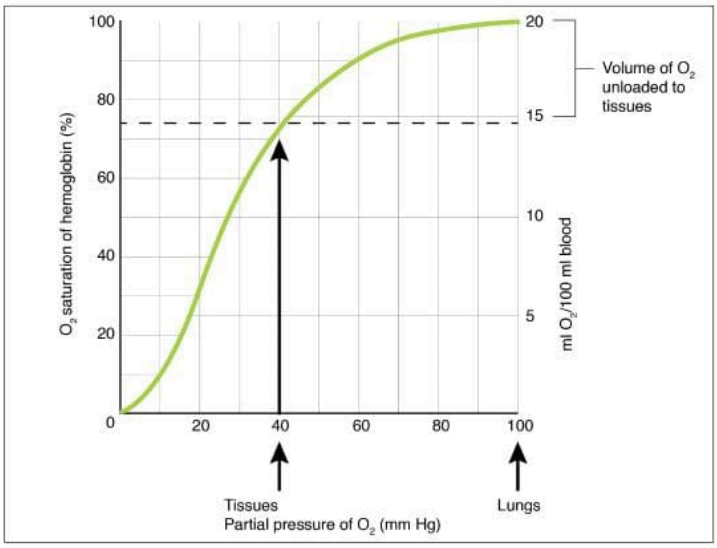
If all four heme sites hold oxygen, the hemoglobin is fully saturated. If only one, two, or three sites hold oxygen, it is partially saturated. When looking at all the red blood cells in the body, the percentage of heme sites that are carrying oxygen is called **hemoglobin saturation**. In healthy individuals, saturation is usually between **95 and 99%**.

Oxygen Dissociation from Hemoglobin

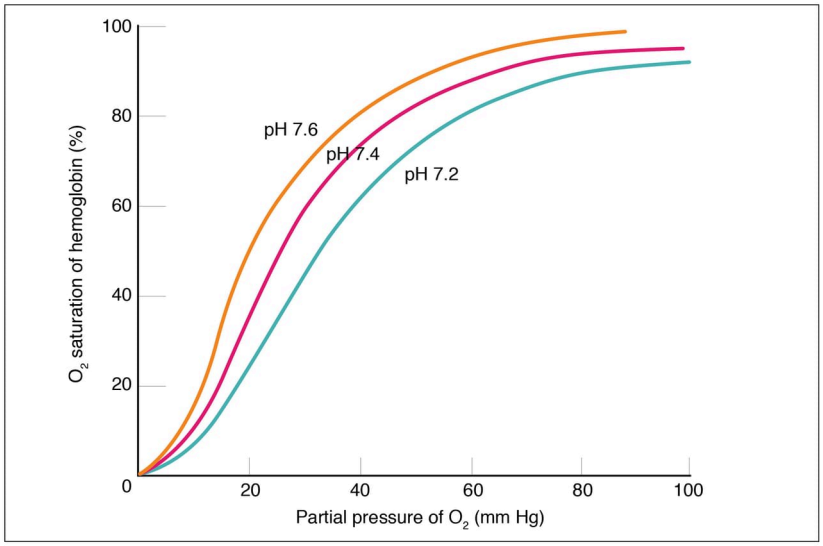
The binding and release of oxygen depend on its partial pressure. As alreay mentioned earlier: oxygen moves from areas of higher partial pressure to areas of lower partial pressure.

An **oxygen–hemoglobin dissociation curve** is a graph that shows how strongly hemoglobin holds on to oxygen at different partial pressures. As the partial pressure of oxygen increases, hemoglobin binds more oxygen. As the partial pressure decreases, hemoglobin releases oxygen more easily.

This means that in the lungs, where the partial pressure of oxygen is high, hemoglobin loads up with oxygen. In the tissues, where the partial pressure of oxygen is lower, hemoglobin releases oxygen so cells can use it.



(a) Partial pressure of oxygen and hemoglobin saturation



(b) Effect of pH

Figure 11.10.2: **Oxygen-Hemoglobin Dissociation Curve.** (a) The graph on the left shows how the amount of oxygen carried by hemoglobin changes with different oxygen pressures. The blood returning from the tissues has a low O_2 pressure (around 40 mm Hg). In the alveoli the partial pressure of O_2 is high (about 100 mm Hg), so so hemoglobin quickly binds to oxygen. (b) The graph on the right shows the effect of pH changes in the blood on the oxygen–hemoglobin dissociation curve. Lower blood pH makes hemoglobin release oxygen more easily (curve shifts right), while higher pH makes it hold oxygen more tightly (curve shifts left).

How the Oxygen–Hemoglobin Curve Helps Control Oxygen Delivery

The oxygen–hemoglobin saturation curve acts like an automatic control system that adjusts how much oxygen is delivered to different tissues. Tissues that are very active, such as working muscles, use oxygen quickly to make ATP. This lowers the tissue's partial pressure of oxygen to about 20 mm Hg. Blood arriving at the tissue has an oxygen pressure near 100 mm Hg, creating a large pressure difference. Because of this steep gradient, hemoglobin releases more oxygen into these active tissues.

Less active tissues, such as adipose tissue, consume far less oxygen. Their oxygen pressure stays relatively high, so hemoglobin releases only a small amount of oxygen. Even though venous blood is often described as deoxygenated, it still carries some oxygen bound to hemoglobin. This remaining oxygen serves as a reserve for times when tissues suddenly need more.

Other Factors That Shift the Oxygen–Hemoglobin Curve

Higher temperature causes hemoglobin to release oxygen more easily. Lower temperature slows this release. Core body temperature does not change much, but active tissues can become warmer as they work. This local rise in heat helps hemoglobin unload extra oxygen right where it is needed.

Blood pH also changes hemoglobin's affinity for oxygen. This relationship is called the Bohr effect.

- Lower pH (more acidic) promotes oxygen release from hemoglobin.
- Higher pH (more basic) slows oxygen release.

Carbon dioxide strongly affects pH. When CO_2 levels rise, more carbonic acid and hydrogen ions form, lowering pH. Active tissues also release metabolic acids such as lactic acid. These drops in pH signal hemoglobin to unload more oxygen into the tissues that need it most.

Carbon Dioxide Transport in the Blood

Carbon dioxide travels from the tissues to the lungs in *three ways:*

1. **Dissolved in plasma**: A small amount of CO_2 simply dissolves into the blood plasma.
2. **As bicarbonate (HCO_3^-)**: Most CO_2 is converted into bicarbonate inside red blood cells, then carried in the plasma.
3. **Bound to hemoglobin**: Some CO_2 attaches to hemoglobin in erythrocytes, forming carbaminohemoglobin, similar to how oxygen binds but at a different site on the molecule.

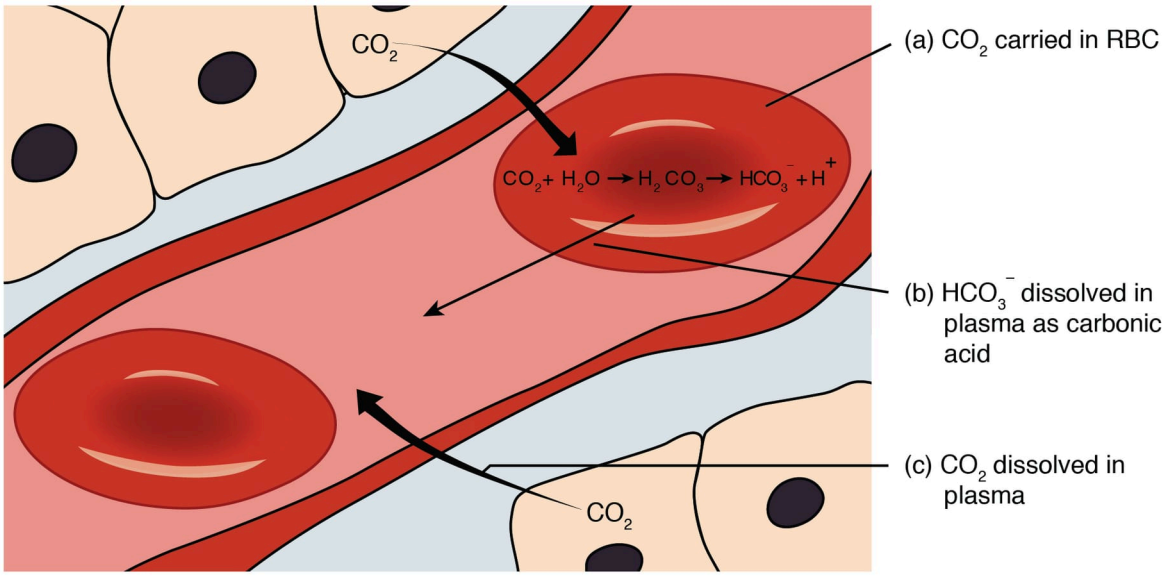


Figure 11.10.3: **Carbon Dioxide Transport.** Carbon dioxide is transported by three different methods: (a) in erythrocytes; (b) after forming carbonic acid (H_2CO_3), which is dissolved in plasma; (c) and in plasma.

1. Dissolved Carbon Dioxide (7–10 percent)

A small amount of carbon dioxide dissolves directly into the blood plasma. This dissolved CO_2 travels to the lungs, crosses the respiratory membrane, and is breathed out.

2. Bicarbonate (About 70 percent)

Most carbon dioxide travels in the blood in the form of **bicarbonate (HCO_3^-) ions**.

Here is the a brief overview of how that happens:

- CO_2 moves from the tissues into red blood cells.
- Inside the RBCs, an enzyme (carbonic anhydrase) quickly turns CO_2 + water into **carbonic acid**, which then splits into **bicarbonate** and **hydrogen ions**.
- As bicarbonate builds up inside the RBC, it moves out into the plasma. A chloride ion moves in to keep the charges balanced. This exchange is called the **chloride shift**.
- In the lungs, the whole reaction reverses: bicarbonate re-enters the RBC, joins with hydrogen ions, and is turned back into CO_2 + water.
- The CO_2 then diffuses into the alveoli and is exhaled.

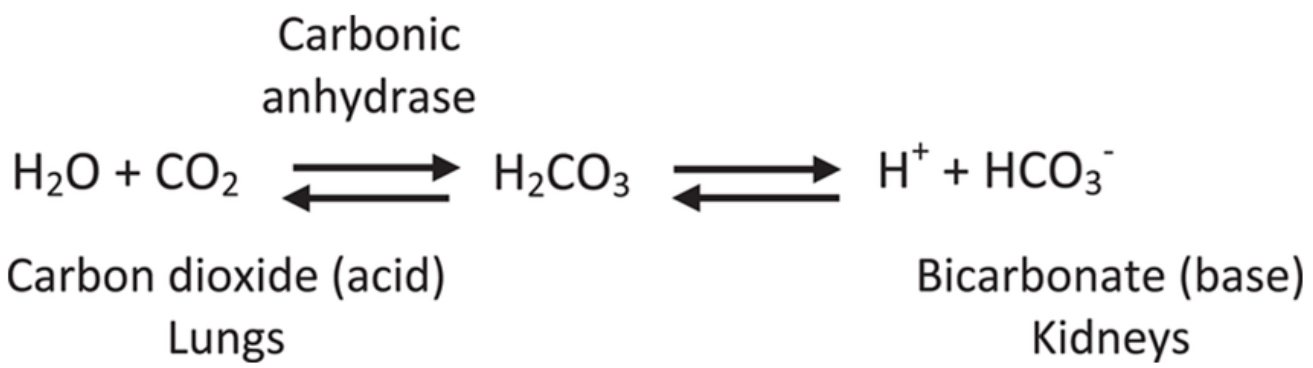


Figure 11.10.4: **Carbonic Acid–Bicarbonate Buffer System.** This chemical equation shows how carbon dioxide (CO_2), water, and bicarbonate (HCO_3^-) work together to maintain the body's pH balance. CO_2 combines with water to form carbonic acid, which can quickly break apart into hydrogen ions (H^+) and bicarbonate. The lungs help regulate this system by adjusting how much CO_2 is exhaled, while the kidneys help regulate pH by controlling how much bicarbonate is kept or removed from the blood.

3. Carbaminohemoglobin (About 20 percent)

Some CO_2 attaches directly to hemoglobin, but not at the iron (like oxygen does). Instead, it attaches to the protein part of hemoglobin and forms **carbaminohemoglobin**. This is also a reversible reaction.

Watch this video to see how oxygen is carried from the lungs to the tissues.

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Why is oxygenated blood bright red, whereas deoxygenated blood tends to be more of a purple color?

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11.11: Internal Respiration

Internal respiration is the process where oxygen moves from the blood into body tissues and carbon dioxide moves from the tissues into the blood, all driven by simple diffusion.

Master this section and you'll be able to:

- Explain how O_2 and CO_2 diffuse between systemic capillaries and tissues.
- Describe how hemoglobin unloads oxygen based on local tissue conditions.
- Identify the three forms of CO_2 transport in the blood.

Gas Exchange between the Blood and the Tissues

Gas exchange between the blood and the tissues — also known as “internal respiration” — is the process where oxygen leaves the blood and enters body cells, while carbon dioxide leaves the cells and enters the blood. It happens in the systemic capillaries that run through organs and tissues all over the body.

Systemic arteries carry oxygen-rich blood from the left side of the heart to tissues, then branch into systemic capillaries that run very close to body cells. In these capillaries, the thin wall (one layer of endothelial cells plus a basement membrane) separates blood from the surrounding interstitial fluid, which bathes the tissue cells.

Because the barrier between the blood and the interstitial fluid is extremely thin, gases move across it easily by simple diffusion, just as they do in the lungs, and no energy-using pumps are required. Gas exchange between the systemic capillaries and the tissues is entirely passive as is the loading up of oxygen and disposal of CO_2 waste in the lungs. Each gas simply moves down its own partial pressure gradient, from an area of higher pressure to an area of lower pressure.

Oxygen Movement into the Tissues

In systemic arterial blood, the partial pressure of oxygen (about 95–100 mm Hg) is much higher than in the interstitial fluid and inside resting cells (around 40 mm Hg or lower). This steep gradient drives oxygen to leave the blood, move through the interstitial fluid, and enter the cells that need it for ATP production.

Most oxygen is carried on hemoglobin inside red blood cells. As oxygen diffuses into the tissues and the plasma PO_2 drops, hemoglobin releases more oxygen to re-establish equilibrium. Active tissues release more CO_2, produce heat, and generate a slightly acidic environment, all of which shift the hemoglobin–oxygen dissociation curve to the right and further increase oxygen unloading where it is needed most.

By the time blood leaves the tissues, its PO_2 has fallen to about 40 mm Hg, and the darker, deoxygenated blood returns to the right side of the heart to be pumped to the lungs for re-oxygenation.

Carbon Dioxide Movement into the Blood

Because cells constantly generate carbon dioxide during metabolism, the partial pressure of CO_2 in the tissues (about 45 mm Hg) is slightly higher than in the incoming arterial blood (about 40 mm Hg). This gradient causes carbon dioxide to diffuse out of the cells, across the interstitial fluid, and into the systemic capillaries.

Once in the blood, carbon dioxide is transported in three forms:

- a small amount **dissolved in plasma**,
- some bound to hemoglobin as **carbaminohemoglobin**,
- and most converted inside red blood cells to **bicarbonate** and hydrogen ions through the action of carbonic anhydrase.

As venous blood leaves the tissues, its PCO_2 has risen to about 45 mm Hg. The blood then returns to the heart and is pumped to the lungs, where external respiration removes the excess carbon dioxide and restores oxygen levels.

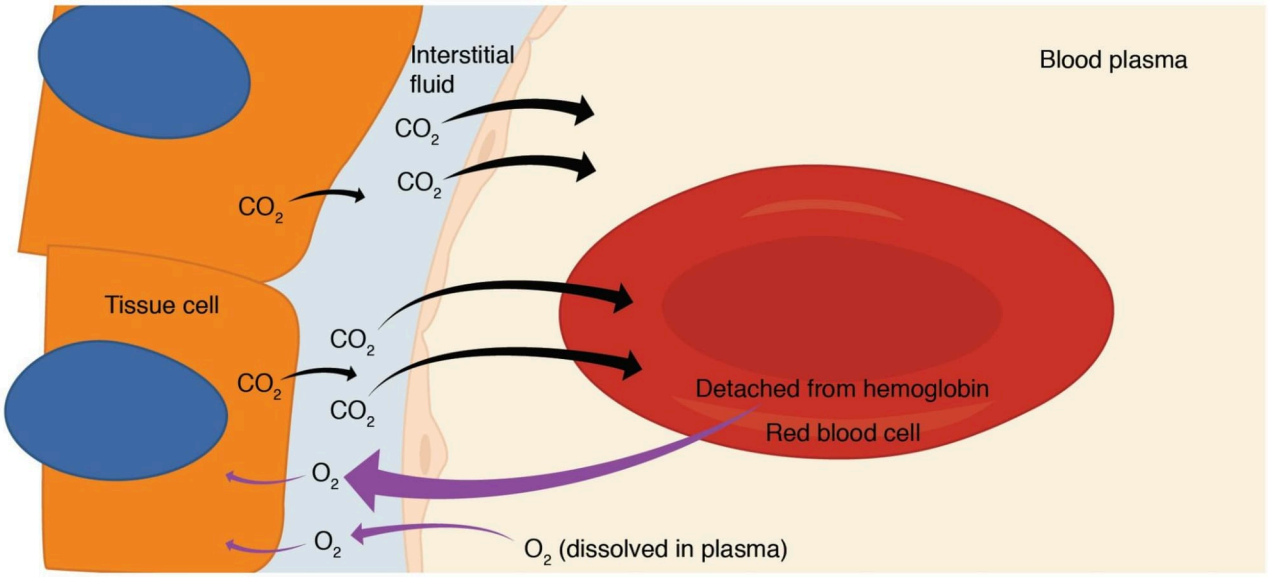


Figure 11.11.1: **Gas Exchange in the Tissues.** Oxygen diffuses out of the systemic capillaries and into nearby tissue cells, while carbon dioxide produced by those cells diffuses in the opposite direction and enters the blood, either dissolving in plasma or binding to hemoglobin inside red blood cells.

Blood Leaving the Tissues



As blood flows through the systemic capillaries, it unloads oxygen into the surrounding tissues and collects carbon dioxide that cells continually produce during metabolism. By the time the blood enters the veins, the **hemoglobin** molecules have released much of their oxygen, and this change alters hemoglobin's shape and the wavelengths of light it reflects. Without O_2 bound, hemoglobin absorbs more red wavelengths and reflects fewer, so venous blood appears **darker, deeper red**.

Nothing in the blood actually turns blue. The color difference is purely a result of **hemoglobin's molecular structure** shifting between an oxygen-bound form and an oxygen-unbound form.

Carbon dioxide is now carried in several forms in the blood, including dissolved CO_2, bicarbonate ions, and carbaminohemoglobin. This deoxygenated, CO_2-rich blood travels back to the right atrium and right ventricle, and is then pumped

to the lungs, where **external respiration** (gas exchange with alveolar air) reloads the blood with oxygen and removes the excess carbon dioxide.

Key Concept

Gas exchange of O_2 and CO_2 during both external respiration (in the alveoli) and internal respiration (in the tissues) occurs entirely by **simple diffusion**. Each gas moves down its own **partial pressure gradient**: O_2 diffuses toward areas where PO_2 is lower, and CO_2 diffuses toward areas where PCO_2 is lower. Local tissue activity can strongly influence these gradients. For example, active tissues use more oxygen, generate more CO_2, increase temperature, and lower pH, all of which encourage hemoglobin to release oxygen. Gas exchange efficiency therefore depends on both the pressure gradients and hemoglobin's ability to carry, release, and reload oxygen as conditions change throughout the body.

Watch this Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

This video shows how oxygen leaves the blood and enters body tissues using partial pressure differences, and how carbon dioxide produced by those tissues diffuses back into the blood to be carried to the lungs.

Everyday Connection

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy uses a sealed chamber to expose a patient to oxygen at a much higher pressure than normal atmospheric air. Increasing the partial pressure of oxygen helps more O_2 dissolve into the blood, which improves oxygen delivery to tissues and enhances healing.



Types of Hyperbaric Chambers

Monoplace chambers
These are designed for a single patient, who lies inside the clear, tube-like unit while staff monitor from the outside. Some facilities use modified monoplace chambers that allow several seated or reclining patients at the same time to reduce feelings of isolation or claustrophobia.

Multiplace chambers
These are larger rooms that can treat multiple patients at once, with medical staff inside the chamber. Patients typically breathe oxygen through a mask or hood while the chamber itself is pressurized with air.

How Hyperbaric Therapy Works

Gas movement follows partial pressure gradients. When the chamber pressure increases, the partial pressure of oxygen increases. This causes more oxygen to dissolve into the bloodstream than would normally be possible at sea level.

Clinical Uses

Carbon monoxide poisoning
Carbon monoxide binds to hemoglobin much more tightly than oxygen. The high oxygen pressure in a hyperbaric chamber helps displace carbon monoxide and rapidly increases the amount of oxygen dissolved in the plasma.

Anaerobic bacterial infections
Anaerobic bacteria grow in low-oxygen environments. Raising oxygen levels in blood and tissues inhibits or kills these bacteria because oxygen is toxic to them.

Wound healing and graft support
Higher oxygen levels increase ATP production and support the energy-intensive processes needed for tissue repair. This promotes faster healing of chronic wounds, grafts, and certain traumatic injuries.

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11.12: When Smoke Meets Biology — The Cost to Your Cells and Tissues

Smoking interferes with normal oxygen transport, reducing how much oxygen the blood delivers to the body and contributing to widespread health effects besides the obvious damage to the respiratory and cardio vascular systems.

Master this section and you'll be able to:

- Describe how carbon monoxide and nicotine from smoking affect oxygen transport and cardiovascular function.
- Summarize the short-term and long-term effects of smoking on the respiratory and cardiovascular systems.

Smoking and Carbon Monoxide: How They Affect Oxygen Transport

Smoking influences the body on several levels, from immediate autonomic changes to long-term structural damage of the lungs and blood vessels. Within minutes of inhaling smoke, nicotine alters heart rate, blood pressure, and the narrowing of airways and blood vessels, changing the normal function of the cardiovascular and respiratory systems. Over time, chronic exposure to smoke particles and toxic chemicals inflames and scars lung tissue, stiffens blood vessel walls, and contributes to chronic diseases such as COPD, atherosclerosis, heart attacks, and stroke.

Cigarette smoke contains **more than 4,000 chemicals**, including hundreds that are toxic and at least 70 that are known carcinogens. **Carbon monoxide (CO)** is one of these chemicals. CO is produced any time a material burns without enough oxygen for complete combustion. This occurs during smoking because tobacco and paper smolder rather than burn cleanly. Incomplete combustion creates CO along with many other harmful gases.



Once inhaled, CO crosses into the bloodstream and binds tightly to hemoglobin at the same location where oxygen normally attaches. This creates **carboxyhemoglobin**. **CO binds more than 200 times more strongly than oxygen**, so hemoglobin will preferentially bind CO even when oxygen levels are normal. As a result, less hemoglobin is available to carry oxygen to body tissues.

Consequences include:

- **Reduced oxygen delivery** to all organs, including the heart and brain
- **Shortness of breath and fatigue**, especially during exercise
- **Increased workload on the heart** as the body attempts to compensate

- **Prolonged recovery time after smoking**, because carboxyhemoglobin has a half-life of about four hours

The level of carboxyhemoglobin rises with each cigarette. In smokers, typical levels range from about 2 to 15%. Because carboxyhemoglobin breaks down with a half-life of roughly four hours, its concentration decreases relatively quickly once a person stops inhaling smoke.

Physiological Effects of Smoking

Smoking has **several immediate and long-term effects** on the body because **nicotine activates the sympathetic, or fight-or-flight, system**.

Immediate physiological effects

- **The effect of nicotine:** nicotine acts on the body within seconds, and its first stop is the brain. Once it arrives, it **switches on the sympathetic, or fight-or-flight, system** and signals the adrenal 2 glands to **release adrenaline**. This creates a **wave of short-term cardiovascular changes** every time a person smokes. Over months and years, this repeated stimulation places chronic stress on the heart, blood vessels, and lungs.

  Here is what happens immediately after smoking:

  - Nicotine enters the bloodstream and reaches the brain and adrenal glands.
  - The sympathetic nervous system becomes activated.
  - Adrenaline is released into the blood.
  - Heart rate rises as the heart beats faster and more forcefully.
  - Blood pressure increases because adrenaline tightens many small arteries.
  - Peripheral vasoconstriction reduces blood flow to the skin and extremities, which can cause cold hands and delayed wound healing.

- **Effects on gas transport and oxygen delivery:** As was discussed above, the carbon monoxide in smoke binds to hemoglobin with much higher affinity than oxygen, forming carboxyhemoglobin and reducing the effective oxygen-carrying capacity of blood. Additionally, when CO attaches to hemoglobin, it also makes the ***remaining*** **hemoglobin hold on to oxygen more tightly.** This means oxygen is not released easily to the tissues, so the tissues can still become starved for oxygen even if a pulse oximeter shows a normal oxygen saturation.

Long-term Chronic Structural Damage

- **Airway and mucociliary changes:** The hot, chemical-laden smoke irritates the airway epithelium, leading to **chronic inflammation** and edema.
  Mucus production increases, but with narrower airways the lungs are less able to clear it. The buildup of mucus in combination with narrowed airways makes smokers more prone to hypoxia, especially during activity or illness.
  Cilia are also damaged and eventually lost, so the mucociliary escalator fails; mucus and inhaled particles accumulate, promoting chronic cough, recurrent infections, and further inflammation.

- **Cardiovascular pathophysiology:** Nicotine and other components of smoke promote endothelial dysfunction, increase oxidative stress, and enhance platelet activation and coagulation, all of which **accelerate atherosclerosis.** Combined effects (sympathetic activation, higher blood pressure, atherosclerosis, and reduced oxygen delivery) greatly increase the risk of coronary artery disease, myocardial infarction, stroke, and peripheral arterial disease.

- **Other chronic adaptations and systemic effects:** Persistent hypoxemia can stimulate **erythropoietin release**, leading to **secondary polycythemia**, which increases **blood viscosity** and further strains the heart.
  Chronic inflammation from smoking contributes to systemic endothelial injury and is linked to **insulin resistance**, **decreased bone density**, **impaired immune function**, and **increased cancer risk in multiple organs**.

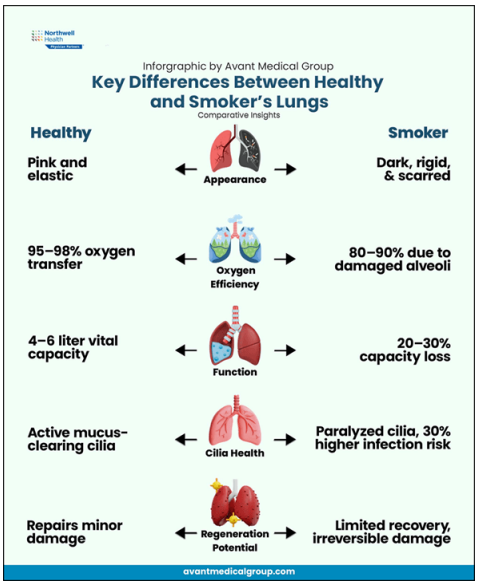


Figure 11.12.1: **Comparison of Healthy and Smoker's Lungs.** Healthy lungs are pink, elastic, and supported by active cilia that help clear mucus, allowing efficient gas exchange and a normal vital capacity. Smoker's lungs become dark, rigid, and scarred over time, with damaged alveoli, reduced lung capacity, paralyzed cilia, and much more limited ability to repair themselves.

In conclusion: Smoking does not just damage the lungs; it also starves the tissues of oxygen. Carbon monoxide and other chemicals in smoke reduce how much oxygen the blood can carry, while nicotine and vessel damage reduce blood flow itself. Together, this means that muscles, the heart, the brain, and even the skin may not get enough oxygen, especially during exercise or illness.

Over time, the tiny alveoli can be destroyed and merge into larger, less efficient spaces, as in **emphysema**. This reduces the total surface area available for gas exchange, so even if a smoker breathes faster or deeper, the lungs simply cannot move oxygen into the blood or remove carbon dioxide as well as healthy lungs can. As a result, smokers become short of breath more easily and are at higher risk of respiratory failure during infections or surgery.

Smoking also interferes with **healing and immune function**. Less oxygen delivery and damaged blood vessels slow the repair of wounds, bone, and other tissues, making surgical complications and infections more likely. At the same time, chronic inflammation and impaired immune cells mean the body is less effective at fighting off pathogens and abnormal (precancerous) cells, further increasing the risk of infections and many types of cancer.

Myths about Smoking and Cigarettes



Smoking is Just a Choice.

The first time? Yes. After just a few cigarettes? No. Addiction to nicotine can happen quickly. It changes the chemical balance in your brain. Smoking may seem like it's just a choice or a habit. In fact, most people who use tobacco are addicted. Breaking nicotine addiction is harder for some people than others. Quitting can take several tries. But don't give up. If you need help to quit, ask your doctor about nicotine replacement, medicines, or coaching.

Filters Make Cigarettes Safer.

Filters do not protect you. They are designed to make smoke particles smaller. That makes nicotine easier to absorb. This increases addiction. Cigarettes have been engineered to speed up nicotine's path to your brain. Their design feeds addiction. Light or low-tar cigarettes may sound less dangerous. They aren't. These misleading labels are no longer allowed. No cigarette is safe. Tobacco smoke contains more than 7,000 chemicals. At least 250 are toxic.

An Occasional Cigarette is no Big Deal.

Smoking doesn't just cause diseases for heavy smokers or longtime smokers. The 2010 Surgeon General's Report shows how breathing tobacco smoke can cause immediate harm. Tobacco smoke can trigger sudden heart attacks and death, even in nonsmokers. Each cigarette you smoke hurts your lungs, your blood vessels, and cells throughout your body. Smoking a few cigarettes a week can cause a heart attack. Cutting back is not enough to protect you. You have to quit entirely.

It's Too Late to Quit — The Damage is Already Done.

It's true that the longer you use tobacco, the more you hurt your body. But at any age, the sooner you quit, the sooner your health can improve. The 2010 Surgeon General's Report shows how using tobacco causes disease almost everywhere in your body. Within 20 minutes after quitting, your body starts to heal. After 2 to 5 years, your risk for stroke is similar to that of a nonsmoker. In 10 years, your lung cancer risk is cut in half.



Secondhand Smoke May Bother People, But it isn't Dangerous.

Tens of thousands of nonsmokers die every year from breathing others' secondhand smoke. Breathing the chemicals in tobacco smoke changes your blood's chemistry almost immediately. Deadly clots can form and block arteries to your heart or brain. When you smoke at work, home, or at a restaurant, everyone there breathes poisons. If you smoke in your car, rolling down a window does not protect your passengers. It is not healthy to breathe any amount of tobacco smoke.

The Little Bit of Smoke that my Kids Get Doesn't Hurt Them.

Don't smoke or let others smoke around your children. They can get bronchitis, pneumonia, and ear infections from smoke. Even if you only smoke by an open window, some of the smoke stays in your house and poisons the air your children breathe. Children with asthma can have a serious, even deadly, asthma attack from breathing secondhand smoke. The best way to protect children is to quit smoking. If you or someone else in your household are not ready to quit, be sure to make your home and car 100% smoke-free.

Smoking vs. Vaping

While smoking burns tobacco to create smoke that is inhaled — exposing the lungs to tar, carbon monoxide, and thousands of combustion-related chemicals — **vaping** does not burn anything. Instead, vaping heats a liquid into an aerosol, containing solvents (like propylene glycol or glycerin) and flavorings, as well as in most cases nicotine.

Vaping is **less harmful** than smoking because it avoids burning tobacco, which is what produces most of the tar and carcinogens in cigarette smoke. However, "less harmful" does **not** mean "safe." Vaping still delivers nicotine, which is addictive, and its aerosols contain chemicals that can irritate airways, trigger inflammation, and potentially harm lung function, especially in young people. So while vaping may be a better alternative for someone trying to quit smoking, it is **not** considered harmless.

Why can toxic chemicals still form when vaping? When vape liquid is heated, especially at high temperatures:

- **Vegetable glycerin and propylene glycol can break down** producing **formaldehyde, acetaldehyde, and acrolein** (all of which are respiratory irritants; formaldehyde is a known carcinogen).
- **Flavoring chemicals** can degrade into toxic compounds as well.
  Some flavorings contain **diacetyl** or related chemicals, which have been linked to a special type of bronchiolitis, known as "popcorn lung", in which the small airways become narrowed or blocked, leading to cough and shortness of breath. It typically occurs as a result of inhaling toxic gases..
- **Metal particles** (nickel, tin, lead) can shed from the heating coil and be inhaled.

So, while vaping does not involve burning or produce smoke like cigarettes do, heating vape liquid can still create harmful chemicals such as formaldehyde, acrolein, and tiny metal particles, so the aerosol is not harmless.

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11.13: Heimlich Maneuver — A Quick Introduction to Choking Rescue

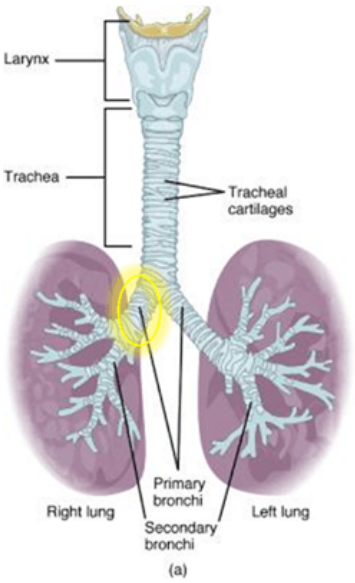
Choking is a time-critical emergency in case of a complete airway blockage, making rapid recognition and immediate action essential for saving a life.

Master this section and you'll be able to:

- Describe the most common location of airway obstruction in adults and children and the signs used to recognize each.
- Explain why complete airway obstruction is a medical emergency.
- Identify and explain the correct steps for relieving choking in adults, pregnant individuals, and infants.

Choking as a Medical Emergency

Choking happens when something blocks the airway and prevents air from reaching the lungs. Because the brain can only survive a few minutes without oxygen, choking is a true, time-critical emergency. Recognizing it quickly is can save lives.



Food is most likely to get stuck in the **right primary bronchus** in adults because it is wider and more vertical, creating a straighter path from the trachea. In children, however, the angles of the bronchi are more symmetrical, so foreign bodies are equally likely to enter either side.

The **left bronchus** is a less frequent site in adults, involved in roughly **40 percent** of aspiration cases. It is uncommon for food to remain in the **trachea**, with only **5 to 11 percent** of adult foreign-body cases occurring there.

When there is a **complete airway blockage**, air cannot move in or out of the lungs. This stops external respiration, so blood leaving the lungs carries little to no oxygen. As oxygen levels fall and carbon dioxide rises, the person becomes weak, confused, and then unconscious. Without rapid intervention, the brain and heart fail from severe hypoxia.

Most adult choking emergencies involve food, especially when it is poorly chewed or swallowed too quickly. Alcohol, dentures, and talking while eating increase the risk. Children often choke on small objects or toys.

A **partial airway blockage** means some air is still moving. The person may cough, gag, or make high-pitched noises. If they can cough forcefully or speak, they may be able to clear the object on their own. A complete airway blockage is far more dangerous. The person cannot talk, cough, or breathe. They may turn blue and use the “universal choking sign” by clutching their throat.

Key signs of complete obstruction include:
- No effective coughing
- No voice or breath sounds
- Increasing cyanosis
- Panic, then rapid loss of consciousness

During a choking emergency, the goal is to quickly create enough internal pressure to push the object out of the airway. For a conscious adult, **abdominal thrusts (the Heimlich maneuver)** can generate this force. If the person becomes unresponsive, **CPR is started immediately**, both to provide circulation and to create upward pressure with chest compressions that may dislodge the object.

If you are on your path to become a paramedic, choking is one of the most urgent airway problems you will encounter. You must be able to recognize obstruction instantly, decide whether it is partial or complete, and respond effectively.

Choking emergencies are often preventable. Chewing food well, avoiding talking or laughing with food in the mouth, and being cautious with high-risk foods (like meat, nuts, and grapes) reduce the risk. Supervising children during eating and play also makes a significant difference.

Key idea: Choking stops airflow, stops gas exchange, and causes life-threatening hypoxia within minutes. Fast recognition and quick action save lives.

Heimlich Maneuver for an Adult Standing or Lying on the Ground

Before you begin, make sure the person really is choking. Ask loudly, **"Are you choking?"** If they nod or cannot speak, tell them you are going to help.

Stand behind the person and wrap your arms around their waist. Your hands should end up in front of their abdomen. Make a fist with one hand and place the thumb side of the fist just **above the belly button**, well below the ribs and sternum.

Place your other hand over your fist. Then give quick, strong **upward abdominal thrusts**. These thrusts create pressure inside the chest that can pop the object out of the airway.

Continue giving thrusts until:
- the object comes out
- the person can breathe, cough, or talk again
- or the person becomes unresponsive

If the person loses consciousness, **lower them to the ground** and begin CPR if you are trained.

If the person is already lying on their back, you can still give abdominal thrusts. Straddle the person near their hips, place your grasped fist above the belly button, and push **inward and upward** the same way you would if they were standing.

Always check that the airway is open afterward and monitor the person closely.

YouTube Video

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Performing the Heimlich maneuver for a person who is standing or seated, according to American Heart Association (2011) guidelines:

Heimlich Maneuver for a Pregnant Woman

If a choking person is pregnant or very large and you cannot reach around their waist, you will need to modify the Heimlich maneuver. Instead of thrusting on their abdomen, you need to place the thrusts on their sternum (breast bone). In other words you must use **chest thrusts** instead of the classical abdominal thrusts.

To start, stand behind the pregnant woman and slide your arms under her armpits so you can wrap your hands around her upper chest. This position allows you to control her safely while keeping all pressure away from the abdomen.

Next, make a fist with one hand and place the thumb side of the fist on **the center of the sternum**, just above where the ribs meet. This location is important because it keeps your thrusts directed at the chest rather than the belly. Place your other hand over your fist for support.

Give quick, firm chest thrusts by pulling straight back toward yourself. The motion is slightly backward and upward, similar to abdominal thrusts but shifted higher on the body. After each thrust, pause briefly to see whether the object has been dislodged. Throughout the procedure, avoid any pressure on the abdomen.

Continue giving chest thrusts until one of the following happens:
- the object is expelled
- the patient can breathe or cough again
- or the patient becomes unresponsive

If the person becomes unresponsive, ease them to the ground and make sure they are lying face up with the airway open. Check whether CPR is needed. If you are not trained in full CPR, begin hands-only CPR. Call 911 right away, and continue CPR until the person starts to move, breathe, or speak, or until help with advanced training arrives.

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Performing Hands-Only CPR:

You should only perform full CPR if you have been trained to do it correctly. If you are not trained, you can still help by providing **hands-only CPR** until someone with more advanced skills arrives.

Hands-only CPR has two simple steps for a teen or adult who suddenly collapses:

- **Call 911** (or your local emergency number).
- **Push hard and fast in the center of the chest**, at about 100 compressions per minute.

This approach keeps blood moving to the brain and heart until trained responders take over, and it can greatly improve the person's chances of survival.

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Choking Care for an Infant

When an infant is choking, you should **never** perform traditional abdominal thrusts (the standard Heimlich maneuver for older individuals). Instead, you start by sitting or kneeling with the infant in your lap. You lay the baby face-down across your forearm and rest your arm on your thigh for support. Use your hand to support the infant's head and neck, holding the jaw gently without squeezing the soft tissues of the throat. The infant's head should be angled downward so gravity can help dislodge the object.

Using the heel of your free hand, deliver **five firm back blows** between the infant's shoulder blades. Stop immediately if the object comes out. If the airway is still blocked, turn the infant face-up as one unit, keeping the head and neck supported at all times. Rest the baby on your lap or thigh with the head still slightly lower than the body.

Next, use **two fingers** on the center of the breastbone to give **five quick chest thrusts**, pressing down about 1½ inches (4 cm). These thrusts should be delivered at a steady rate of about one per second. After the five thrusts, check again to see if the object has been expelled.

You can continue alternating **five back blows** with **five chest thrusts** until the object is removed or the infant becomes unresponsive. If the infant loses consciousness, call 911 and begin CPR if you are trained.

Any infant who has had a choking episode, even if the object is removed, should be evaluated by a healthcare provider. It is also important to document what happened and notify your supervisor if this occurs in a care setting.

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Check your knnowlege

1. Put the steps of performing the Heimlich maneuver on an adult in order:

a). Make a fist with one hand.
b). Thrust inward and upward.
c). Grasp the fist against the abdomen with your free hand.
d). Place your thumb against the person's abdomen, just above their belly button.
e). Stand behind the person.

Show Answer

1. E, A, D, C, B

Show Feedback

The correct sequence is: stand behind the person; make a fist with one hand; place your thumb against the abdomen just above the belly button; grasp the fist with your other hand; and thrust inward and upward until the object is dislodged.

2. When performing the Heimlich maneuver on an infant, you should provide 5 back thrusts with the baby face down and then 5 chest thrusts with the baby face up until the object is dislodged. True or False? _____

Show Answer

2. False

Show Feedback

2. Performing abdominal thrusts on an infant is different than an adult. 5 back slaps between the shoulder blades (infant face-down) followed by 5 chest thrusts (infant face-up) are performed until the object is dislodged. Care should always be taken to support the head and neck of the infant.

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11.14: Cystic Fibrosis

Cystic fibrosis is an inherited disorder that causes abnormally thick mucus to build up in the airways and other organs, leading to chronic lung infections and long-term breathing difficulties.

Master this section and you'll be able to:

- Describe the cause of cystic fibrosis.
- Explain the consequences of the CFTR mutations.
- Summarize major treatments for cystic fibrosis.

Cystic fibrosis (CF) is an inherited disorder that affects epithelial cells of the exocrine glands of not only the lungs, but also the pancreas, intestines, and bile ducts. We will focus only on the pulmonary aspects here and see how CF produces an obstructive lung disease.

***Cystic fibrosis (CF)** is an **autosomal recessive genetic disorder**. An autosomal recessive disorder appears only when a person inherits **two nonworking copies of a gene**, one from each parent. “Autosomal” means the gene is located on one of the numbered chromosomes that both males and females share, so the condition affects all sexes equally. “Recessive” means that **one working copy of the gene is enough to prevent the disease**, so individuals with only one mutated copy are healthy carriers and do not show symptoms.

CF is caused by mutations in the **CFTR gene**, which provides instructions for making a protein that helps chloride and sodium ions move across epithelial cell membranes. When the CFTR protein does not work properly, glands that normally make thin, watery fluids instead produce **very thick, sticky mucus**. This mucus buildup interferes with normal function in many organ systems, especially the lungs and digestive tract.

In summary:
A person develops CF only when they inherit **two mutated CFTR alleles**, one from each parent. Individuals with one normal and one mutated allele are **carriers** and remain symptom-free.

Inside the Biology of Cystic Fibrosis

Control of the airway fluid relies on the action of ion channels in the apical membranes of epithelial cells, and there are two channels to focus on: CFTR and ENaC. The CFTR channels let chloride out of the cell, while the ENaC lets sodium in (top panel, figure 1.19).

This exchange helps maintain a healthy fluid layer in the airway, but fails in CF because of a nonfunctioning CFTR channel (right panel on the figure below).

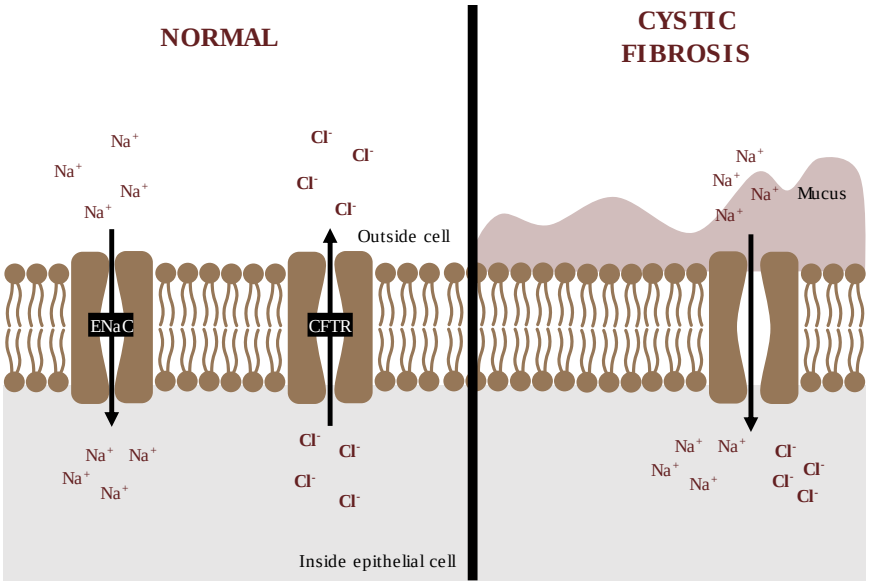


Figure 11.14.1: **Ion Transport Differences in Normal vs. Cystic Fibrosis Airway Cells.** In a healthy airway cell (left), a working CFTR channel allows chloride to exit the cell and helps keep sodium and water movement balanced, resulting in thin, well-hydrated mucus. In cystic fibrosis (right), the CFTR channel is defective, chloride cannot move out, and excess sodium is drawn into the cell, pulling water with it. The airway surface becomes dehydrated, leading to the buildup of thick, sticky mucus.

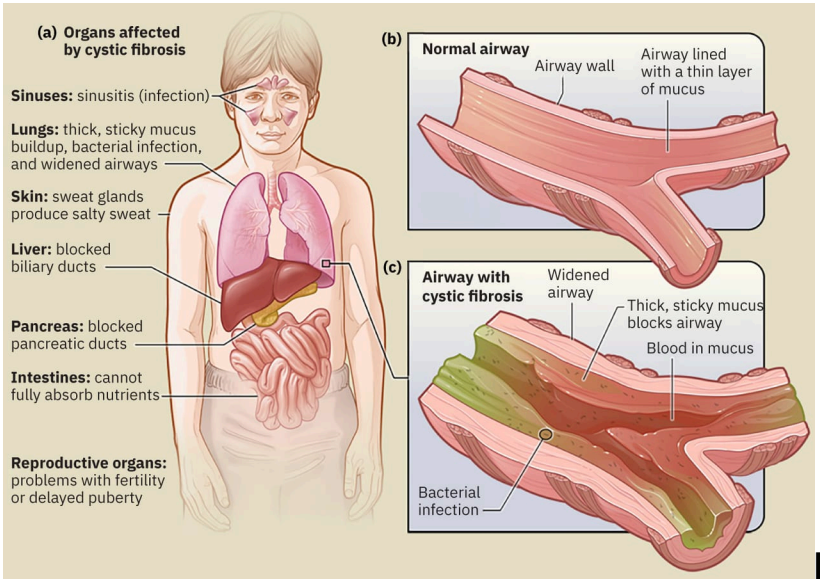
There are numerous mutations that are known to produce a dysfunctional CFTR channel. So what are the consequences of CFTR dysfunction?

Chloride ends up being trapped inside the cell and this leads to a greater influx of sodium through the ENaC down its electrochemical gradient, leaving a **higher concentration of salt inside the cells that pulls water in from the airway lumen.** The low fluid volume in the airway results in:

- **heavy, viscous mucus**, and
- **collapse of cilia.**

The defective CFTR channel causes thick mucus to build up in the airways, which blocks airflow and traps bacteria. This reduces alveolar ventilation and sets the stage for repeated lung infections. In people with cystic fibrosis, the two most common infectious organisms are *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Chronic infection and inflammation can lead to several serious complications, including atelectasis (partial or complete collapse of part of a lung), pneumonia, bronchiectasis (permanently widened and damaged bronchi), and other structural airway changes.

Although cystic fibrosis affects many organs such as the pancreas, modern treatments help manage most non-pulmonary problems. Lung disease, however, remains the major cause of illness because pulmonary involvement can begin at any time — from just weeks after birth to later in childhood.



How Cystic Fibrosis Affects the Body

Lungs

- Change in the composition of the fluid lining the airways leads to thick mucus blocking airways and trapping bacteria.
- This leads to **chronic cough, frequent infections** (bronchitis and pneumonia) **, and progressive breathing problems.**

Pancreas

- Mucus blocks digestive enzyme release.
- Causes **poor nutrient absorption, slow growth, and vitamin deficiencies.**

Other Effects

- Chronic sinus infections.
- Male infertility (due to blocked or absent vas deferens).
- Salty tasting skin due to high salt content in sweat.
- Poor growth, poor weight gain despite a normal food intake.

Lung disease in CF develops because the thick, sticky mucus clogs the airways, reduces normal mucociliary clearance, and triggers chronic inflammation. Over time, inflammation and repeated infections damage lung tissue and change the structure of the airways.

Early symptoms often include persistent coughing, large amounts of phlegm, and reduced exercise tolerance. Many of these problems occur when bacteria trapped in the thick mucus multiply and cause pneumonia.

In later stages, structural changes such as bronchiectasis widen and distort the major airways, making breathing even more difficult. Ultimately, lung transplantation is often necessary as CF worsens.

CF is most common among **Caucasians** and can be diagnosed before birth by genetic testing, or by a sweat test in early childhood.

Since 2010, essentially **all newborn babies in the United States** are **screened** for Cystic fibrosis (CF) shortly after birth.

Treatment of Cystic Fibrosis

Treatment Overview for Cystic Fibrosis

Many individuals with cystic fibrosis take one or more antibiotics regularly to suppress chronic airway infections. When pneumonia is suspected or lung function declines, antibiotics become essential and are chosen based on sputum culture results and how the patient has responded in the past. Staying current with vaccinations for respiratory illnesses is also an important part of preventive care.

Airway clearance therapy is necessary because it helps move the thick airway secretions out of the lungs. Several inhaled medications thin the mucus and improve clearance. Airway clearance may involve manual chest percussion or the use of a high-frequency chest wall oscillation vest. The vest connects to a compressor that rapidly moves air in and out of the vest, creating vibrations and pressure that loosen thick mucus and make it easier to clear.



Figure 11.14.2: **High-Frequency Chest Wall Oscillation Vest for Airway Clearance.** This vest uses rapid vibrations to loosen and mobilize thick mucus in the airways. The vest connects to a control unit that pumps air in short bursts, helping patients with cystic fibrosis clear their lungs more effectively. (CC BY 4.0; Rice University & OpenStax)

As lung disease progresses, some patients may be candidates for a bilateral lung transplant. A successful transplant can extend life by about five years in children and about eight years in adults.

In children under eighteen, high-dose ibuprofen can slow the loss of lung function. During times when symptoms worsen, corticosteroids help reduce inflammation and inhaled bronchodilators help reduce airway narrowing.

Gene therapy is being studied as a possible long-term treatment by delivering a normal copy of the CFTR gene into affected epithelial cells. If these cells could produce even a small amount of functional CFTR, about five to ten percent of normal, many lung symptoms could be prevented.

Because the CFTR mutation affects more than the lungs, additional care is often needed. Many patients experience digestive problems due to pancreatic insufficiency and require pancreatic enzyme supplements. Most male patients lack a vas deferens but still produce sperm, so sperm retrieval and assisted conception are options for those who want to have children.

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12: DIGESTIVE SYSTEM

12.1: Overview of the Digestive System
12.2: Liver, Pancreas, and Gallbladder — Accessory Digestive System Organs
12.3: Structural Organization of the Intestinal Wall and Peritoneum
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12.1: Overview of the Digestive System

The digestive system is a coordinated set of organs that break down food, absorb nutrients, and eliminate waste to support the body's energy needs and overall health.

Master this section and you'll be able to:

- List the organs of the digestive tract from proximal to distal, and briefly state their functions.
- Identify the accessory digestive organs and briefly state their primary function.
- Describe the six core digestive processes and where they occur.

The digestive system breaks down the foods you eat by releasing enzymes that mix with food, free the nutrients, and allow those nutrients to be absorbed into the body. Although the small intestine does most of this work, every organ in the system contributes to the overall process. The figure below shows the digestive tract, a continuous tube that runs from the oral cavity through the esophagus, stomach, small intestine, and large intestine, ending at the anus. It also includes important accessory organs, such as the salivary glands, liver, gallbladder, and pancreas.

The digestive system works around the clock, even though we seldom notice the complex, coordinated tasks it performs. When you eat something as simple as an apple, you taste it only briefly, but long after you stop thinking about it, your stomach and intestines quietly digest it, absorb its nutrients, and move along anything your body cannot use. In the sections that follow, we will explore the structures that carry out digestion and the processes that turn food into usable fuel.

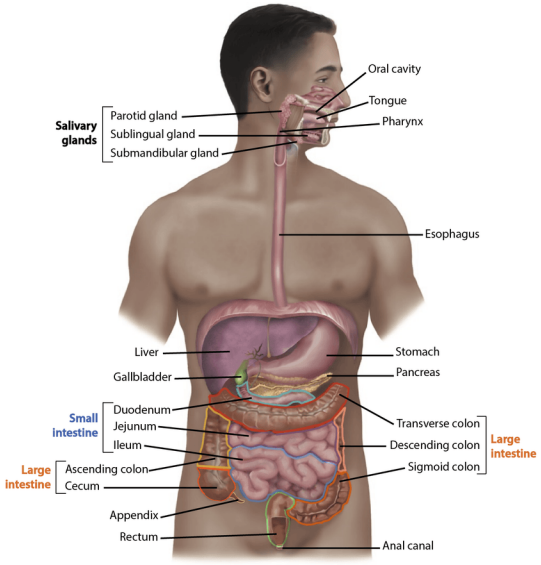


Figure 12.1.1: **Organs of the Digestive System**. As food moves through the organs of the digestive tract it is broken down into component molecules which are absorbed into the body. The accessory organs (salivary glands, liver, pancreas and gallbladder) secrete digestive enzymes and other substances to assist and regulate the processes. *(Image credit: "Components of the Digestive System" by Jennifer Lange and Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of original by KnowledgeWorks .)*

Digestive System Organs

The simplest way to understand the digestive system is to divide its organs into two main categories.

The first category is the **digestive tract**, also called the **alimentary canal or gastrointestinal (GI) tract**, or simply "gut", which is the long tube food travels through.

The second category is the **accessory digestive organs**, which release **exocrine secretions** into the tract to help break food

down and allow the body to absorb nutrients. Despite the term “accessory,” these organs are essential for normal digestive function.

Digestive Tract Organs

The digestive tract is a one-way tube about 7.62 meters (25 feet) long during life and closer to 10.67 meters (35 feet) after death, when smooth muscle tone is lost. Its primary function is to nourish the body. The tube begins at the oral cavity and ends at the anus, and along the way it is regionally modified as the pharynx, esophagus, stomach, and small and large intestines to meet the body’s needs.

In this system, structures closer to the oral cavity are considered “**proximal**,” and those closer to the anus are “**distal**.” Because both the oral cavity and anus open to the external environment, the materials within the tract — food and waste — are **technically outside the body**. Only through absorption, when nutrients move from the tract into the bloodstream, do they enter and support the body’s internal environment.

Accessory Organs

Each accessory digestive organ contributes to the breakdown of food. In the oral cavity, the teeth and tongue begin mechanical digestion, and the salivary glands begin chemical digestion. Once food enters the small intestine, the gallbladder, liver, and pancreas release secretions such as bile and digestive enzymes that allow digestion to continue. These structures are called accessory organs because they originate as outgrowths of the developing gut (mucosa) and support its function. You could not survive without the essential roles of the liver and pancreas, and many serious diseases result when they malfunction. These organs are connected to the gut through a system of ducts. The accessory digestive organs are summarized in the Table below.

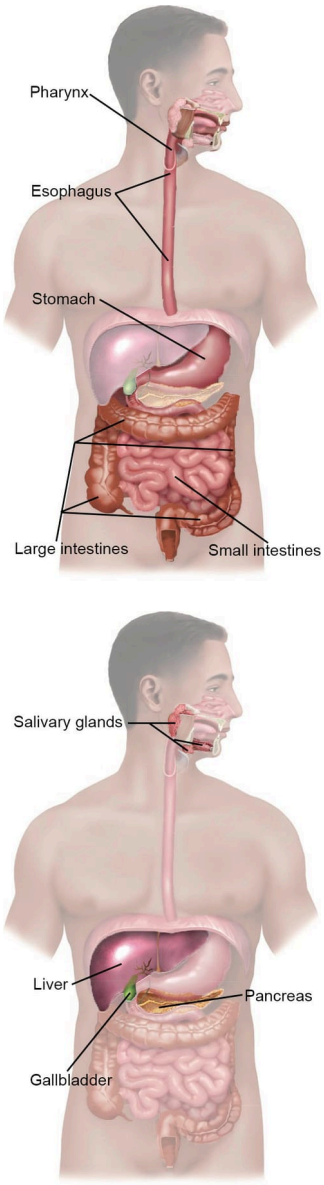


Figure 12.1.2: **The Alimentary Canal and its Accessory Organs.** On the left is the tube called the alimentary canal with its main subdivisions. On the right the critical accessory organs. *(Image credit: "Main Digestive Organs" by John Polos is licensed under CC BY-NC-SA 4.0, modification of original by KnowledgeWorks .)*

Organs of the Digestive System

Tract Organ	Accessory Organ
Oral Cavity: Ingestion. Site of mechanical digestion; start of chemical digestion.	**Salivary Glands**: Produce saliva; empty into oral cavity through ducts. The three pairs of salivary glands are: • parotid glands • submandibular glands • sublingual glands **Teeth**: Grinding, tearing, crushing of food. **Tongue**: Moves food to contact teeth; moves food into pharynx.
Esophagus: Moves food to stomach.	
Stomach: Chemical digestion of proteins and mechanical breakdown of food. Moves food to small intestine.	
Small Intestine: Finish chemical digestion and absorbs food. Moves food to large intestine. Three regions are: • Duodenum • Jejunum • Ileum	**Liver**: Produces bile that emulsifies fat. Empties into duodenum through hepatic ducts. **Gallbladder**: Stores bile. Empties into duodenum through cystic duct. **Pancreas**: Produces pancreatic juice which contains enzymes to digest lipids, proteins, and starch. Empties into duodenum through pancreatic duct(s).
Large Intestine: Reabsorbs water and absorbs some vitamins and minerals; bacteria ferment soluble fiber. Five regions are: • Cecum • Ascending Colon • Transverse Colon • Descending Colon • Sigmoid Colon	
Rectum: Collects and stores fecal matter.	

The Six Core Processes of Digestion: An Overview

The proper functioning of the gastrointestinal (GI) tract is imperative for our well being and life-long health. A non-functioning or poorly-functioning GI tract can be the source of many chronic health problems that can interfere with your quality of life.

Here is a look at the importance of the digestive system functions grouped into six core processes:

Getting Food Ready for the Trip: Ingestion, Moistening, Breakdown, and Swallowing

Digestion begins in the mouth. A brain reflex triggers the flow of saliva when we see or even think about food. **Saliva** moistens the food and begins its chemical breakdown, and the salivary glands together produce about three liters of saliva each day. The **teeth** contribute mechanical breakdown by chewing the food into smaller pieces so digestive enzymes can reach it more easily. Once food is moistened, shaped, and ready to swallow it is called a **bolus**.

Swallowing begins when the muscles of the tongue and mouth move the bolus into the pharynx. This step requires the coordinated action of about twenty-five muscles working at the same time.

The pharynx is a short passageway, only about five inches long, that carries both food and air. A small flap of tissue called the **epiglottis** closes over the opening to the trachea to keep food from entering the airway and causing choking. The bolus is then directed into the **esophagus**, a muscular tube that uses coordinated waves of contraction called peristalsis to move food toward the stomach.

While food travels through the digestive tract, it is technically **passing through the body** rather than being inside the body. Only after nutrients are absorbed do they truly enter the internal environment.

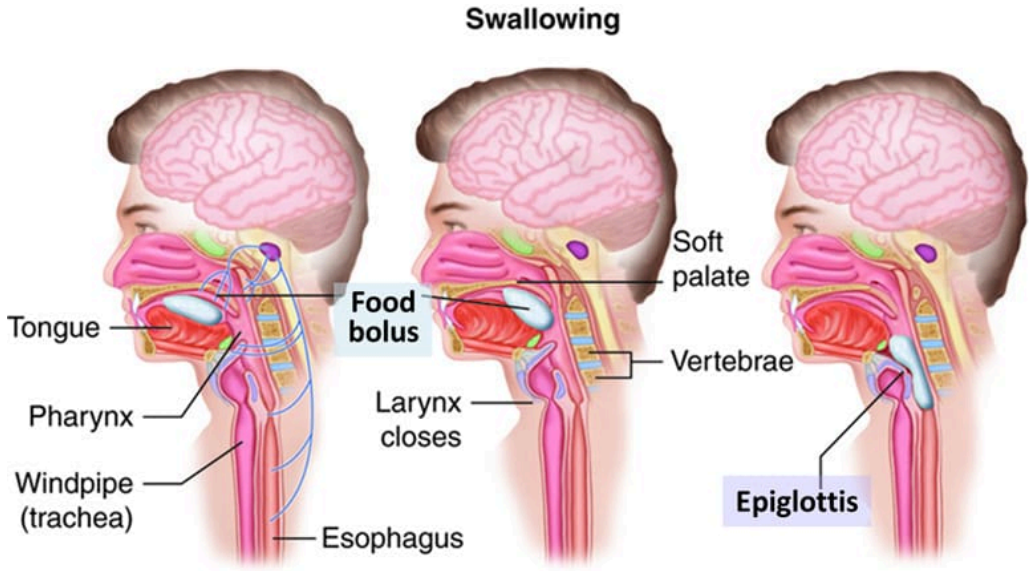


Figure 12.1.3: **Stages of Swallowing (Deglutition).** Tongue, soft palate, and epiglottis work together to safely move a food bolus from the mouth into the esophagus. In the first panel, the tongue pushes the bolus toward the pharynx. In the middle panel, the soft palate elevates to block the nasal cavity while the larynx rises and begins to close. In the final panel, the epiglottis folds down to cover the trachea so the bolus can enter the esophagus, preventing food from entering the airway. This work by Cenveo is licensed under a Creative Commons Attribution 3.0 United States (http://creativecommons.org/licenses/by/3.0/us/).

Secretion

Cells along the digestive tract, and in nearby glands, release fluids that help you break down food and protect your organs. With every meal, several liters of fluid enter the digestive tract. These secretions **include enzymes, mucus, acids, and bicarbonate-rich fluids, as well as hormones that help coordinate the whole process.**

In the mouth, salivary glands release saliva that contains the enzyme **amylase**, which begins breaking down starches into smaller sugars. In the stomach, glands in the lining secrete **hydrochloric acid** (HCl), which helps unfold proteins and kills many microbes, and **pepsin**, an enzyme that begins protein digestion. The stomach also secretes thick **mucus** that protects its own tissue from being damaged by the acid.

As food moves into the small intestine, the pancreas, liver, and gallbladder add their own secretions. The pancreas releases **digestive enzymes t**hat break down carbohydrates, proteins, and fats, along with **bicarbonate that neutralizes stomach acid** so the intestinal lining is not harmed. The liver produces **bile**, which is stored in the gallbladder and then squirted into the small

intestine to help emulsify fats so enzymes can reach them more easily. **Hormones** such as gastrin, secretin, and cholecystokinin (CCK) act as chemical messengers that tell different organs when to increase or decrease their secretions, depending on what kind of food has arrived. It is important understanding these secretions matters because problems such as ulcers, pancreatitis, or gallbladder attacks often involve abnormal secretion or blockage of these fluids, which can cause serious pain, bleeding, or changes in vital signs.

Mixing and Propulsion

Mixing and propulsion describe how the digestive tract keeps food moving and blends it with digestive juices. Once you swallow, waves of smooth muscle contraction called **peristalsis** push the food bolus from the esophagus down toward the stomach. In the stomach, strong muscular contractions churn the food and mix it with acid and enzymes to form a semi-liquid called chyme. This churning action increases contact between the food and digestive secretions so that chemical digestion can proceed efficiently.

As the food — now called chyme — enters the small intestine, the muscle in the intestinal wall continues to move it along, but now with a combination of peristalsis and a back-and-forth action called **segmentation**. Segmentation does not push food very far forward. Instead, it repeatedly squeezes and relaxes different segments of the intestine so that chyme is thoroughly mixed with enzymes and brought into close contact with the absorptive surface of the intestinal wall. Farther along, in the large intestine, slower peristaltic waves and occasional stronger “mass movements” propel the remaining material toward the rectum.

Digestion

Food is the body’s source of fuel. The nutrients in food give the body’s cells the energy they need to operate. Digestion is the process of breaking food down into small enough pieces that your body can absorb and use. It has two main parts: **mechanical digestion** and **chemical digestion.** Mechanical digestion is the physical breakdown of food into smaller pieces. It starts in the mouth, where teeth tear, grind, and mash food. In the stomach, strong muscular contractions continue this process by churning the food into a semi-liquid mixture called chyme. This mechanical breakdown increases the surface area of the food, making it easier for enzymes to do their job.

Chemical digestion uses enzymes and other chemicals to break large molecules into their building blocks. In the mouth, salivary amylase begins breaking down starch. In the stomach, acid helps unfold proteins, and the enzyme pepsin begins to digest them. Most chemical digestion happens in the small intestine, where enzymes from the pancreas and the intestinal lining break carbohydrates into simple sugars, proteins into amino acids, and fats into fatty acids and glycerol. Bile from the liver helps with fat digestion by emulsifying large fat droplets into smaller ones.

Absorption

During absorption, the nutrients that come from food (such as proteins, fats, carbohydrates, vitamins, and minerals) actually enter the body’s internal environment by passing through the wall of the intestinal tract and into the bloodstream. Most absorption happens in the **small intestine**, which is lined with folds, villi, and microvilli that greatly increase the surface area, making it look like a plush carpet under the microscope. This huge surface allows nutrients to move efficiently from the lumen of the intestine into blood vessels and lymphatic vessels. Simple sugars from carbohydrates and amino acids from proteins are absorbed into tiny blood capillaries, while most fats are packaged into small droplets and absorbed into lymphatic vessels called lacteals. Water, vitamins, and electrolytes are also absorbed, mainly in the small intestine, with additional water and electrolyte absorption in the large intestine.

Once nutrients are absorbed, they do not just float around randomly. Blood from the intestines first travels through the **hepatic portal vein** to the liver, where many substances are processed, stored, modified, or detoxified before they enter the general circulation. Glucose can be stored as glycogen or released back into the blood to maintain a stable blood sugar level. Amino acids may be used to build new proteins, and fats can be stored in adipose tissue or used for energy. Cells throughout the body use these absorbed nutrients to make ATP, repair tissues, support growth, and maintain normal function.

Waste Compaction and Elimination

Waste compaction and elimination are the final processes of digestion, where the body deals with what it cannot digest or absorb. After most nutrients and a large amount of water have been removed in the small intestine, the remaining material enters the **large intestine**. Here, the colon slowly moves the contents along while **absorbing additional water and electrolytes**, which helps compact the material into feces. Helpful gut bacteria living in the large intestine also break down some remaining substances, producing gases and certain vitamins, such as vitamin K, that can be absorbed. Mucus is secreted to help the contents move more smoothly and protect the lining of the colon.

As **feces** become more solid, they are stored in the rectum until stretch receptors in the rectal wall are stimulated, triggering the **defecation reflex**. This reflex involves coordinated contraction of the rectum and relaxation of the internal anal sphincter, along with voluntary control over the external anal sphincter, which allows a person to decide when it is socially appropriate to go to the bathroom. If stool moves too slowly, too much water is absorbed and constipation can occur; if it moves too quickly, there is not enough time to reabsorb water, leading to diarrhea and possible dehydration.

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12.2: Liver, Pancreas, and Gallbladder — Accessory Digestive System Organs

Chemical digestion in the small intestine depends on the coordinated actions of the liver, gallbladder, and pancreas, which supply bile and digestive enzymes to break down nutrients efficiently.

Master this section and you'll be able to:

- Describe the roles of the liver, gallbladder, and pancreas in releasing bile and pancreatic juice to support chemical digestion in the small intestine.
- Distinguish between the pancreas's exocrine enzyme secretion and endocrine hormone release.

Chemical digestion in the small intestine relies on the activities of three accessory digestive organs: the **liver**, **pancreas**, and **gallbladder** (see figure below). The digestive role of the liver is to produce **bile** and export it to the duodenum. The gallbladder primarily stores, concentrates, and releases bile. The pancreas produces **pancreatic juice**, which contains **digestive enzymes and bicarbonate ions**, and delivers it to the duodenum.

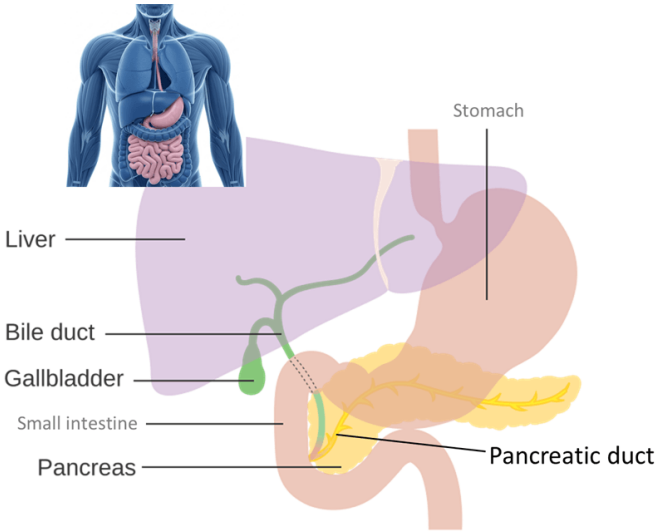


Figure 12.2.1: **Accessory Digestive Organs and Their Ducts.** The liver, gallbladder, and pancreas work together to release bile and digestive enzymes into the duodenum (1st part of the small intestine), where they help break down fats, proteins, and carbohydrates. This diagram highlights the location of each organ and shows how the bile ducts and pancreatic duct empty into the first part of the small intestine to support digestion.

Liver

The **liver** is the largest gland in the body, weighing about three pounds in an adult. It is also one of the most important organs. In addition to being an accessory digestive organ, it plays a number of roles in metabolism and regulation. The liver lies inferior to the diaphragm in the right upper quadrant of the abdominal cavity and receives protection from the surrounding ribs.

The liver is divided into two primary lobes: a large **right lobe** and a much smaller **left lobe**. In the right lobe, some anatomists also identify an inferior **quadrate lobe** and a posterior **caudate lobe**, which are defined by internal features. The liver is connected to the abdominal wall and diaphragm by five peritoneal folds referred to as ligaments. The lesser omentum tethers the liver to the lesser curvature of the stomach.

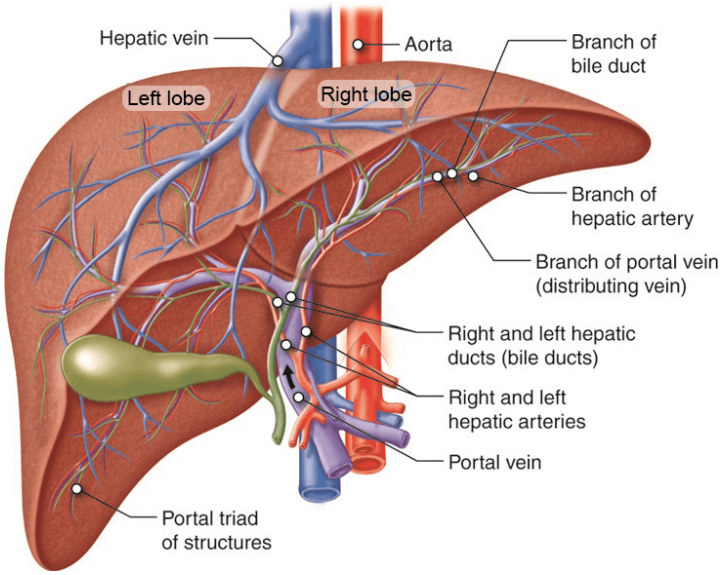


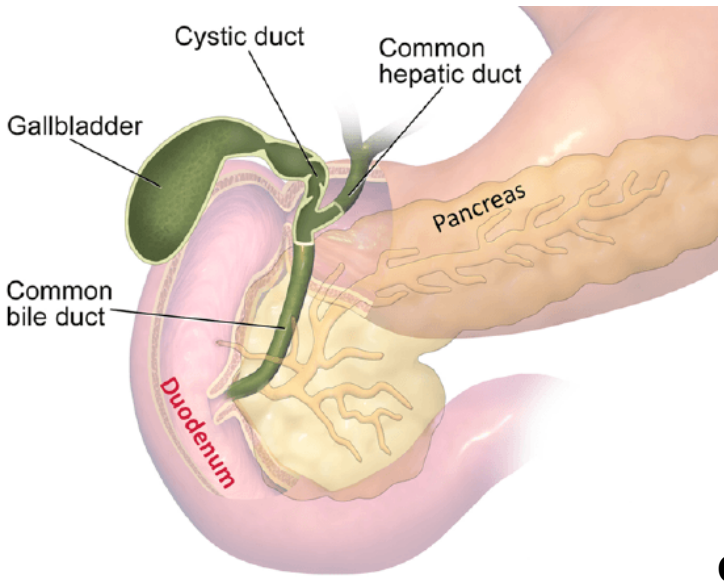
Figure 12.2.2: **Liver Blood Flow and Bile Drainage.** Blood arrives from two sources: the hepatic arteries, which supply oxygenated blood, and the portal vein, which carries nutrient-rich blood from the digestive tract. Inside the liver, these vessels branch extensively and travel alongside bile ducts. As the liver processes nutrients and detoxifies blood, cleaned blood exits through the hepatic veins and returns to the heart. Bile produced by hepatocytes drains into small ducts that merge into the right and left hepatic ducts and eventually flow toward the gallbladder and small intestine. *(Image credit: "Cenveo - Drawing Liver anatomy and vascularisation - English labels" by Cenveo, license: CC BY, modifications by Jennifer Lange.)*

The liver is one of the body's most versatile and essential organs, often described as a metabolic powerhouse because nearly every nutrient absorbed from the digestive tract passes through it for processing. After digestion, the liver adjusts nutrient levels in the blood by storing some molecules, converting others, and releasing them as needed to maintain stable internal conditions. It also detoxifies harmful substances, transforms ammonia into urea, breaks down old red blood cells, and helps recycle iron. With hundreds of chemical reactions occurring at any moment, the liver plays a central role in keeping metabolism balanced and supporting overall health.

The liver performs both exocrine and endocrine functions. Its major **exocrine** role is the **production and secretion of bile**, a fluid that contains bile salts needed for the emulsification and absorption of dietary lipids. Bile flows through a duct system and is stored in the gallbladder until it is released into the small intestine during digestion.

In addition to being a huge metabolic and detoxifying organ, the liver quietly behaves like an **endocrine gland** and helps regulate growth, blood pressure, blood cell production, iron balance, and calcium homeostasis.

Last but not least, besides its many metabolic, and endo-and exocrine function, the liver also releases other important substances directly into the bloodstream, including p**lasma proteins such as albumin and clotting factors**.



Gallbladder

The gallbladder is a small, muscular sac, about 8–10 cm (3–4 in) long, nestled in a shallow depression on the underside (posterior aspect) of the right lobe of the liver. It **stores and concentrates bil**e produced by the liver, then releases it into the duodenum through the **common bile** duct when needed for digestion. The gallbladder connects to the liver via the cystic duct, which joins the hepatic duct to form the common bile duct. Structurally, the gallbladder has three regions: the fundus is the widest portion, which tapers into the body; the body narrows into the neck, which bends slightly upward as it approaches the hepatic duct. The cystic duct is a short (1–2 cm) passage that connects the neck of the gallbladder to the hepatic duct.

The inner lining of the gallbladder is a simple columnar epithelium arranged in folds called rugae, similar to the rugae of the stomach. There is no distinct submucosa. The middle layer of the wall is made of smooth muscle; when this muscle contracts, bile is squeezed out through the cystic duct and into the bile duct. The outer surface is covered by visceral peritoneum that reflects from the liver capsule, helping hold the gallbladder tightly against the liver. As bile sits in the gallbladder, its mucosa absorbs water and ions, concentrating the bile by up to about tenfold. Over time, some people develop gallstones within the gallbladder , and in many of these cases the gallbladder is surgically removed along with the stones.



Figure 12.2.3: **Gallstones**. Ultrasound image of a stone in the gallbladder. *(Image credit: "Gallstone" by © Nevit Dilmen is licensed under CC BY-SA 3.0, via Wikimedia Commons.)*

Pancreas

The oblong, glandular pancreas lies transversely in the **retroperitoneal space behind the stomach**. Its head fits snugly into the c-shaped curve of the duodenum, while the body extends to the left about 15 cm (6 in) and narrows into a tapering tail that reaches the hilum of the spleen. The pancreas **performs both exocrine functions (secreting digestive enzymes into ducts) and endocrine functions (releasing hormones into the blood).** On histologic examination, you can see round clusters of acinar cells connected to the pancreatic ducts, as well as larger clusters of lighter-staining endocrine cells called pancreatic islets.

The **exocrine portion** of the pancreas is organized into many small, grape-like clusters of serous cells called acini (singular: acinus) at the terminal ends of the pancreatic ducts. These acinar cells secrete enzyme-rich **pancreatic juice** into tiny ducts that merge to form two main ducts. The main pancreatic duct joins the common bile duct at the hepatopancreatic ampulla, just before entering the duodenum through the main duodenal papilla. A ring of smooth muscle called the sphincter of the hepatopancreatic ampulla regulates the release of both pancreatic juice and bile into the small intestine. In about 30 percent of people, a second, smaller accessory pancreatic duct (duct of Santorini) carries secretions directly into the duodenum about 2.5 cm (1 in) above the main opening; when present, it is a persistent remnant of pancreatic development.

Scattered among the exocrine acini are small “islands” of endocrine cells called **pancreatic islets** (islets of Langerhans). These cells release several important hormones into the bloodstream, including **insulin**, **glucagon**, somatostatin, and pancreatic polypeptide. Together, these hormones help regulate blood glucose levels and coordinate other metabolic functions throughout the body.

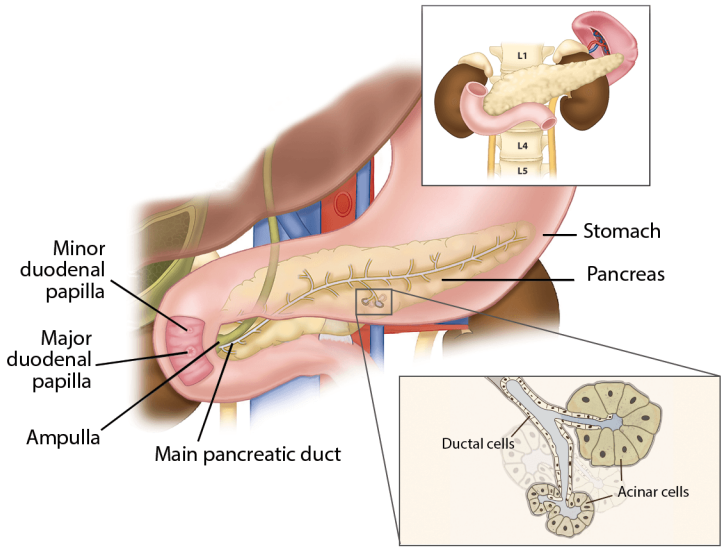


Figure 12.2.4: **Exocrine Pancreas**. The pancreas is located posterior to the stomach. The acinar and ductal cells secrete enzymes and bicarbonate into the pancreatic duct(s) that empty into the duodenum at the duodenal papilla(e). *(Image credit: "Exocrine Pancreas" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original illustration by BlueLink.)*

Pancreatic Juice

The pancreas produces more than a liter of clear, watery pancreatic juice each day. This fluid contains salts, **sodium bicarbonate**, and **several digestive enzymes**. Sodium bicarbonate gives pancreatic juice its slightly alkaline pH (7.1 to 8.2), which helps neutralize acidic chyme arriving from the stomach, inactivates pepsin, and creates the proper pH for the enzymes that work in the small intestine. Pancreatic enzymes participate in breaking down carbohydrates, proteins, and fats.

Protein-digesting enzymes are **released in inactive forms** so they do not harm pancreatic tissue. These enzymes are activated only after they reach the duodenum. A brush border enzyme called enteropeptidase triggers the first activation step, which then sets off a cascade that turns the remaining protein-digesting enzymes into their active forms.

Enzymes that digest starch (amylase), fats (lipase), and nucleic acids (nuclease) are released already active, because they do not pose a risk of damaging the pancreas the way active protein-digesting enzymes would.

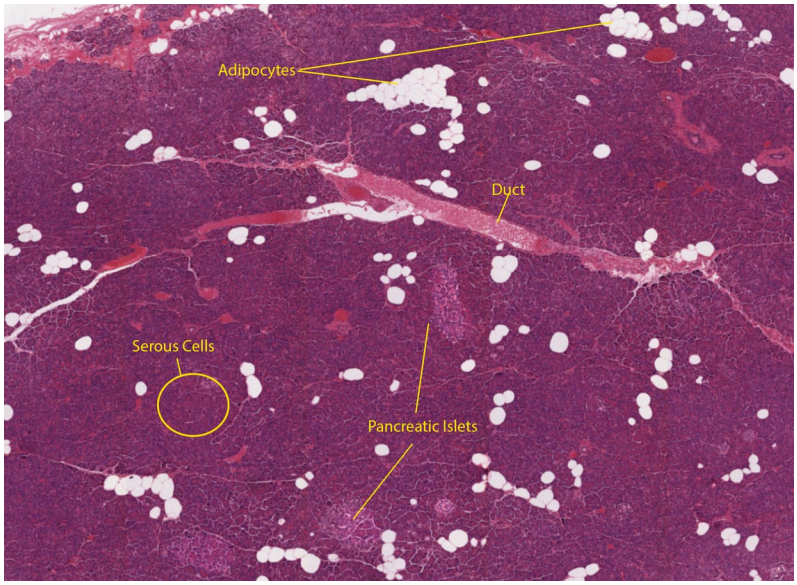


Figure 12.2.5: **Pancreas Histology**. This shows that he pancreas is made up of lots of serous cells. However, at this power, you cannot see the acini. *(Image Credit: "Pancreas Histology @ 100x" micrograph provided by the Regents of University of Michigan Medical School © 2012.)*

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12.3: Structural Organization of the Intestinal Wall and Peritoneum

The digestive tract is organized into four layers that vary by region depending on the specific function of that region.

Master this section and you'll be able to:

- Describe the four main tissue layers of the digestive tract and how each contributes to digestive function.
- Compare how the mucosa, submucosa, muscularis, and serosa/adventitia vary among the different digestive organs shown.

Histology of the Digestive Tract Organs

Throughout its length, the digestive tract is built from **four main tissue layers — mucosa, submucosa, muscularis, and serosa (or adventitia)** — each arranged slightly differently to support the specific functions of different regions. The figure below also highlights the mesentery, which contains the blood vessels and nerves that run between the two serosal layers, and will be discussed a little later.

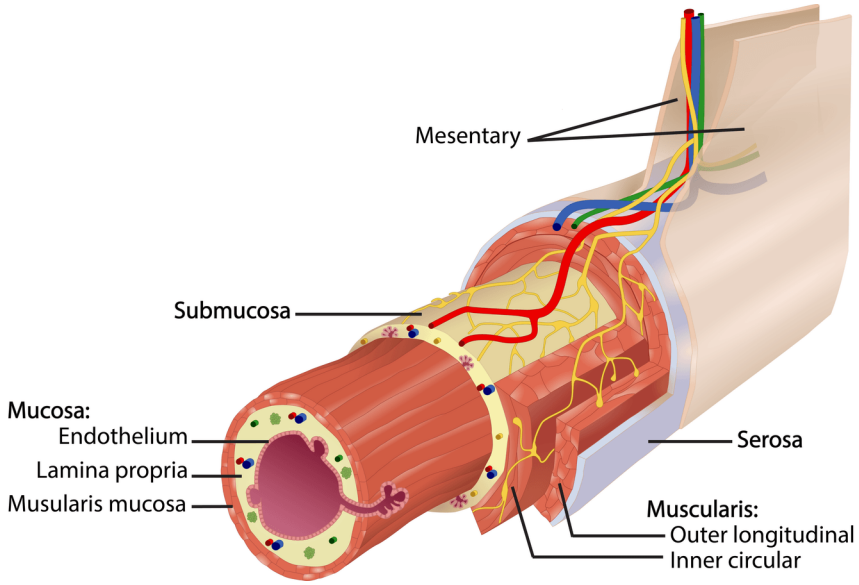


Figure 12.3.1: **Layers of the Digestive Tract.** The digestive tract is made up of four distinctive layers: the most inner layer is the **mucosa**, formed by the epithelium, lamina propria, and muscularis mucosae. Outside of it lies the supportive **submucosa**, followed by the **muscularis** with its inner circular and outer longitudinal smooth-muscle layers that drive mixing and propulsion. The outermost serosa connects to the mesentery, a double-layered fold of peritoneum that holds the digestive organs in place and provides a pathway for vessels and nerves to reach them. Mucosa

Mucosa

The mucosa is often called a mucous membrane because producing mucus is one of the hallmarks of the gut epithelium. This inner lining includes an epithelial layer that directly contacts ingested food, a layer of areolar connective tissue, and a thin sheet of smooth muscle known as the muscularis mucosa. This muscularis mucosa should not be confused with the thicker muscularis layer located farther outward in the digestive tract wall.

Epithelium:

In the oral cavity, pharynx, esophagus, and anal canal, the epithelial lining is mostly **non-keratinized stratified squamous epithelium**, which provides protection against abrasion.

In the stomach and intestines, it **shifts to simple columnar epithelium specialized for secretion and absorption.** Because this epithelium is in direct contact with the lumen, its cells constantly encounter food, chemicals, and microbes. **Goblet cells** scattered among the epithelial cells release **mucus** and fluid into the lumen, while **enteroendocrine cells secrete hormones** into the surrounding interstitial spaces to influence digestive activity. These epithelial cells have a short lifespan — from only a few days in the mouth to about a week in the intestines — allowing the mucosa to renew itself quickly despite continual wear.

Lamina propria:

The lamina propria is a layer of **areolar connective tissue** containing an extensive network of blood and lymphatic vessels that carry absorbed nutrients away from the digestive tract. It also plays a key immune role by housing clusters of lymphocytes known as mucosa-associated lymphoid tissue (MALT). These immune structures are especially well developed in the distal ileum, where they form Peyer's patches. Because the gut is constantly exposed to food-borne microbes and foreign materials, this immune defense is crucial for maintaining digestive tract health.

Muscularis mucosa:

The muscularis mucosa is a thin sheet of smooth muscle that keeps the mucosal surface in gentle motion. In the stomach and small intestine, this movement creates small folds that greatly increase the surface area available for digestion and absorption.

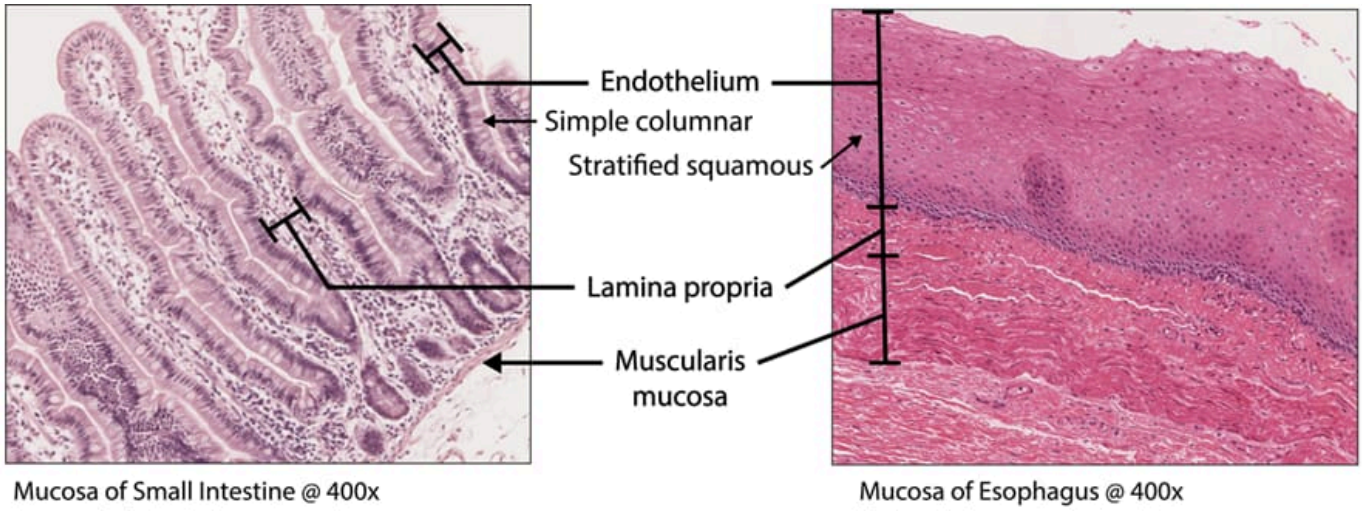


Figure 12.3.2: **Comparing the Mucosa of the Small Intestine and Esophagus.** Both images show the mucosa, the innermost layer of the digestive tract, but each organ's mucosa is adapted to a different job. The small intestine (left) has simple columnar epithelium with tall villi that increase surface area for nutrient absorption. In contrast, the esophagus (right) has a protective non-keratinized stratified squamous epithelium suited for resisting abrasion from swallowed food. Both epithelia are backed by backed by a lamina propria and muscularis mucosa. *Image credit: "Mucosa of the GI Tract" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, incorporating illustration by Goran tek-en with edits made by Collectivedogs via Wikimedia Commons and slides provided by the Regents of the University of Michigan Medical School © 2022.)*

Submucosa

As its name implies, the submucosa lies immediately beneath the mucosa. This broad layer of **connective tissue** varies in thickness along the digestive tract. Positioned between the muscularis mucosa and the muscularis, it contains blood and lymphatic vessels that transport absorbed nutrients, along with scattered submucosal glands that release digestive secretions. The submucosa also houses a dense branching network of nerves called the submucosal plexus, which helps regulate local secretions and blood flow.

Muscularis

The muscularis (or muscularis externa) is the third major layer of the digestive tract. It is composed of **two layers of smooth muscle: an inner circular layer that wraps around the tube, and an outer longitudinal layer that runs along its length.** The coordinated contractions of these layers help **mechanically break down food, mix it with digestive secretions, and propel it forward through the canal.**

In the most proximal and distal regions of the tract, including the oral cavity, pharynx, the upper portion of the esophagus, and the external anal sphincter, the muscularis consists of **skeletal** muscle. This arrangement allows voluntary control over swallowing and defecation.

Several organs modify the basic two-layer pattern. The **stomach adds a third,** deep **oblique** layer that strengthens its ability to churn and mix chyme. The large intestine retains two layers; however, its outer longitudinal layer is gathered into three narrow bands called the teniae coli, which create the characteristic pouch-like appearance of the colon.

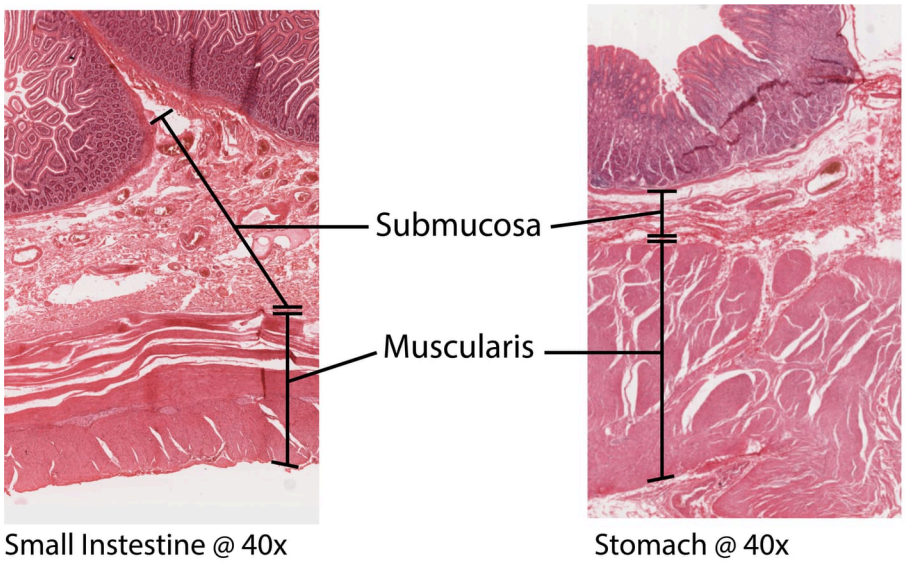


Figure 12.3.3: **Comparing the Submucosa and Muscularis of the Small Intestine and Stomach.** These paired histology images highlight how the same two digestive tract layers — the submucosa and muscularis — look different depending on the organ. The small intestine's submucosa supports tall villi and contains scattered glands, while its muscularis shows the typical two smooth-muscle layers used for peristalsis. In contrast, the stomach has a thicker, more gland-rich submucosa and a much more robust muscularis, which includes an additional oblique layer that helps churn and mix food during mechanical digestion.

Serosa or Adventitia

The serosa is the **outermost layer** of the digestive tract in regions that lie **within the abdominal cavity**. It consists of a thin sheet of visceral peritoneum resting on loose connective tissue. Because it is derived from the peritoneum, the serosa provides a smooth, lubricated surface that allows abdominal organs to slide past one another as they move.

In contrast, the oral cavity, pharynx, and esophagus lie outside the abdominal cavity and are not surrounded by the peritoneum. These structures therefore lack a serosa. Instead, they are wrapped in a tougher outer covering called the **adventitia**, a dense layer of collagen fibers that anchors them in place near the ventral surface of the vertebral column.

The Peritoneum

The peritoneum is a serous membrane that lines the abdominal cavity (**parietal peritoneum**) and covers most abdominal organs (**visceral peritoneum**). It is made of a thin sheet of simple squamous epithelial cells that produces a smooth, slippery lining, very much alike other serous membranes, including the pleura and pericardium. A small amount of lubricating fluid reduces friction between organs as they move. The peritoneum also protects and supports the abdominal organs and serves as a passageway for blood vessels, lymphatic vessels, and nerves that supply them.

The abdominal cavity is the large internal space enclosed by the diaphragm, abdominal wall, vertebrae, and pelvic floor. Within this cavity is the intraperitoneal space, which is wrapped in peritoneum. The large, open portion of the peritoneal cavity that you enter as soon as the parietal peritoneum is pierced is called the **greater sac** (see image below). It fills most of the space between the parietal peritoneum and the visceral peritoneum covering the abdominal organs. Almost all intraperitoneal organs — such as the stomach, liver, and small intestine — lie within or project into this space.

Not all organs inside the abdominal cavity are surrounded by peritoneum though. For example, the kidneys are located in the abdominal cavity but lie behind the peritoneum, making them **retroperitoneal** rather than intraperitoneal.

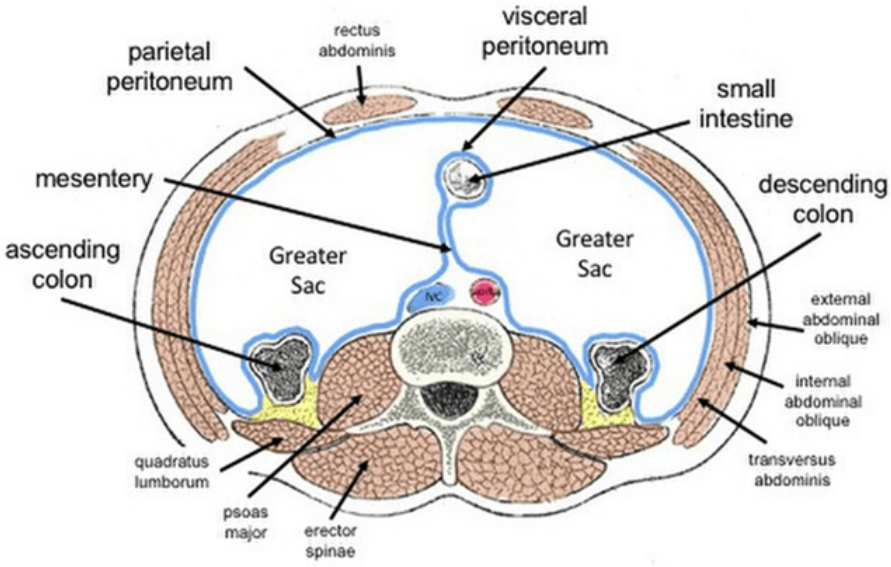


Figure 12.3.4**: Peritoneal Cavity in Cross-Section.** This cross-section of the abdomen shows how the **parietal peritoneum** lines the inner body wall and how the **visceral peritoneum** covers the abdominal organs. The space between these layers forms the peritoneal cavity. The **mesentery**, a double layer of peritoneum, anchors the small intestine to the posterior abdominal wall and carries its blood vessels, nerves, and lymphatics.

Although they ultimately form one continuous sheet, there are two layers of peritoneum and potential space between those layers.

- The outer layer, called the p**arietal peritoneum**, is attached to the abdominal wall.
- The inner layer, the **visceral peritoneum**, is **wrapped around the internal organs** that are located inside the intraperitoneal cavity.
- The potential space between these two layers is the **peritoneal cavity**. It is filled with a small amount of slippery serous fluid that allows the two layers to slide freely over each other.

The term **mesentery** is often used to refer to a **double layer of visceral peritoneum.** There are generally blood vessels, nerves, and other structures between these layers. The space between the two layers is technically outside of the peritoneal sac, and thus not in the peritoneal cavity.

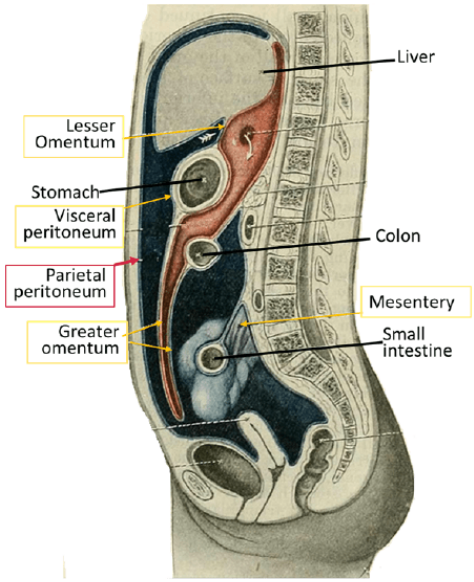


Figure 12.3.5**: Relationship of Abdominal Organs to the Peritoneum.** The peritoneum folds around the abdominal organs to create two main spaces: the intraperitoneal space and the retroperitoneal space. The parietal peritoneum lines the inner surface of the abdominal wall, while the visceral peritoneum covers selected organs. Organs such as the stomach and much of the intestines are wrapped in visceral peritoneum and suspend within the peritoneal cavity, which includes the large central region called the greater sac (shown in dark blue in the drawing). In contrast, structures such as the kidneys, pancreas, and portions of the duodenum lie behind the peritoneal lining in a region known as the retroperitoneal space.

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12.4: From the Mouth to the Stomach

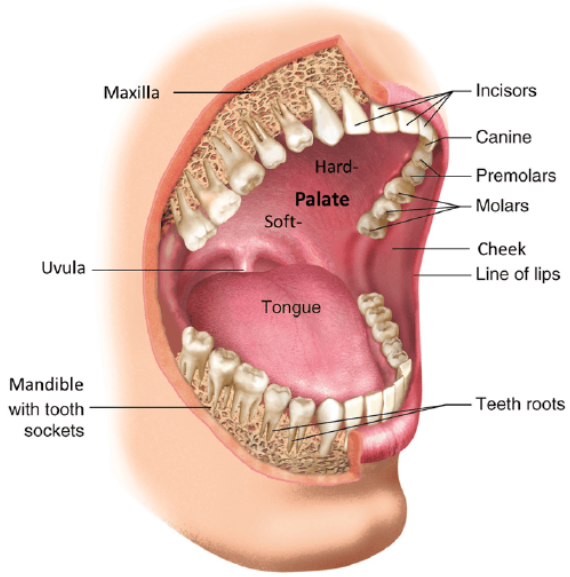
The mouth, pharynx, esophagus, and stomach work together to begin digestion by mechanically and chemically processing food, safely directing it toward the stomach, and mixing it with secretions that transform it into chyme for the small intestine.

Master this section and you'll be able to:

- Identify the major structures of the mouth, salivary glands, teeth, pharynx, and esophagus, and explain how they begin digestion and move a bolus safely from mouth to stomach.
- Label the main regions and curvatures of the stomach, and summarize how stomach structure, secretory cells, and protective mechanisms support mechanical and chemical digestion.

Mouth, Pharynx, and Esophagus

Let's start with a quick overview of the anatomy and functions of the three main organs of the upper alimentary canal — the mouth, pharynx, and esophagus — as well as two associated accessory organs — the salivary glands, and teeth.



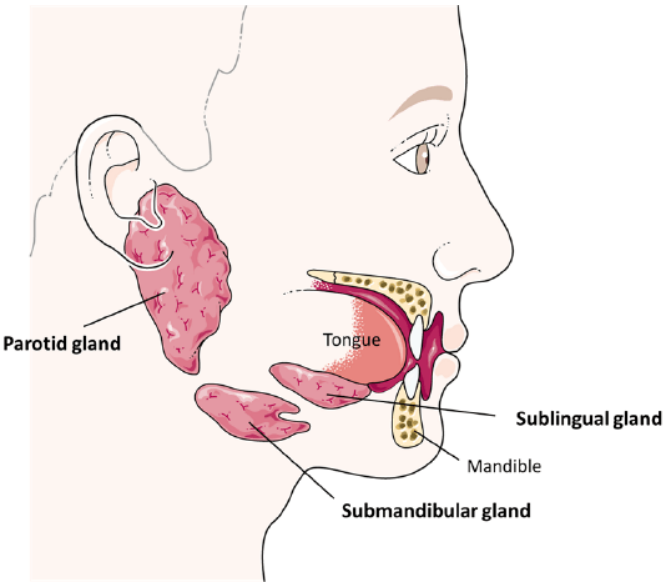
The Mouth (Oral Cavity)

The cheeks, lips, tongue, and palate frame the mouth, also called the **oral cavity**. The lips mark the entrance to the mouth and are highly vascular, which gives them their reddish color. A small fold of tissue, the labial frenulum, connects each lip to the gums. The cheeks form the sidewalls of the oral cavity and contain the **buccinator muscles**, which help keep food in your mouth while you chew and speak.

The space between the lips/cheeks and the gums/teeth is called the oral vestibule. Farther inside is the oral cavity proper, which extends back to the opening to the throat (oropharynx).

The **palate** forms the roof of the mouth and separates the oral and nasal cavities. The front portion, the **hard palate**, is made of bone and provides a firm surface for the tongue during chewing. The back portion, the **soft palate**, is made of skeletal muscle and can move during swallowing, yawning, or speaking. Hanging from the soft palate is the **uvula**, a small projection that helps prevent food and liquids from entering the nasal cavity during swallowing.

On either side of the uvula are two muscular arches. Between them lie the **palatine tonsils**, part of the immune system that helps protect the pharynx. Additional lymphoid tissues, the **lingual tonsils**, are located at the base of the tongue.



The Salivary Glands

Scattered throughout the lining of the mouth and tongue are many small salivary glands that constantly release tiny amounts of saliva, even when you sleep. Their job is to keep the mouth moist and comfortable. When you begin eating, saliva production increases so food can be moistened, shaped into a bolus, and chemically broken down.

In addition to these hundreds of small glands, three pairs of major salivary glands supply most of the saliva that enters the mouth:

- **Parotid glands** – located near the ears and about the size of a prune. They send saliva into the mouth through the parotid duct near the second upper molar.
- **Submandibular glands** – found along the floor of the mouth and about the size of a walnut. Their ducts open just under the tongue.
- **Sublingual glands** – sitting beneath the tongue and about the size of an almond. They release saliva through several small ducts in the floor of the mouth.

Together, all salivary glands produce about 1 to 1.5 liters of saliva each day.

Saliva

Saliva is mostly water, but it contains important substances that help with digestion, protection, and lubrication. One key enzyme, **salivary amylase**, begins the chemical breakdown of **carbohydrates** in the mouth and continues to work until the food reaches the acidic environment of the stomach. Saliva also contains mucus that helps lubricate food for swallowing, as well as antimicrobial molecules such as lysozyme and immunoglobulin A, which help protect the mouth from pathogens.

Each major salivary gland produces slightly different saliva. The parotid glands produce a thin, watery saliva rich in amylase. The submandibular glands make a mixture of watery and mucous saliva. The sublingual glands primarily secrete thicker, mucus-rich saliva with smaller amounts of amylase. This combination ensures that the mouth stays moist and that chewing, swallowing, and early digestion occur smoothly.

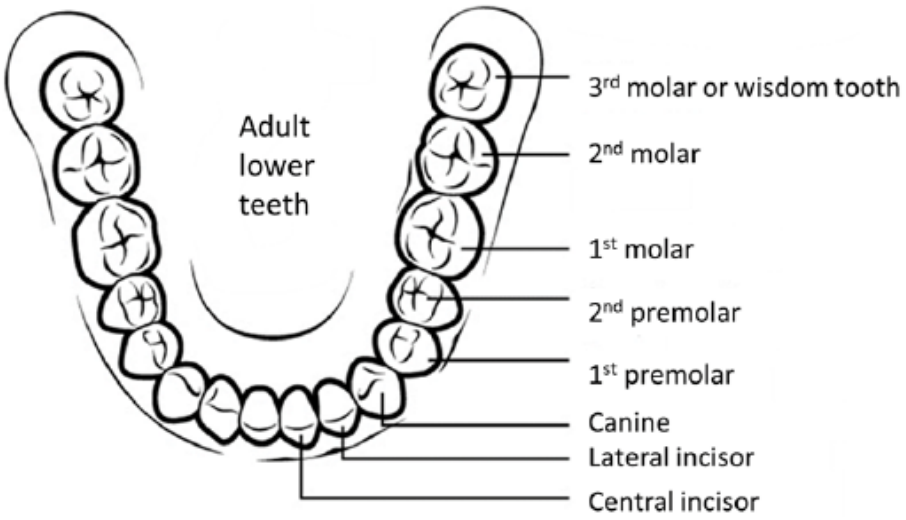
Viral Mischief: Mumps in the Parotid Gland



Infections of the nasal passages and pharynx can involve any of the salivary glands, but the **parotid glands are the classic site of infection** with the **mumps virus**, a paramyxovirus. Mumps typically causes painful enlargement and inflammation of one or both parotid glands, producing the familiar swelling between the ears and jaw. Symptoms often include fever, headache, and sore throat, and swallowing acidic drinks such as orange juice can be especially uncomfortable. CDC1(opens in new window)

In some adolescents and adults, the virus spreads beyond the salivary glands. After puberty, mumps can cause **inflammation of the testes (mumps orchitis)** in a substantial fraction of infected males, especially if they are unvaccinated; the condition is usually unilateral and painful, can lead to testicular shrinkage, but only rarely results in permanent sterility. Mumps can also inflame the ovaries or breast tissue, the pancreas, the coverings of the brain and spinal cord (meningitis), or the brain itself, and can occasionally cause hearing loss. CDC2(opens in new window)

The good news is that routine use of the **measles–mumps–rubella (MMR) vaccine** has reduced U.S. mumps cases by more than 99 percent compared with the pre-vaccine era, when well over 100,000 cases occurred each year. Today, most years see only a few hundred to a few thousand reported cases, often clustered in outbreaks on college campuses or in other close-contact settings, and vaccinated people who do get mumps usually have milder disease and fewer complications.



The Teeth

You develop **two sets of teeth in your lifetime.** The first 20 baby (**deciduous**) teeth begin to appear around 6 months of age. Between ages 6 and 12, they are replaced by **32 permanent teeth.** From front to back, the teeth include incisors for cutting, canines for tearing, premolars for mashing, and molars for crushing food. The third molars are the **wisdom teeth**; they often erupt in early adulthood and may stay trapped in the bone or gum tissue without being able to fully erupt into the mouth. This is why they are commonly removed.

Each tooth sits in a socket in the upper or lower jaw and is held in place by the gums and a strong periodontal ligament. A tooth has two main regions: the crown above the gum line and the root anchored in the jaw. Inside is the pulp cavity, which contains blood vessels and nerves. Surrounding the pulp is **dentin**, a hard tissue covered by cementum in the root and by enamel in the crown. **Enamel** is the hardest substance in the body, but it can still be damaged by acids.

Tooth decay (cavities) occurs when bacteria feeding on sugars produce acids that dissolve enamel and irritate deeper tissues. Good brushing, flossing, and limiting sugary foods help keep enamel intact and protect the rest of the tooth.

The Pharynx

The wall of the **oropharynx** is similar to the lining of the mouth, with a **protective stratified squamous epithelium and mucus-secreting glands.** During swallowing, skeletal muscles in the pharynx lift and widen the space to receive the bolus of food, then relax as the constrictor muscles squeeze it into the esophagus to begin **peristalsis**. At the same time, the **soft palate and uvula rise to seal off the nasopharynx**, and the larynx moves upward so the **epiglottis can fold down over the glottis to protect the airway.** If a small amount of food slips into the trachea, the cough reflex usually expels it and sends it back toward the pharynx.

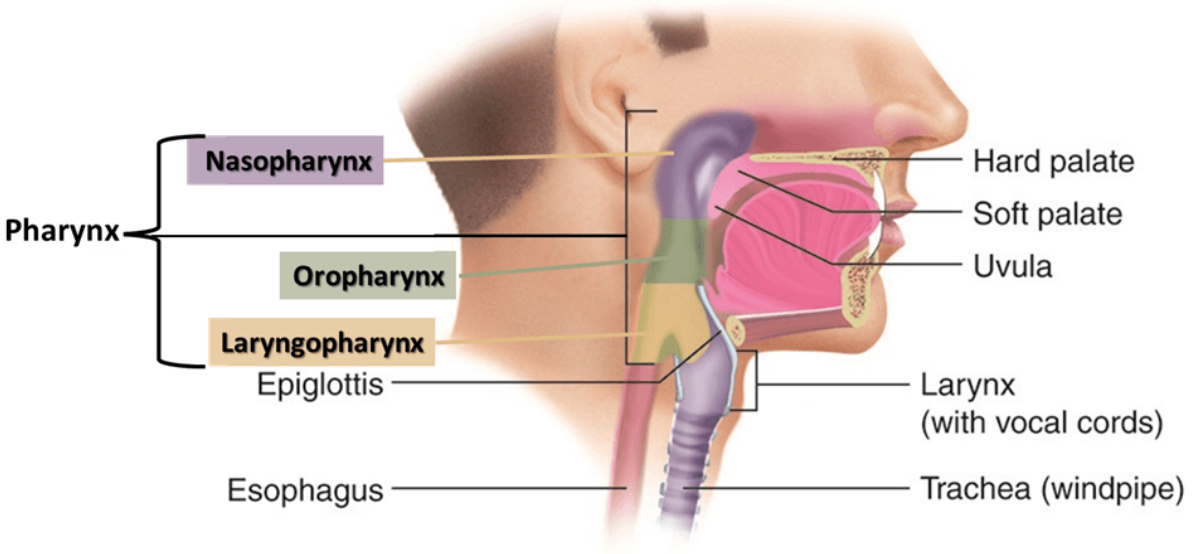


Figure 12.4.1: **Regions of the Pharynx and Nearby Structures.** A midsagittal view of the head and neck highlights the three divisions of the pharynx and how they connect the nasal cavity, oral cavity, and larynx. The **nasopharynx** sits behind the nasal cavity and is separated from the oral cavity by the hard and soft palates. The **oropharynx**, located behind the mouth, is where both food and air pass. Inferior to this is the **laryngopharynx**, which serves as the final pathway before air enters the larynx and food enters the esophagus. The image also shows key structures involved in swallowing and airway protection, including the uvula, soft palate, epiglottis, and the opening to the trachea.

The Esophagus

The esophagus is a muscular tube that carries food from the pharynx to the stomach. It is about 25 cm (10 in) long, lies **posterior to the trachea**, and stays collapsed except during swallowing. As shown in the figure, the esophagus travels straight **through the mediastinum** of the thorax and enters the abdomen by passing through the **esophageal hiatus of the diaphragm.**

The **upper esophageal sphincter (UES)** controls the entry of food from the pharynx. The upper two-thirds of the esophagus contain both skeletal and smooth muscle fibers, while the lower third is entirely smooth muscle. Waves of peristalsis begin near the top of the esophagus and push the bolus downward. Mucus secreted by the esophageal lining lubricates both the tube and the food as it travels.

At the stomach entrance, the **lower esophageal sphincter LES)** relaxes so the bolus can enter the stomach, then contracts to prevent acidic stomach contents from refluxing upward. The surrounding diaphragm also helps keep this sphincter closed between swallows. When the sphincter does not close completely, gastric contents can move into the esophagus and cause

heartburn or **GERD** (gastroesophageal reflux disease).

The esophageal mucosa is lined with **non-keratinized stratified squamous epithelium**, which protects the surface from abrasion. The lamina propria contains mucus-secreting glands that help lubricate the lumen.

The muscularis layer changes along the length of the esophagus: the upper third is skeletal muscle, the middle third is a mix of skeletal and smooth muscle, and the lower third is entirely smooth muscle. The outermost layer is the adventitia, a connective tissue covering that lacks the visceral peritoneum found on the stomach and intestines.

Table 1: Esophageal Actions During Swallowing.

Action	Outcome
Upper esophageal sphincter relaxation	Bolus moves from the laryngopharynx into the esophagus
Peristalsis	Propels the bolus through the esophagus
Lower esophageal sphincter relaxation	Bolus enters the stomach and reflux is prevented
Mucus secretion	Lubricates the bolus and eases passage

Deglutition (Swallowing)

Deglutition, or swallowing, is the process that moves a bolus of food from the mouth to the stomach. It normally takes only a few seconds and depends on smooth cooperation between the tongue, pharynx, esophagus, and plenty of lubricating saliva. Swallowing begins voluntarily but soon becomes an automatic reflex. The three phases are:

- **Voluntary (oral) phase:** The tongue pushes the bolus to the back of the mouth to start swallowing.
- **Pharyngeal phase:** Breathing briefly pauses while muscles guide the bolus safely past the airway and into the esophagus.
- **Esophageal phase:** Peristaltic waves move the bolus through the esophagus and relax the lower esophageal sphincter so it can enter the stomach.

Watch this animation to see how swallowing is a complex process that involves the nervous system to coordinate the actions of upper respiratory and digestive activities. During which stage of swallowing is there a risk of food entering respiratory pathways and how is this risk blocked?

YouTube Video

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Stomach

Situated just below the esophagus, the stomach forms a muscular, expandable chamber that links the esophagus to the

duodenum. Although anchored at both ends, it is highly dynamic in between, shifting shape and rhythmically contracting to aid mechanical digestion. When empty, it is roughly the size of a fist, yet it can expand to hold up to 4 liters of food and fluid — more than **75 times its resting volume** — and then return to its original size. Stomach size does not predict how much a person typically eats; instead, it simply stretches more when larger meals, such as holiday dinners, are consumed.

The stomach does not operate as an open tube; instead, it is bounded by **two muscular gates** that regulate what enters and leaves this organ. A **sphincter** is a muscular ring that can tighten like a drawstring to control the passage of materials from one region of the digestive tract to another. The stomach has two of these muscular gates. At the **top** — as you learned further up — is the **lower esophageal sphincter** helping to prevent acidic stomach contents from flowing backward into the esophagus. At the **bottom**, the **pyloric sphincter** regulates the release of small amounts of chyme from the stomach into the duodenum.

Chemical digestion begins in the mouth with amylase breaking down starch, but it accelerates in the stomach. However, despite common belief, the stomach is not where most digestion occurs; that job belongs to the small intestine. Instead, the stomach functions primarily as a **temporary storage and mixing chamber.** Because you can eat much faster than your small intestine can process nutrients, the stomach holds food, mixes it with digestive secretions, and releases small amounts of **chyme** into the **duodenum** at a controlled pace.

Anatomy of the Stomach

There are **four main regions** in the **stomach**: the cardia, fundus, body, and pylorus. It is unique with **three layers of the muscularis externa**: outer longitudinal layer, middle circular layer, and inner oblique layer. The **cardia** (or cardiac region) is the point where the esophagus connects to the stomach and through which food passes into the stomach. Located inferior to the diaphragm, above and to the left of the cardia, is the dome-shaped **fundus**. Below the fundus is the **body**, the main part of the stomach. The funnel-shaped **pylorus** connects the stomach to the duodenum. The wider end of the funnel, the **pyloric antrum**, connects to the body of the stomach. The narrower end is called the **pyloric canal**, which connects to the duodenum. The smooth muscle **pyloric sphincter** is located at this latter point of connection and controls stomach emptying. In the absence of food, the stomach deflates inward, and its mucosa and submucosa fall into large folds called **rugae**.

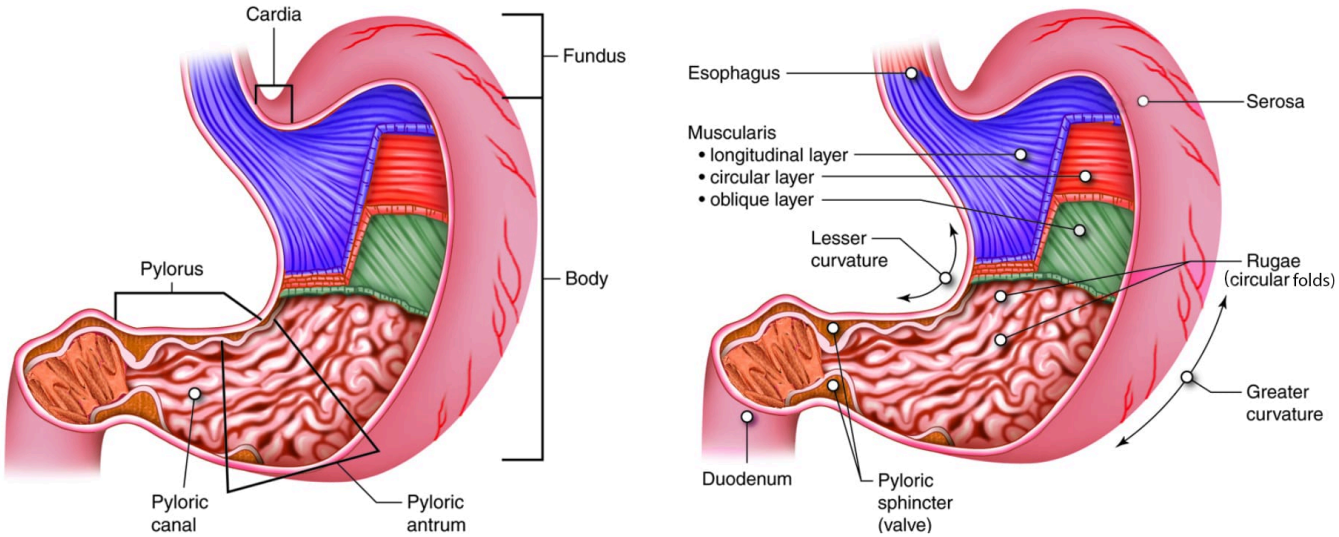
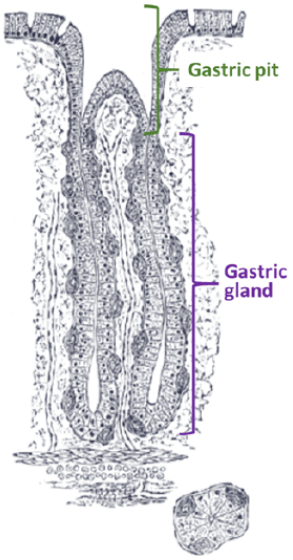


Figure 12.4.2: **Regions and Layers of the Stomach.** The four major anatomical regions of the stomach are the cardia, fundus, body, and pylorus. The stomach has three smooth muscle layers of the muscularis externa (unlike the remaining parts of the digestive tract): longitudinal, circular, and the stomach-specific oblique muscle layer. They work together to churn and mix the food bolus into chyme. The internal surface folds, called rugae, allow the stomach to expand after eating. (Image credit: "Layers of the Stomach" by "KnowledgeWorks - Drawing Abdominal organs - no labels" by KnowledgeWorks Global Ltd. and Open Learning Initiative, license: CC BY-NC-SA. Edited by Gabrielle Spurlock(opens in new window)

Histology

The wall of the stomach is built from the same four layers that line most of the alimentary canal, but **its mucosa and muscularis**

include special adaptations that support the stomach's unique roles in digestion.



Mucosa: Gastric Pits and Gastric Glands

The surface of the mucosa is not smooth. Countless indentations give it the appearance of a well-used pincushion. The **shallow openings** on the surface are the **gastric pits.** Each pit serves as the opening to deeper exocrine tubules called **gastric glands.**

What Do Gastric Pit Cells Produce?

The **cells on the surface of the stomach and the ones lining the gastric pits** are called **surface mucous cells**. Their main job is to secrete a **thick, alkaline (bicarbonate-rich) mucus**. This coating of alkaline mucus shields the stomach lining, preventing the acid and enzymes in gastric juice from damaging the stomach wall.

What Do Gastric Gland Cells Produce?

Beneath the gastric pits lie the gastric glands. These deeper tubules contain several types of secretory cells that collectively produce the components of **gastric juice**. Their secretions include hydrochloric acid, digestive enzymes, and mucus, all of which work together to support efficient digestion in the stomach.

Mucous neck cells
Located in the upper "neck" region of the glands, these cells secrete a thinner, slightly acidic mucus. This mucus helps lubricate the gland and mixes with the secretions moving upward through the pit.

Parietal cells
Found mainly in the middle of the gastric glands, the parietal cells produce **hydrochloric acid (HCl)**, which creates the highly acidic environment of the stomach (pH 1.5 to 3.5). This **acidity activates pepsin**, helps break down proteins, and kills many microbes in food. Parietal cells also release **intrinsic factor**, a glycoprotein **required for vitamin B12 absorption in the small intestine**.

Chief cells
Located deeper in the glands, chief cells secrete **pepsinogen**, the **inactive precursor of pepsin**, and a small amount of gastric lipase. Pepsinogen is converted to pepsin by HCl and begins the digestion of proteins, while gastric lipase contributes modestly to fat digestion.

Enteroendocrine cells (including G cells)
Scattered among the glandular cells, these cells release hormones into the surrounding tissue fluid rather than into the gland lumen. In the pyloric region, G cells produce gastrin, a hormone that stimulates the parietal and chief cells and increases stomach

motility.

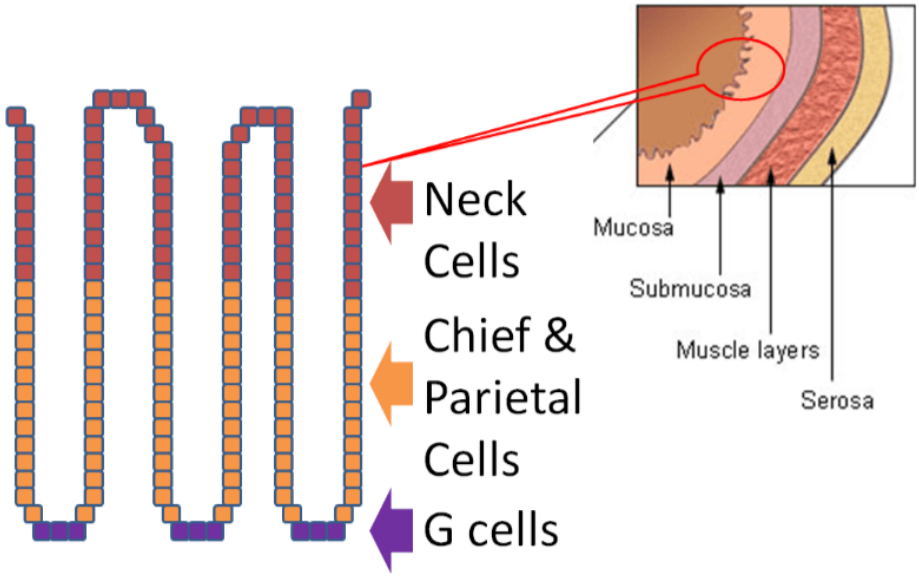


Figure 12.4.3: **Cell Types in a Gastric Gland.** This diagram highlights the major secretory cells found within the gastric glands of the stomach mucosa. Near the top of each gland, ***mucous neck cells*** release mucus that helps protect the lining from acid. Deeper in the gland, ***parietal cells*** secrete hydrochloric acid and intrinsic factor, while ***chief cells*** produce pepsinogen and gastric lipase for protein and fat digestion. At the base of the gland, ***G cells*** release the hormone gastrin, which stimulates the upper cells to increase their secretions and supports overall gastric activity.

Watch This Video

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Cells Involved in the Digestive Processes in the Stomach

Type of Cell	Secrete
Neck	Mucus
Chief	Pepsinogen and gastric lipase
Parietal	Hydrochloric acid
G	Gastrin

Muscularis Externa: A Third Layer in the Stomach

Most regions of the digestive tract contain two layers of smooth muscle in the muscularis externa, an inner circular layer and an outer longitudinal layer. The stomach is an exception. It includes a **third, inner oblique layer of smooth muscle.**

Why Does the Stomach Have an Oblique Layer?
The added oblique layer strengthens the stomach's contractions. Working together, the three layers create powerful mixing motions that blend food with gastric juice and mechanically break it into very small particles. This vigorous mixing helps transform the food into **chyme**, the **semi-fluid material** that moves into the duodenum.

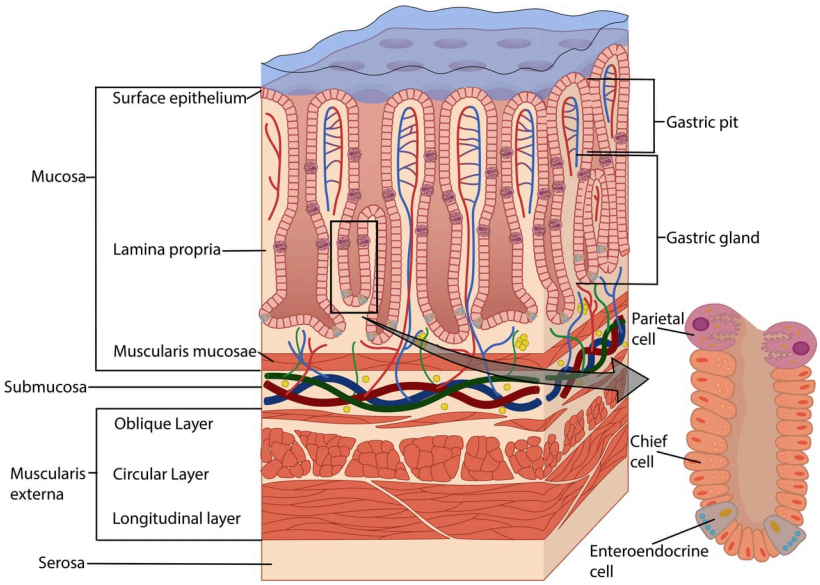


Figure 12.4.4: **Histology of the Stomach.** The stomach wall is adapted for the functions of the stomach. In the epithelium, gastric pits lead to gastric glands that secrete gastric juice. The gastric glands (one gland is shown enlarged on the right) contain different types of cells that secrete a variety of enzymes, including hydrochloric acid, which activates the protein-digesting enzyme, pepsin. (Image credit: "Histology of the Stomach" by Collectivedogs is licensed under Creative Commons Attribution-Share Alike 4.0 International license. Labeled by John Polos)

Watch this video

For a quick visual review, this short Khan Academy video offers a helpful overview of stomach physiology.

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Digestive Functions of the Stomach

The stomach participates in virtually all the digestive activities with the exception of ingestion and defecation. Although almost all digestions and absorption takes place in the small intestine, the stomach does absorb some nonpolar substances, such as **alcohol and aspirin**.

Mechanical Digestion in the Stomach

Within a few moments after food enters your stomach, rhythmic **mixing waves** begin about every 20 seconds. These waves represent a special type of peristalsis that blends and softens food with gastric juices, forming a **thick, creamy mixture called chyme.** Early waves are gentle, but they become stronger as they move from the body of the stomach toward the pylorus. By the time your sushi approaches the pyloric sphincter, it no longer resembles the sushi you originally ate.

The pylorus, which holds about 30 mL (1 fluid ounce) of chyme, acts like a selective gatekeeper. Only liquids and very small particles pass through the mostly closed **pyloric sphincter.** During gastric emptying, each wave pushes roughly **3 mL** of chyme into the duodenum. Sending more than this at once would overwhelm the small intestine. The chyme that does not pass through is pushed back into the stomach to continue mixing until the next wave repeats the cycle. Such mixing waves occur roughly every 20 seconds.

Gastric emptying is controlled by both the stomach and the duodenum. As chyme enters the duodenum, receptors there trigger signals that slow gastric secretion and delay further emptying. This coordination ensures the duodenum receives chyme only at a rate it can safely process.

Chemical Digestion in the Stomach

Hydrochloric Acid (HCl) from Parietal Cells
Parietal cells release hydrochloric acid, creating the stomach's extremely acidic environment. This acidity helps **denature dietary proteins, unfolding them so enzymes can reach their chemical bonds.** It **also converts the inactive enzyme precursor pepsinogen into its active form, pepsin,** which begins the chemical breakdown of proteins.

Pepsinogen and Gastric Lipase from Chief Cells
Chief cells secrete pepsinogen, an inactive enzyme (= zymogen) that becomes the active enzyme pepsin when exposed to HCl. **Pepsin** is the stomach's primary **protease** — protein digesting enzyme — and begins cleaving large **proteins into smaller peptides.** Chief cells also release gastric **lipase**, which initiates the digestion of triglycerides. Gastric lipase is a relatively weak fat-digesting enzyme compared to those of the small intestine, but it contributes to the early breakdown of dietary fats.

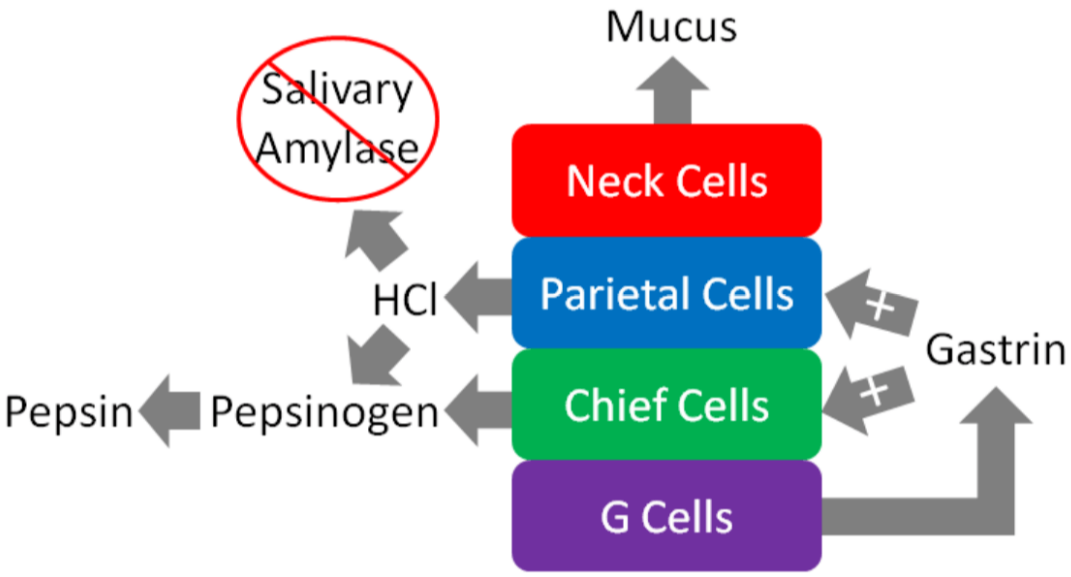


Figure 12.4.5: **Actions of Gastric Secretions in the Stomach.** Mucus helps protect the stomach lining. **Hydrochloric acid (HCl)** stops the action of salivary amylase and creates the acidic environment needed to activate pepsinogen into pepsin. The hormone gastrin, finally, stimulates both parietal and chief cells to increase their secretory activity.

Its numerous digestive functions notwithstanding, there is only one stomach function necessary to life: the production of intrinsic factor. The intestinal absorption of vitamin B_{12}, which is necessary for both the production of mature red blood cells and normal neurological functioning, cannot occur without intrinsic factor. People who undergo total gastrectomy (stomach removal) — for life-threatening stomach cancer, for example — can survive with minimal digestive dysfunction if they receive vitamin B_{12} injections.

The contents of the stomach are completely emptied into the duodenum within 2 to 4 hours after you eat a meal. Different types of food take different amounts of time to process. Foods heavy in carbohydrates empty fastest, followed by high-protein foods. Meals with a high triglyceride content remain in the stomach the longest. Since enzymes in the small intestine digest fats slowly, food can stay in the stomach for 6 hours or longer when the duodenum is processing fatty chyme. However, note that this is still a fraction of the 24 to 72 hours that full digestion typically takes from start to finish.

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12.5: Anatomy of the Small Intestine

The small intestine is a long, folded tube designed to finish digestion and efficiently absorb nutrients.

Master this section and you'll be able to:

- Describe the overall structure of the small intestine and explain how its regions and surface adaptations support digestion and absorption.
- Compare circular folds, villi, and microvilli and summarize how each increases the absorptive surface area of the small intestine.
- Differentiate between intraperitoneal and retroperitoneal organs and explain the role of the peritoneum and mesentery in supporting the intestines.

The word intestine is derived from a Latin root meaning “internal”, and indeed, the intestinal tract nearly fills the whole interior of the abdominal cavity. Also known as the small and large bowel — or colloquially the “guts” — they constitute the greatest mass and length of the alimentary canal and, with the exception of ingestion, perform all digestive system functions.

The **small intestine** is the **primary site of digestion and absorption** in the human body. After food leaves the stomach, it enters this long, highly folded tube where nutrients are broken down into their simplest forms and moved into the bloodstream. Although called “small,” it is actually the longest part of the digestive tract, and its internal surface is vastly expanded by circular folds, villi, and microvilli that maximize contact with chyme. As it moves through the **duodenum**, **jejunum**, and **ileum**, chyme encounters enzymes, bile, and bicarbonate that complete digestion and create ideal conditions for absorption. The small intestine’s structure and function work together to ensure that nearly all usable nutrients from a meal are efficiently extracted before the remaining material passes into the large intestine.

Anatomy of the Small Intestine

Chyme released from the stomach enters the **small intestine**, which is the primary digestive organ in the body. Not only is this where most digestion occurs, it is also where practically all absorption occurs. The longest part of the alimentary canal, the small intestine is about **3 meters (10 feet) long** in a living person (but about twice as long in a cadaver due to the loss of muscle tone). Since this makes it about **five times longer than the large intestine**, you might wonder why it is called “small.” In fact, its name derives from its relatively **smaller diameter of only about 2.5 cm (1 in), compared with 7.5 cm (3 in) for the large intestine.** As we will see shortly, in addition to its length, the folds and projections of the lining of the small intestine work to give it an enormous surface area, which is approximately **200 m^2, more than 100 times the surface area of your skin.** This large surface area is necessary for complex processes of digestion and absorption that occur within it.

The coiled tube of the small intestine is subdivided into three regions. From proximal (at the stomach) to distal, these are the duodenum, jejunum, and ileum (see the figure below).

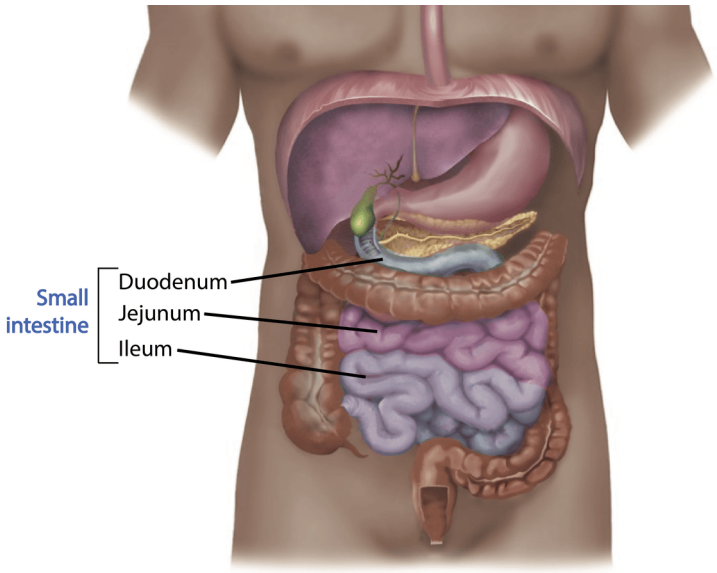
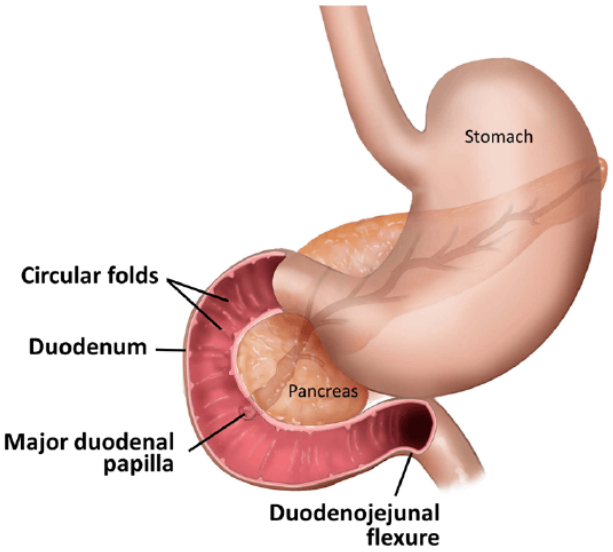


Figure 12.5.1: **Regions of the Small Intestine.** The three regions of the small intestine, from proximal to distal, are the duodenum, jejunum, and ileum. *(Image credit: "Regions of the Small Intestine" by Jennifer Lange is licensed under CC BY-NC-SA, modification of original "Drawing of Abdominal Organs" by KnowledgeWorks Global Ltd. and Open Learning Initiative.)*

Duodenum



The duodenum is the first and **shortest segment** of the small intestine, measuring about 25 centimeters (10 inches). It begins immediately at the pyloric sphincter. Just past this point, the duodenum curves backward behind the **peritoneum**, becoming **retroperitoneal**, and then forms a C-shaped loop around the head of the pancreas. After this curve, it travels upward and forward to reenter the peritoneal cavity and connect with the jejunum.

Within the wall of the duodenum is the hepatopancreatic ampulla, the site where the bile duct — carrying bile from the liver (via the gallbladder) — and the main pancreatic duct join. This shared duct system opens into the duodenum at the **major duodenal papilla**, allowing bile and pancreatic juice to enter and assist in digestion.

Jejunum

The jejunum is about 0.9 meters (3 feet) long (in life) and runs from the duodenum to the ileum. Jejunum means "empty" in Latin and supposedly was so named by the ancient Greeks who noticed it was always empty at death. No clear demarcation exists between the jejunum and the final segment of the small intestine, the ileum.

Ileum

Measuring about 1.8 meters (6 feet), the ileum is the longest portion of the small intestine. Compared with the jejunum, it is slightly thicker and more highly vascularized, and it contains more prominent mucosal folds. At its distal end, the ileum meets the cecum, the first part of the large intestine, at the **ileocecal valve (or sphincter)**, which helps regulate the flow of intestinal contents. Both the jejunum and ileum are suspended from the posterior abdominal wall by the **mesentery**, and together these regions are framed on all sides by the large intestine.

The small intestine receives **dual autonomic innervation**, with parasympathetic fibers supplied by the vagus nerve and sympathetic fibers arriving through the thoracic splanchnic nerves. Its primary blood supply comes from the superior mesenteric artery, while veins that run alongside these arteries drain into the superior mesenteric vein. From there, nutrient-rich blood travels directly **to the liver through the hepatic portal vein** for processing and storage.

Histology of the Small Intestine

The wall of the small intestine is composed of the same four layers typically present in the digestive tract wall. However, three features of the mucosa and submucosa are unique. These features, which increase the absorptive surface area of the small intestine more than 600 times, include **circular folds** (**plicae circulares**), **villi**, and **microvilli** (see figure below). These adaptations are most abundant in the proximal two-thirds of the small intestine, where the majority of absorption occurs.

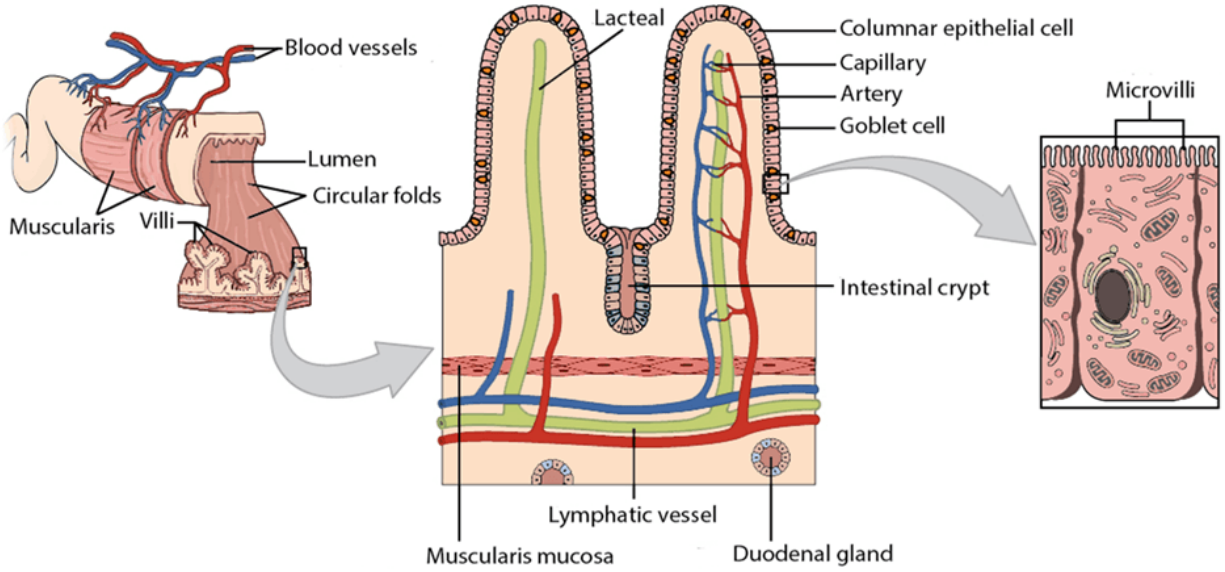


Figure 12.5.2**: Structural Features That Increase Absorptive Surface Area in the Small Intestine.** The small intestine maximizes nutrient absorption through multiple levels of folding. Circular folds create large ridges in the mucosa and submucosa, each covered with numerous fingerlike villi that contain blood vessels and a central lacteal for transporting absorbed nutrients. At an even smaller scale, the apical surfaces of the epithelial cells form countless microvilli, together called the brush border, which further increase surface area and hold digestive enzymes.*l lustration" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax; slides b-d provided by the Regents of the University of Michigan Medical School © 2022.)*

Circular Folds

Also called a **plica** circulare, a circular fold is a tall ridge of the mucosa and submucosa (see image above). These transverse folds can be up to 1 cm high and are easily visible to the naked eye. They begin near the proximal duodenum and extend to about the midpoint of the ileum, increasing the surface area available for absorption. Their curved shape also causes chyme to spiral rather than move straight through the lumen, slowing its flow and allowing more time for nutrients to be absorbed.

Villi

Within the circular folds are small (0.5–1 mm long) hairlike, vascularized projections of the epithelium and lamina propria called **villi** (singular: villus). Each square millimeter of mucosa contains roughly 20 to 40 villi, greatly expanding the surface area for absorption. The villi are covered by **simple columnar epithelium**, made mostly of absorptive cells.

Each villus contains connective tissue, a small amount of smooth muscle, **a capillary bed (one arteriole and one venule)**, and a lymphatic capillary called a **lacteal**. Sugars and amino acids, produced from the digestion of carbohydrates and proteins, enter the bloodstream through these capillaries. In contrast, lipid breakdown products are absorbed into the lacteals and reach the bloodstream later via the lymphatic system (see image above).

Microvilli

As their name implies, microvilli (singular: microvillus) are much smaller than villi, measuring only about 1 micrometer in length. These tiny cylindrical projections extend from the apical (luminal) surface of the epithelial cells lining the mucosa. Each microvillus is supported internally by microfilaments, which help maintain its shape.

Although individual microvilli are too small to be seen clearly with a light microscope, the many thousands on each absorptive cell create a fuzzy, bristle-like appearance known as the ***brush border***. Embedded in the membranes of the microvilli are enzymes that complete the digestion of carbohydrates and proteins, as well as transporter proteins that assist with nutrient uptake.

The small intestine contains an estimated 200 million microvilli per square millimeter. This enormous number dramatically increases the surface area of the epithelial membrane, greatly improving the efficiency of absorption.

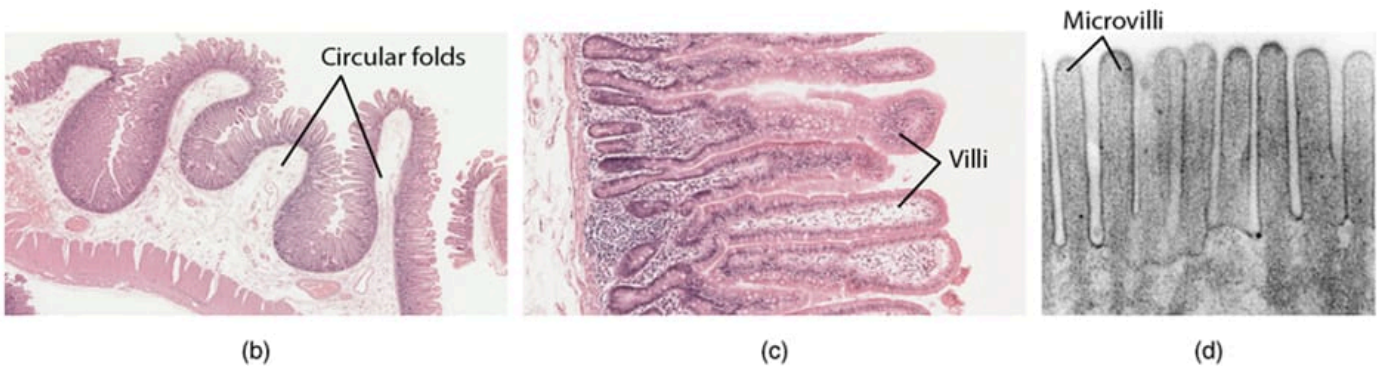


Figure 12.5.3**: Structural Adaptations That Increase Absorptive Surface Area in the Small Intestine.** Shown are the three levels of surface area amplification in the small intestine. **(b)** Circular folds are large ridges of mucosa and submucosa that slow the movement of chyme and increase contact time with the intestinal wall. **(c)** Villi are fingerlike projections of the mucosa that further expand the absorptive surface and contain blood vessels and a lacteal for nutrient uptake. **(d)** Microvilli form tiny membrane extensions on each epithelial cell, creating the brush border where many final digestive enzymes are located.

Intestinal Glands

In addition to the three specialized absorptive features just discussed, the mucosa between the villi is dotted with deep crevices that each lead into a tubular **intestinal gland** (crypt of Lieberkühn), which is formed by cells that line the crevices. These produce **intestinal juice**, a slightly alkaline (pH 7.4 to 7.8) mixture of water and mucus. Each day, about 1 to 1.9 liters (1 to 2 quarts) are secreted in response to the distention of the small intestine or the irritating effects of chyme on the intestinal mucosa. In addition to the exocrine glands making intestinal juice, there are enteroendocrine cells to secrete many regulatory hormones that communicate with other digestive organs including the pancreas and gallbladder.

The submucosa of the duodenum is the only site of the complex mucus-secreting **duodenal glands** (Brunner's glands), which produce a bicarbonate-rich alkaline mucus that buffers the acidic chyme as it enters from the stomach.

Lymphatic Nodules

The layer of loose connective tissue that lies just under the epithelium of the mucosa in the small intestine contains clusters of immune cells called mucosa-associated lymphoid tissue (MALT). In the **ileum**, these clusters form larger groups known as **Peyer's patches,** which help prevent bacteria in the intestine from getting into the bloodstream. Peyer's patches are easiest to see in younger people and become less noticeable with age, similar to the overall activity of the immune system.

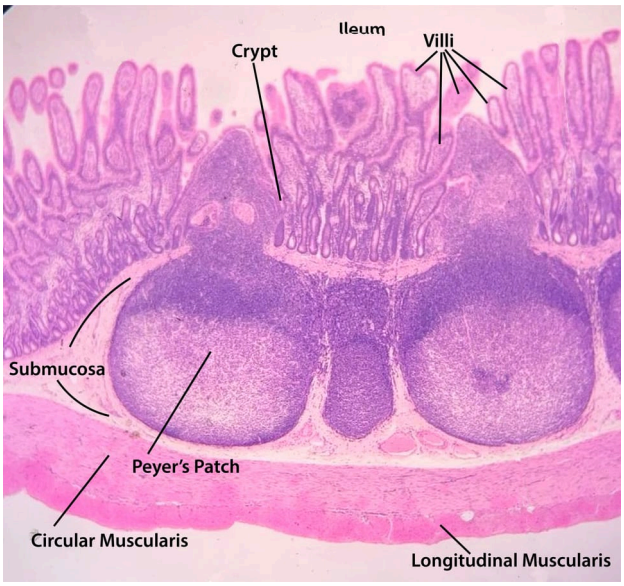


Figure 12.5.4**: Histology of the Ileum with Peyer's Patches.** This section of the ileum shows several key features of the small intestine. Fingerlike villi project into the lumen to increase the surface area for absorption, while the intestinal crypts sit between them as sites of cell renewal. Beneath the mucosa lies the submucosa, where large clusters of lymphoid tissue called Peyer's patches help monitor and protect against bacteria entering from the gut. Below this region, the circular and longitudinal layers of the muscularis work together to mix and move intestinal contents.

Visualizing the Intestine: Colonoscopy

Learn more about colonoscopy by watching the video below. A colonoscope is the special tool used to perform a colonoscopy. It is a thin, flexible, tubular 'telescope' with a light and video camera that your doctor carefully guides through your colon in order to see and determine the health of your colon. Watch this animation to learn about the features of the colonoscope, how the colonoscopy procedure is performed and how polyps are removed, and the follow-up care you and your doctor should talk about after your procedure.

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12.6: Activities of the Small Intestine

The small intestine is where most digestion and absorption occur, as pancreatic enzymes and bile break food into its simplest components so that they can enter the body.

Master this section and you'll be able to:

- Describe how pancreatic enzymes, brush border enzymes, and bile complete the digestion of carbohydrates, proteins, and lipids in the small intestine.
- Explain how monosaccharides, amino acids, and lipid components are absorbed across the intestinal lining.
- Trace how digested nutrients enter the bloodstream or lymphatic system and are processed or transported in the body.

Digestion and Absorption of the Major Food Groups in the Small Intestine

The small intestine is the primary site of chemical digestion. Most of the digestive enzymes that function in the small intestine come from the **pancreas** and enter the duodenum through the **pancreatic duct.** When nutrients enter the small intestine, they trigger the release of the hormone cholecystokinin, which stimulates the pancreas to release **enzyme-rich pancreatic juice**.

At the same time, the hormone secretin prompts the pancreas to add bicarbonate ions, which neutralize the acidic chyme arriving from the stomach.

As you have learned, the inner surface of the small intestine is lined with tiny fingerlike projections called **villi**, and each villus is covered with even smaller folds called **microvilli**. These microvilli form the **brush border** — a fuzzy-looking edge under the microscope. **Brush border enzymes** are digestive enzymes that are embedded in the membranes of these microvilli. Because they sit right on the surface of the intestinal lining, they finish the **final steps** of digestion just before nutrients are absorbed.

In short, **pancreatic enzymes do most of the early work**, and **brush border enzymes finish the job**, breaking nutrients into their simplest absorbable forms — single sugars and amino acids — right at the site of absorption.

Three major classes of nutrients undergo digestion in the small intestine:

Carbohydrate Digestion

Carbohydrate digestion begins with understanding the types of carbohydrates in the diet. About half of the average American diet consists of carbohydrates, which can be **grouped by their number of sugar units**.

Carbohydrates have to be digested into **simple sugars** (**monosaccharides**) in order to be absorbed. Pancreatic amylase breaks down **starch** into shorter chains called **oligosaccharides** (oligo = few). Brush border enzymes then convert these oligosaccharides into **glucose, galactose, and fructose**, which are monosaccharides and are absorbed across the intestinal wall. Carbohydrates that remain undigested move into the large intestine, where they may be fermented (broken down) by gut bacteria.

- **Monosaccharides** such as glucose, galactose, and fructose are the simplest sugars and are readily absorbed.
- **Disaccharides** include sucrose (table sugar: glucose + fructose), lactose (milk sugar: glucose + galactose), and maltose (grain sugar: glucose + glucose).
- **Polysaccharides** such as starch and glycogen are long chains of glucose units. The body lacks enzymes to digest most fibrous plant polysaccharides, such as cellulose, but these indigestible carbohydrates provide dietary fiber that helps move material through the alimentary canal.

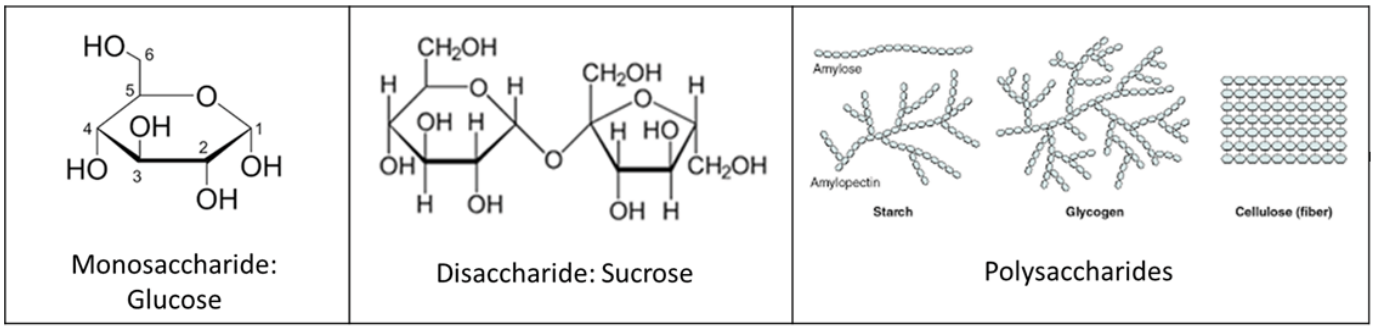


Figure 12.6.1: **Types of Carbohydrates.** Comparison of three levels of carbohydrate structure. On the left is a ***monosaccharide*** (**glucose**), the simplest carbohydrate unit. In the center is a ***disaccharide*** (**sucrose** = table sugar), made by joining two monosaccharides. On the right are examples of *polysaccharides* — large, complex chains such as starch, glycogen, and cellulose. **Amylose** is a long, mostly unbranched chain of glucose found in **plant starch**, while **glycogen** is a highly branched storage form of glucose in **animals** that can be broken down very quickly. These structures illustrate how small sugar units can link together to create larger molecules with different functions in the body and in plants.

The chemical digestion of starch (**amylose**) begins in the **mouth**, where **salivary amylase** starts breaking large starch molecules into smaller fragments as you chew. In the small intestine, **pancreatic amylase** continues this work and produces **short chains of glucose** that are still too large to absorb. **Brush border enzymes** on the intestinal lining then complete digestion by clipping off individual glucose units from the ends of these chains. The resulting monosaccharides can be absorbed into the bloodstream.

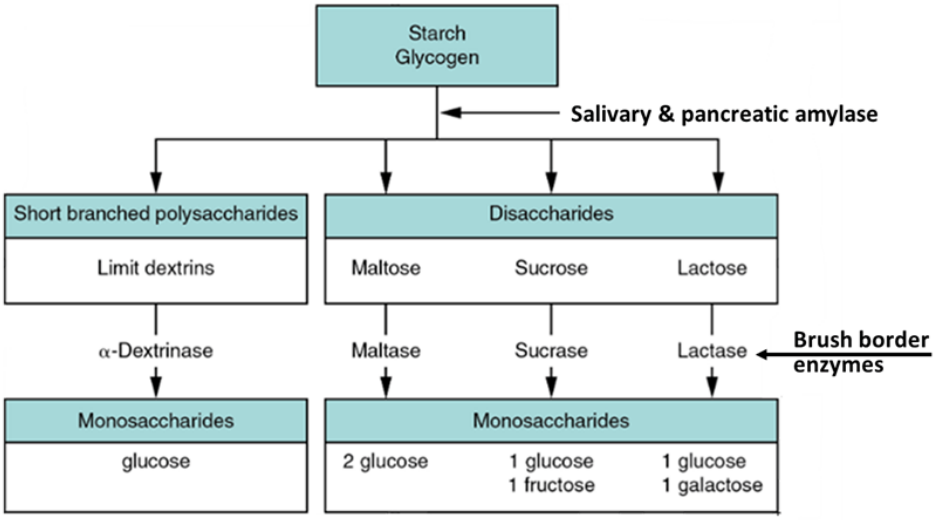


Figure 12.6.2: **Overview of Carbohydrate Digestion.** Complex carbohydrates (starch and glycogen) are first partially digested by **amylase**, forming shorter carbohydrate chains and also disaccharides. In the small intestine, **brush border enzymes** (α-dextrinase, maltase, sucrase, and lactase) located on the intestinal microvilli complete digestion by splitting these molecules into their **monosaccharide end products**: **glucose**, **fructose**, and **galactose**, which can then be absorbed into the bloodstream.

Carbohydrate Absorption

Carbohydrates can be absorbed only after they have been completely broken down into monosaccharides. The small intestine is remarkably efficient at this task, absorbing up to about 120 grams of monosaccharides per hour. All digestible carbohydrates are taken up, while indigestible fibers move on to the large intestine and eventually exit the body.

Once monosaccharides reach the intestinal lining, transport proteins in the cell membranes quickly move them into the bloodstream. From there, the blood carries glucose, fructose, and galactose directly to the liver. The liver converts galactose into glucose, breaks fructose into smaller carbon units, and either stores glucose as glycogen or returns it to the blood. How much glucose the liver releases is regulated by hormones, and even glucose itself plays a role in maintaining stable blood levels.

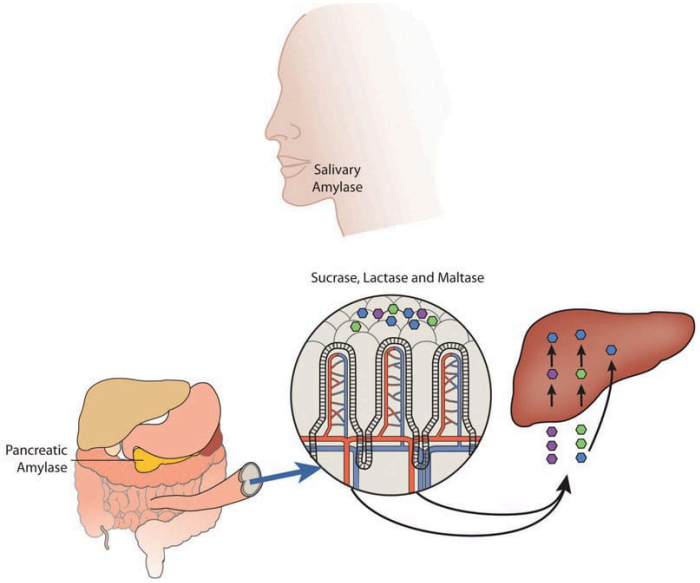


Figure 12.6.3**: Digestion and Absorption of Carbohydrates.** Digestion begins in the mouth, where **salivary amylase** starts splitting starch into smaller pieces. In the small intestine, **pancreatic amylase** continues this process. Final digestion occurs at the brush border of the intestinal villi, where enzymes such as **sucrase, lactase, and maltase** convert disaccharides into absorbable monosaccharides. These monosaccharides then enter the bloodstream and travel first to the **liver**, where they are processed and distributed to the rest of the body.

Almost all carbohydrates are digested and absorbed, except for dietary fiber and resistant starches, which our enzymes cannot break down. Some of these indigestible carbohydrates are fermented by **bacteria** in the large intestine, producing **short-chain fatty acids and gases**. The short-chain fatty acids can be used by the bacteria for growth, absorbed by the colon to support its functions, or transported in small amounts to the liver where they are metabolized for energy. Humans gain only about 2 kilocalories per gram from fiber, with soluble fibers and resistant starches providing more energy than insoluble fibers. Because fiber digests slowly and does not raise blood glucose rapidly, foods rich in fiber, such as whole grains, are associated with less weight gain and a lower risk of Type 2 diabetes and cardiovascular disease.

Protein Digestion

Proteins are long chains of amino acids linked by peptide bonds, and digestion must reduce them to individual amino acids before absorption. About 15 to 20 percent of the calories you eat typically come from protein.

Protein digestion **begins in the stomach,** where **hydrochloric acid unfolds** the protein and **pepsin** breaks it into smaller polypeptides. The chyme then leaves the stomach and enters the small intestine, where the majority of protein digestion occurs.

Pancreatic enzymes — **trypsin** and **chymotrypsin** — continue the process by cutting specific peptide bonds. Trypsin also activates other protein-digesting enzymes called **proteases**, and together, **these enzymes break proteins down to tripeptides, dipeptides, and individual amino acids.** Finally, brush border enzymes including aminopeptidase and dipeptidase clip off the remaining amino acids from the ends of the small peptides, producing molecules that are small enough to be absorbed into the bloodstream.

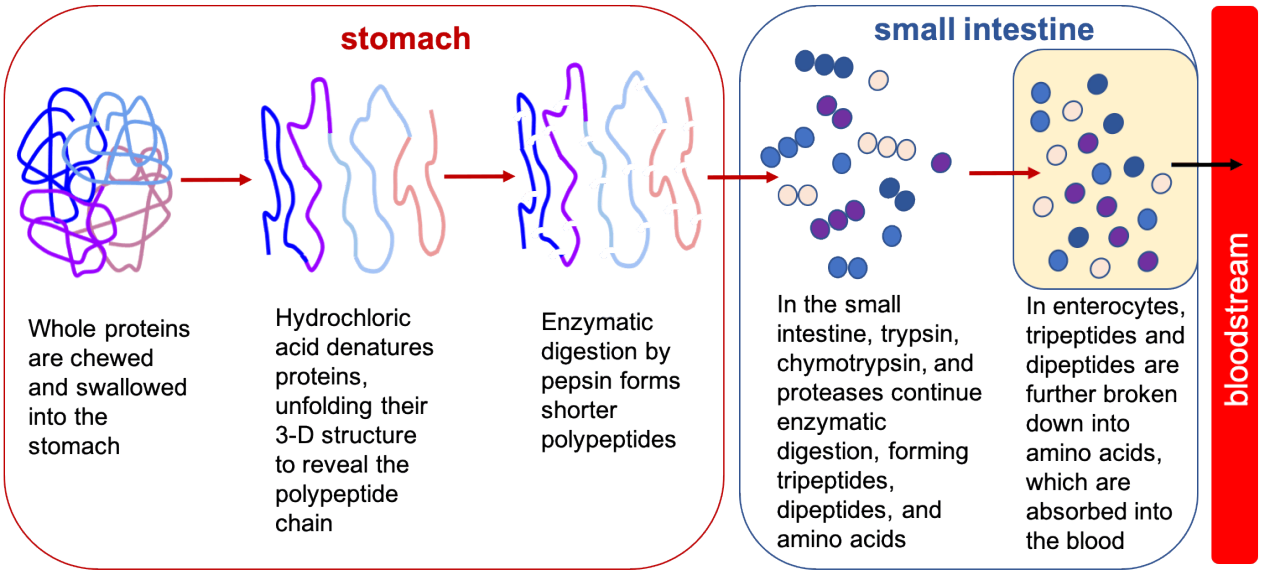


Figure 12.6.3: **Overview of Protein Digestion.** Protein digestion starts in the stomach and continues in the small intestine. Large dietary proteins are gradually broken into **amino acids** that can enter the bloodstream. In the stomach, **hydrochloric acid unfolds (denatures) protein structure**, and pepsin cuts the long polypeptide chains into shorter fragments. In the small intestine, pancreatic enzymes such as **trypsin** and **chymotrypsin** continue digestion, producing tripeptides, dipeptides, and free amino acids. Inside the absorptive cells of the small intestine, any remaining small peptides are split into individual amino acids, which then enter the blood for transport throughout the body.

Proteins that are not fully digested in the small intestine pass into the large intestine and are eventually excreted in the feces. Plant-based proteins are a bit less digestible than animal proteins, because some proteins are bound in plant cell walls.

Protein Absorption

Active transport mechanisms, primarily in the duodenum and jejunum, absorb most proteins as their breakdown products, **amino acids**. Almost all (95 to 98 percent) protein is digested and absorbed in the small intestine. Amino acids are absorbed in the lower small intestine through a series of carrier-mediated steps rather than by simple diffusion. At the apical surface of the intestinal villus, most free amino acids enter the enterocytes by Na⊕-dependent co-transporters that rely on the sodium gradient created by the Na⊕/K⊕ pump, which uses ATP.

To leave the enterocyte from the basolateral side and enter the bloodstream, amino acids move through specific membrane carriers that typically use facilitated diffusion or other Na⊕-independent mechanisms. Overall, amino acid absorption from the intestinal lumen to the blood is an active, carrier-mediated process at the point of entry and a facilitated, carrier-mediated process at the point of exit.

Fat Digestion

A healthy diet limits lipid intake to 35 percent of total calorie intake. The most common dietary lipids are **triglycerides**, which are made up of a **glycerol molecule bound to three fatty acid chains.** Small amounts of dietary cholesterol and phospholipids are also consumed.

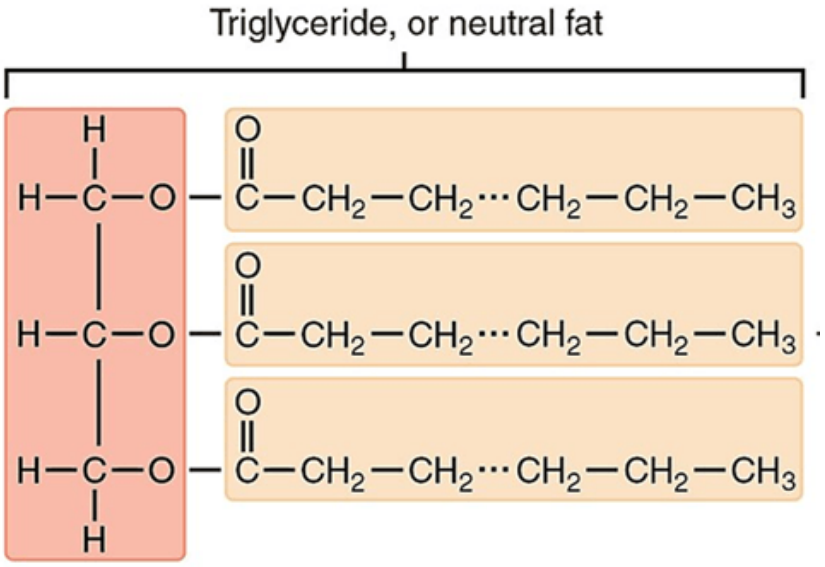


Figure 12.6.4: **Structure of a Triglyceride (Neutral Fat).** Triglycerides are the most common type of fat found in foods as well as the most common form of stored fat in the human body. Whether the fat comes from plants (like oils, nuts, and seeds) or animals (like meat, dairy, and eggs), most of it is made of triglycerides. Triglycerides are important for long-term energy storage, insulation, and cushioning of organs.

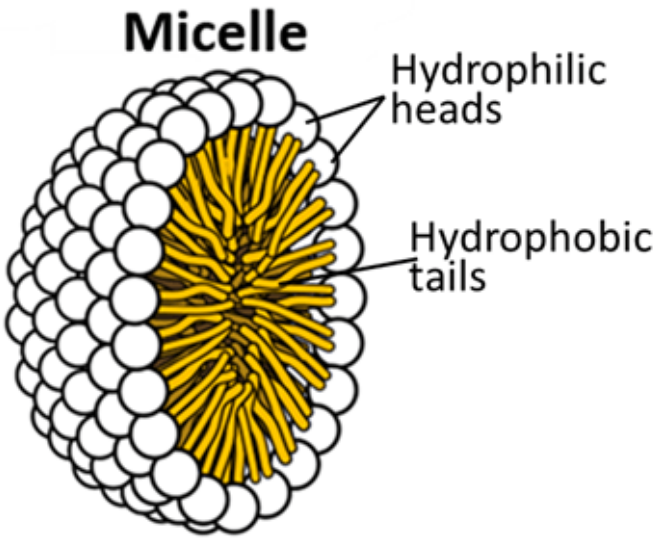
As stomach contents enter the small intestine, the digestive system must solve a small challenge: fats and water do not mix. To deal with this, the liver produces bile, which contains **bile salts**, lecithin, and cholesterol-derived molecules. These components act as **emulsifiers**, allowing fat droplets to disperse into tiny particles that can mix with the watery intestinal fluid. Emulsification increases the surface area of lipids dramatically, making them far more accessible to digestive enzymes.

The three lipases responsible for lipid digestion are lingual lipase, gastric lipase, and **pancreatic lipase.** However, because the pancreas is the only consequential source of lipase, virtually all lipid digestion occurs in the small intestine. Once emulsified, pancreatic lipase breaks down each triglycerides into two **free fatty acids and a monoglycerides**. However, these products must still cross the watery mucus layer covering the intestinal lining. Bile solves this problem again. Bile salts surround the fatty acids and monoglycerides to form **micelles**, which have a water-soluble exterior and a fatty core. Micelles ferry the lipids through the watery layer to the microvilli of the intestinal epithelium, where the lipids are released and absorbed.

Fat Absorption

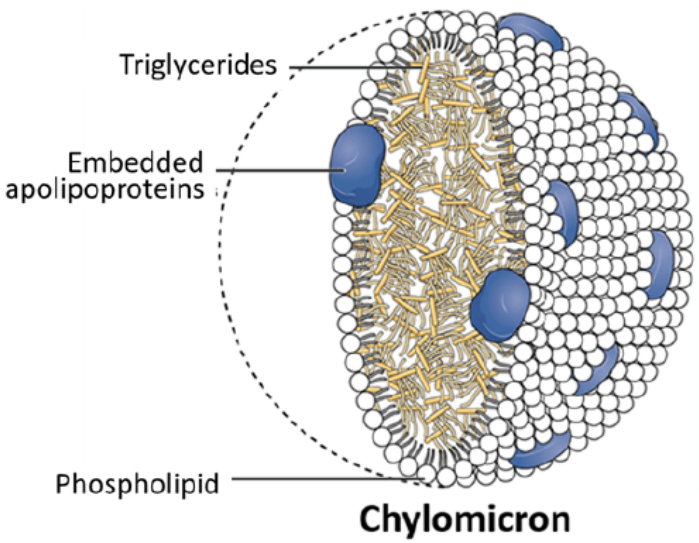
About 95 percent of dietary lipids are absorbed in the small intestine. **Bile salts** are again essential for this process because they not only aid lipid digestion but also make it possible for the end products to reach the absorptive epithelial cells (enterocytes).

Short-chain fatty acids are small and relatively water-soluble. They diffuse directly across the apical membrane of enterocytes and then move into the blood capillaries of a villus, following the same route as monosaccharides and amino acids.



Long-chain fatty acids and monoglycerides are large and hydrophobic, so they do not mix well with intestinal chyme. Bile salts help to solve this problem again by forming **micelles**, tiny spheres whose hydrophilic surfaces face the watery environment and whose hydrophobic interiors hold long-chain fatty acids, monoglycerides, cholesterol, and fat-soluble vitamins.

Micelles can slip between the microvilli and bring lipids close to the enterocyte surface. There, the lipid components leave the micelle and diffuse into the cell.



Inside the absorptive enterocyte, long-chain fatty acids and monoglycerides are **reassembled into triglycerides.** These triglycerides combine with phospholipids and cholesterol and are coated with protein, forming **chylomicrons** (see image on the right). The chylomicrons are water-soluble lipoproteins. After being processed by the Golgi apparatus, chylomicrons are released from the basal surface of the cell.

Because chylomicrons are too large to enter blood capillaries, they instead move into the large pores of **lacteals**, the lymphatic capillaries of the small intestine. The lacteals merge into larger lymphatic vessels, and the chylomicrons eventually enter the bloodstream through the thoracic duct and subclavian vein.

Cholesterol is absorbed less efficiently than phospholipids and triacylglycerols. Its absorption improves when dietary fat is present but decreases when the diet is high in fiber. This is why high-fiber foods such as fruits, vegetables, and oats can help lower blood cholesterol. Fiber binds bile salts and cholesterol in the intestine, preventing their reabsorption and carrying them out of the body through the feces.

Once in the blood, the enzyme **lipoprotein lipase** breaks down the triglycerides carried by chylomicrons into free fatty acids and

glycerol. These products move into tissues to be used for energy or stored in adipose cells. The liver then processes the remaining chylomicron remnants and packages them into **other lipoproteins that distribute cholesterol throughout the body.**

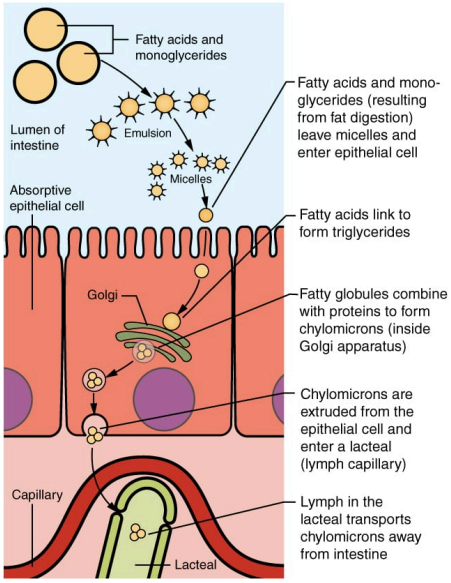


Figure 12.6.5: **Lipid Absorption.** Unlike amino acids and simple sugars, lipids are transformed as they are absorbed through epithelial cells.

Table: Absorbable End Products of Digestion.

Source	Substance
Carbohydrates	**Monosaccharides: glucose, galactose, and fructose**
Proteins	**Single amino acids, dipeptides, and tripeptides**
Triglycerides	**Monoglycerides, glycerol, and free fatty acids**

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12.7: Anatomy of the Large Intestine

The large intestine is the final region of the digestive tract, where the body reclaims water, houses beneficial bacteria, and transforms the remaining material from the small intestine into feces for elimination.

Master this section and you'll be able to:

- Identify the anatomical regions of the large intestine and explain the role of the ileocecal valve in regulating movement of chyme.
- Compare the histological features of the large intestine to those of the small intestine.
- Trace the pathway of food from its point of entry into the body through its exit from as feces.
- Summarize key risk factors, early signs, and prevention strategies for colorectal cancer.

The l**arge intestine** is the final stretch of the digestive tract. While some absorption is finished off, the large intestine is mainly responsible for **reclaiming water, compacting indigestible material, and preparing waste for elimination.** After leaving the **ileum**, the remaining chyme enters a wider, slower-moving tube where helpful bacteria break down some of what is left, producing vitamins and gases. As water and electrolytes are absorbed, the material gradually transforms into feces, which is stored until defecation. Although its job seems simple, the large intestine plays an essential role in maintaining fluid balance, supporting a healthy **gut microbiome**, and completing the digestive process.

Anatomy of the Large Intestine

The large intestine **runs from the appendix to the anus** *(see figure below).* It frames the small intestine on three sides. Despite its being about one-half as long as the small intestine, it is called **large** because it has a **diameter** that is more than twice the diameter of the small intestine, about 3 inches.

The large intestine is subdivided into four main regions: the **cecum**, the **colon**, the **rectum**, and the **anus**. The **ileocecal valve** (or sphincter), located at the opening between the ileum and the large intestine, controls the flow of chyme from the small intestine to the large intestine.

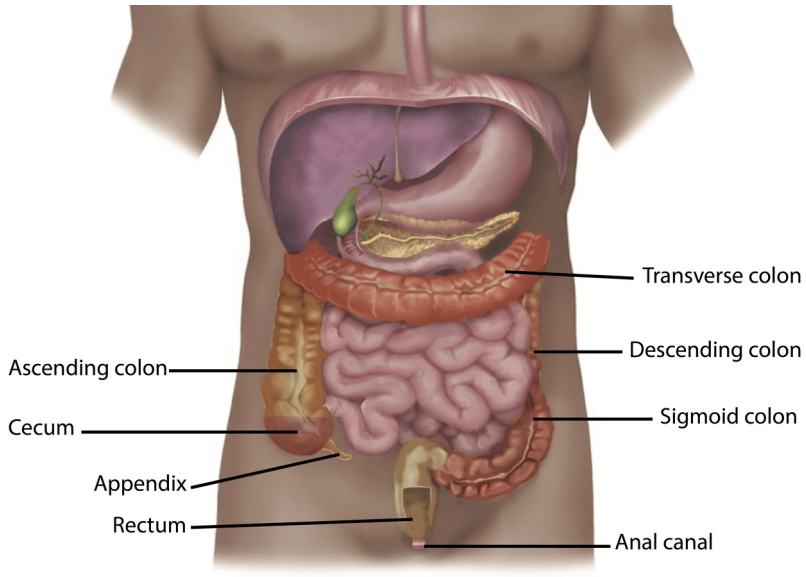


Figure 12.7.1: **Regions of the Large Intestine.** The large intestine frames the coils of the small intestine and includes the cecum (with its attached appendix), the ascending, transverse, descending, and sigmoid colon, and finally the rectum and anal canal. *(Image credit: "Regions of the Large Intestine" by Jennifer Lange is licensed under CC BY-NC-SA, modification of original "Drawing of Abdominal Organs" by KnowledgeWorks Global Ltd. and Open Learning Initiative.)*

Cecum

The first part of the large intestine is the **cecum**, a sac-like structure that is suspended **distal to the ileocecal valve.** It is about **6 cm (2.4 in) long**, receives the contents of the ileum, and continues the absorption of water and salts. The **appendix** (or vermiform appendix) is a winding, dead-end tube that attaches to the cecum. Although the 7.6-cm (3-in) long appendix contains lymphoid tissue, suggesting an immunologic function, this organ is generally considered **vestigial** (a structure present in our ancestors that has over time lost its original function). However, at least one recent report postulates a survival advantage conferred by the appendix: in diarrheal illness, the appendix may serve as a bacterial reservoir to repopulate the enteric bacteria for those surviving the initial phases of the illness. Moreover, its twisted anatomy provides a haven for the accumulation and multiplication of enteric bacteria.

Rectum

Food residue leaving the sigmoid colon enters the **rectum** in the pelvis near the third sacral vertebra. Although the word *rectum* comes from a Latin term meaning “straight,” it is not straight. Instead, it follows the curved contour of the sacrum and contains three lateral bends that form internal transverse folds called rectal valves. These valves help separate feces from gas so that each can pass at appropriate times.

Anal Canal

The final segment of the large intestine is the **anal canal**, **located in the perineum, completely outside the abdominopelvic cavity.** This short canal, measuring about 4–5 cm (1.5–2 in), opens to the exterior at the **anus**. The anal canal contains **two sphincters.** The **internal** anal sphincter is composed of **smooth muscle** and contracts involuntarily. The **external** anal sphincter is composed of **skeletal muscle** and is under voluntary control. Except during defecation, both sphincters normally remain closed.

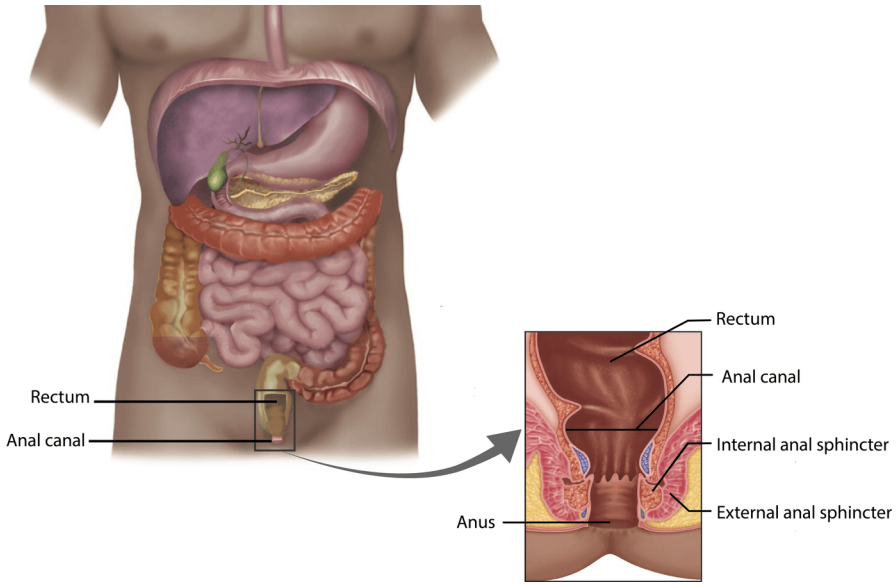


Figure 12.7.2**: Rectum, Anal Canal, and Anal Sphincters.** The rectum forms the final segment of the large intestine and stores feces before elimination. The anal canal extends from the rectum to the exterior of the body at the anus. Two sphincters control the passage of feces: the internal anal sphincter, made of smooth muscle and under involuntary control, and the external anal sphincter, made of skeletal muscle and under voluntary control. *(Image credit: "Anal Canal" by Jennifer Lange is licensed under CC BY-NC-SA, modification of original “Drawing of Abdominal Organs” by KnowledgeWorks Global Ltd. and Open Learning Initiative.)*

DISORDER OF THE...

Digestive System: Colorectal Cancer (CRC)

Colorectal cancer is still one of the most common cancers worldwide, but the pattern of who gets it is changing. The American Cancer Society estimates that

Right now in the United States, the American Cancer Society estimates that:

- in **2025 about 154,270 people** will be diagnosed with colorectal cancer (around 107,320 colon + 46,950 rectal cancers). Cancer.org
- colorectal cancer will cause about **52,900 deaths in 2025,** , making it one of the most deadly malignancies. Cancer.org

In people over 50, rates and deaths have been dropping thanks to better screening and treatment. At the same time, cases in younger adults are rising: about 1 in 5 new CRC cases now occur in people under 55, and it has become a leading cause of cancer death in men under 50 and a top cause in women under 50.

Because of these trends, major guidelines now recommend that average-risk adults start routine colorectal cancer screening at age 45 instead of 50. Screening can be done with **stool tests** (like FIT or stool DNA tests) or procedures that look directly at the colon (like colonoscopy), and any abnormal stool test needs a follow-up **colonoscopy**. People with higher risk, such as a strong family history or certain genetic syndromes, often need to start even earlier and be screened more often.

Researchers are also sharpening the picture of risk factors. Long-known **risks** include diets high in processed and red meats, low fiber intake, obesity, inactivity, smoking, alcohol, and chronic inflammation in the gut. Newer studies highlight ultra-processed foods as a concern and suggest that dietary patterns may harm the gut microbiome and increase polyp and cancer risk, especially in the colon. On the treatment side, there has been major progress in personalized medicine and immunotherapy, especially for tumors with specific genetic features, which is improving outcomes for many patients.

Colorectal cancer may be signaled by constipation or diarrhea, cramping, abdominal pain, and rectal bleeding. Bleeding from the rectum may be either obvious or occult (hidden in feces). Since most colon cancers arise from benign mucosal growths called **polyps**, cancer prevention is focused on identifying these polyps. The **colonoscopy is both diagnostic and therapeutic**. Colonoscopy not only allows identification of precancerous polyps, the procedure also enables them to be removed before they become malignant.

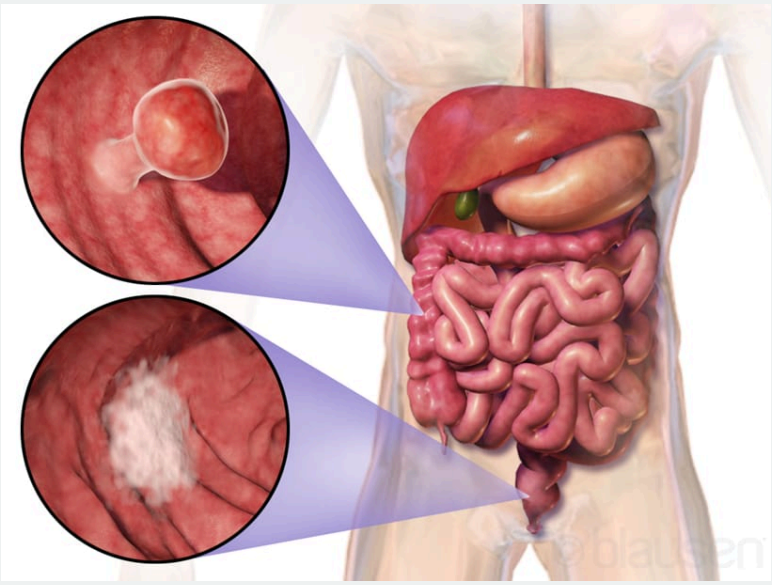


Figure 12.7.3**: Polyps and Early Tumor Changes in the Large Intestine.** Highlighted are two common findings seen during colonoscopy. The upper inset shows a small, raised polyp projecting from the lining of the large intestine. Polyps are growths of mucosal tissue that can be harmless at first but may develop into cancer over time if not removed. The lower inset shows an area where the tissue has become irregular and abnormal in appearance, representing early malignant change.

Incidence and mortality are not equal across groups. In the US, CRC incidence is highest in American Indian/Alaska Native populations, followed by non-Hispanic Black individuals, and lowest in Asian American/Pacific Islander groups. Mortality is about **43% higher in men than women** overall. Disparities reflect a mix of access to screening, differences in risk factors, and broader social determinants of health. Cancer.org

Histology

The walls of the large intestine differ in several important ways from those of the small intestine. Unlike the small intestine, the large intestine has very few enzyme-secreting cells, and it lacks circular folds and villi.

The mucosa of the colon (except in the anal canal) is lined by simple columnar epithelium made mostly of **absorptive enterocytes** with **microvilli** and **many goblet cells**. Compared to the small intestine, the colon contains a much greater number of **intestinal glands**. These glands are packed with enterocytes and goblet cells.

Goblet cells secrete **mucus** that lubricates the passage of feces and **protects the mucosa from acids and gases produced by resident bacteria**. The **enterocytes absorb water, salts, and vitamins** that are synthesized by your intestinal microbiota.

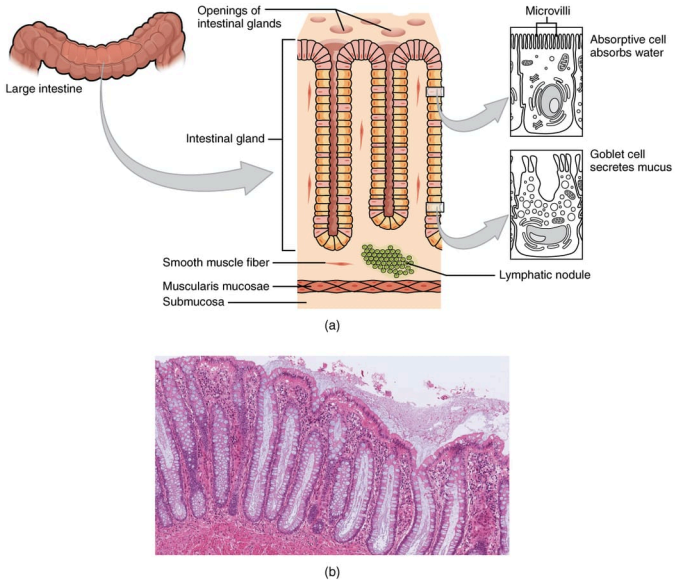


Figure 12.7.4: **Histology of the Large Intestine.** (a) The mucosa of the large intestine contains many straight, tube-shaped intestinal glands lined mainly by absorptive cells and numerous mucus-secreting goblet cells. Absorptive cells remove water and electrolytes, while goblet cells produce the thick mucus that helps feces move smoothly through the colon. Beneath the mucosa, the muscularis mucosae and submucosa provide support, and lymphatic nodules offer immune protection. In contrast to the small intestine, the large intestine does **not** have villi.
(b) A histological section of the large intestine shows the densely packed intestinal glands and abundant goblet cells characteristic of this region. LM x 464. Micrograph provided by the Regents of University of Michigan Medical School © 2012.
(Image credit: "Histology of Large Intestine" by OpenStax is licensed under CC BY 3.0)

Special Features of the Large Intestine

Teniae Coli and Haustra

The **teniae coli** (also spelled taenia) are **three narrow bands of smooth muscle** that form the longitudinal layer of the muscularis in the large intestine, except near its terminal end. These bands run along the length of the colon and are spaced roughly the same distance apart around the circumference of the tube. Tonic contractions of the teniae coli pull on the colon wall and pucker it into a series of pouch-like segments called **haustra** (singular = haustrum). These haustra give the colon its characteristic lumpy or segmented appearance.

The rectum and anal canal do not have teniae coli or haustra. Instead, they contain thick, continuous layers of smooth muscle within their muscularis, which produce the strong contractions required during defecation.

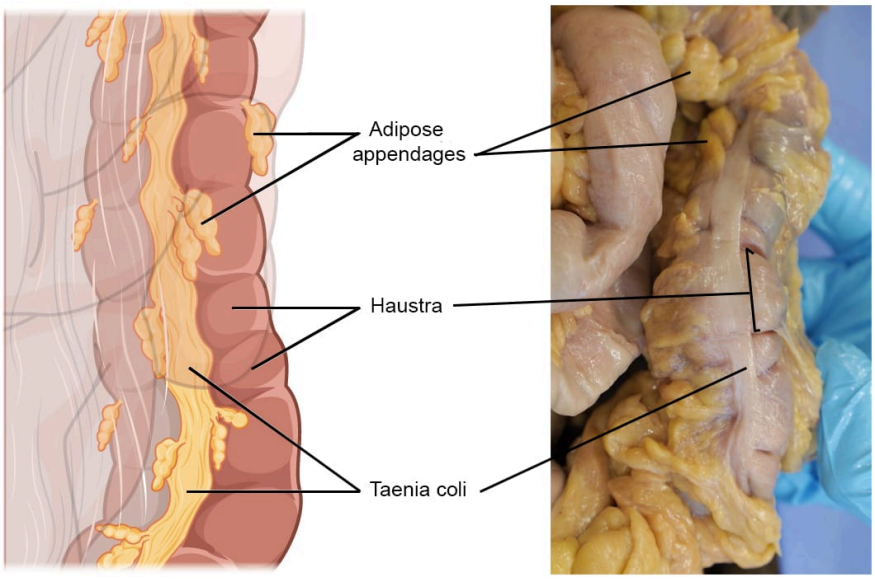


Figure 12.7.5: **External Features of the Large Intestine.** Compared are a schematic drawing (left) with a cadaver specimen (right) to highlight three key external structures of the large intestine. The **taeniae coli** are three narrow bands of longitudinal smooth muscle that run along the colon and create the segmented, pouch-like **haustra** seen on the surface. Together with the small, fat-filled peritoneal pouches called **adipose appendages** these features help identify the large intestine and distinguish it from the small intestine in both anatomical drawings and real specimens. *(Image credit: "Large Intestine Structural Features by Jennifer Lange is licensed under CC BY-NC-SA 4.0 , modification of originals "Teniae Coli, Haustra, Epiploic Appendage" by OpenStax and "Leiden MOOC - Reader Anatomy on the Table - The Large Intestine" by O. Paul Gobée, LUMC.)*

Epithelium of the Anal Canal

The **stratified squamous epithelial mucosa** of the anal canal connects to the skin on the outside of the anus. This mucosa varies considerably from that of the rest of the colon to accommodate the high level of abrasion as feces pass through. Depressions within the canal's wall secrete mucus that facilitates defecation.

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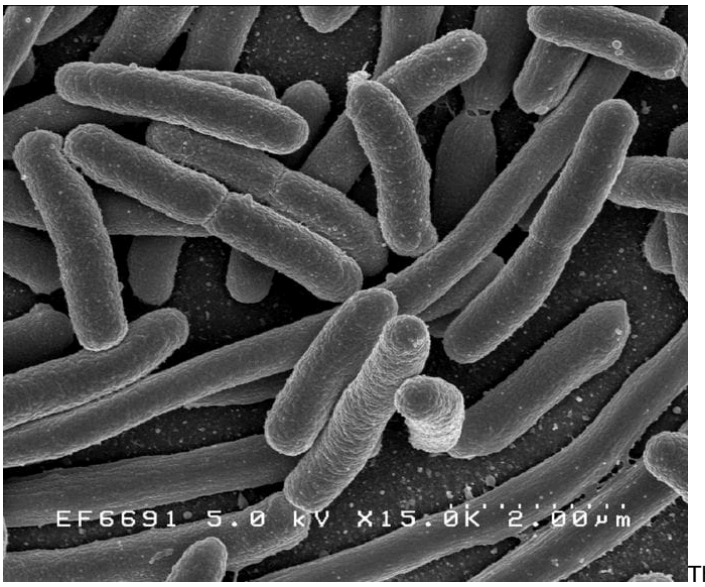
12.8: Activities of the Large Intestine

The large intestine hosts a diverse community of microbes that assist with digestion and vitamin production while the organ itself absorbs water, compacts waste, and prepares feces for elimination.

Master this section and you'll be able to:

- Describe the gut microbiome and explain how intestinal microorganisms contribute to the well-being of their host.
- Explain the processes of digestion and absorption and feces formation in the large intestine.

Gut Microbiome: Overview



The term *gut microbiome* refers to the enormous community of microorganisms living in your digestive tract. Most are bacteria, but the community also includes viruses, fungi, archaea, and tiny single-celled eukaryotes. Together, these microbes assist with digestion, produce certain vitamins, support immune function, and help protect the body from harmful pathogens — tasks your body cannot perform alone.

Composition and Location

Most microbes that enter the digestive tract are destroyed earlier in digestion by lysozyme, defensins, stomach acid, or protein-digesting enzymes. However, trillions of microorganisms, collectively called the *gut microbiota* (historically called the "bacterial flora"), survive and thrive in the large intestine. More than 700 species have been identified. Most are nonpathogenic commensal organisms that stay safely within the gut lumen and provide important benefits to the host. In the image you can see *Escherichia coli (E. coli* for short), a common inhabitant of the human gut.

Roles in Digestion and Absorption

These microbes are active participants in digestion. Bacteria break down **undigested polysaccharides** — dietary fiber — and metabolize them into **short-chain fatty acids** that are absorbed by passive diffusion and provide several important benefits once they are inside our body. Because the bacterial metabolism produces acids, the large intestine secretes bicarbonate to help neutralize the acidity.

Several bacterial species also synthesize vitamins that humans cannot make on their own, including **biotin** (**B7**), **pantothenic acid** (**B5**), and **vitamin K.** Although this bacterial vitamin supply provides only a modest portion of the daily requirement, it

becomes especially important when dietary intake is low or inconsistent.
Antibiotic treatment can disrupt this process because antibiotics often kill helpful microbes along with harmful ones, which may lead to deficiencies if the gut flora is suppressed for long periods.

Immune Support and Barrier Protection

Some members of the gut microbiota also strengthen immune responses and help maintain a stable intestinal environment. However, it is essential that these microbes stay inside the intestinal lumen. The large intestine maintains a tightly regulated barrier system — including epithelial cells sealed by tight junctions, a protective mucus layer, and continuous immune surveillance — that keeps the microbiota from crossing into deeper tissues.

Absorption and Feces Formation

Absorption and feces formation in the large intestine center on reclaiming water and electrolytes from the remaining chyme while compacting indigestible material into solid waste. The material gradually becomes feces that can be stored and later eliminated.

Digestive Functions of the Large Intestine

The material that enters the large intestine is what remains of chyme after most digestion and absorption have already occurred. It contains very few nutrients other than water. As this residue moves slowly through the large intestine, usually over 12 to 24 hours, much of the remaining water is reabsorbed.

Because the large intestine mainly absorbs water and does not play a major role in nutrient absorption, it can be completely removed without severely disrupting digestion. In some patients with severe inflammatory bowel disease, surgeons remove the large intestine in a procedure called a colectomy. If possible, they form a new internal fecal pouch from a segment of the small intestine and connect it to the anus so that defecation can still occur through the normal route. If this is not feasible, an ileostomy is created by bringing the distal ileum out through the abdominal wall. In that case, the watery intestinal contents empty into a bag-like adhesive appliance attached to the skin.

Mechanical Digestion

Mechanical digestion in the large intestine begins when chyme passes from the ileum into the cecum. This movement is regulated by the ileocecal valve (sphincter). After a meal, peristalsis in the ileum pushes chyme through the sphincter. When the cecum becomes distended, the sphincter tightens to prevent material from moving backward into the small intestine.

Once chyme reaches the cecum, the colon begins its characteristic movements: the **haustral contractions.** These slow, segmenting movements occur mainly in the transverse and descending colon. When a haustrum becomes stretched by chyme, its circular muscle contracts and pushes the residue into the next haustrum. These contractions occur about every 30 minutes and last roughly 1 minute. They also mix the residue, which helps with water absorption.

Peristalsis also occurs in the large intestine, but it is slower than in the small intestine. These waves help gradually move the residue forward along the colon.

A third and more powerful type of motion is the **mass movement.** These forceful contractions begin in the transverse colon and quickly drive the contents toward the rectum. **Mass movements typically occur three or four times each day,** usually during a meal or shortly after. Stretching of the stomach and the presence of nutrients in the small intestine trigger the gastrocolic reflex, which increases motility in the colon and helps initiate these strong waves.

Adequate fiber intake helps the colon perform all these functions effectively. Fiber softens the stool and enhances the strength of colonic contractions, improving motility and reducing the risk of constipation.

Chemical Digestion

Although the glands of the large intestine secrete mucus, they do not release digestive enzymes. As a result, any chemical digestion that occurs in the large intestine is carried out entirely by the bacteria living in the colon. Through a process called **saccharolytic fermentation**, these bacteria **break down some of the remaining carbohydrates.** This activity produces **hydrogen**, **carbon dioxide**, and **methane gases,** which together form **flatus** (intestinal gas). Flatulence refers to excessive flatus. On average, the colon generates up to 1500 mL of flatus per day, and even more when foods high in indigestible sugars and complex carbohydrates, such as beans and soluble dietary fiber, are consumed.

Water Absorption and Formation of Feces

The small intestine absorbs nearly 90 percent of the water you ingest, whether it comes from liquids or from solid food. The large intestine absorbs most of what remains, gradually **converting liquid chyme into semisolid feces.** Feces contain undigested food residues, unabsorbed nutrients, millions of bacteria, shed epithelial cells from the mucosa, inorganic salts, waste products, and enough water to allow smooth passage out of the body. Of the approximately 500 mL (about 17 ounces) of residue that enters the cecum each day, only about 150 mL (5 ounces) leave the body as feces.

The Defecation Reflex

Defecation is a coordinated blend of involuntary reflexes and voluntary control that safely and efficiently clears waste from the digestive system. It begins when powerful mass movements sweep fecal material into the rectum, stretching its walls and activating the defecation reflex. This spinal cord–mediated, parasympathetic reflex contracts the sigmoid colon and rectum, relaxes the internal anal sphincter, and briefly tightens the external anal sphincter. As feces enter the anal canal, sensory signals reach the brain, giving you the choice to either relax the external anal sphincter to proceed or keep it contracted to delay the process.

If the urge is postponed, the rectum gradually relaxes and some material may even be moved back into the colon by reverse peristalsis, where additional water is absorbed. This reduces pressure for the moment, but the next mass movement will trigger the reflex again. Delaying defecation for too long causes the stool to harden as more water is absorbed, which can lead to constipation. On the other hand, if fecal material moves too quickly through the intestines, not enough water is absorbed, resulting in diarrhea. Everything from hydration and diet to stress levels influences how often these reflexes occur, which is why normal bowel habits vary widely among healthy individuals.

When you decide to defecate, voluntary effort works together with the reflex. The abdominal muscles contract to increase intra-abdominal pressure and the perineal wall lowers, reducing the anorectal angle from about 90 degrees to nearly straight. The external anal sphincter relaxes, and coordinated contractions of the rectum, internal anal sphincter, and puborectalis muscle help propel feces out of the body. These final adjustments essentially pull the anal canal up and over the passing stool, completing one of the most fundamental yet finely tuned processes your body carries out each day.

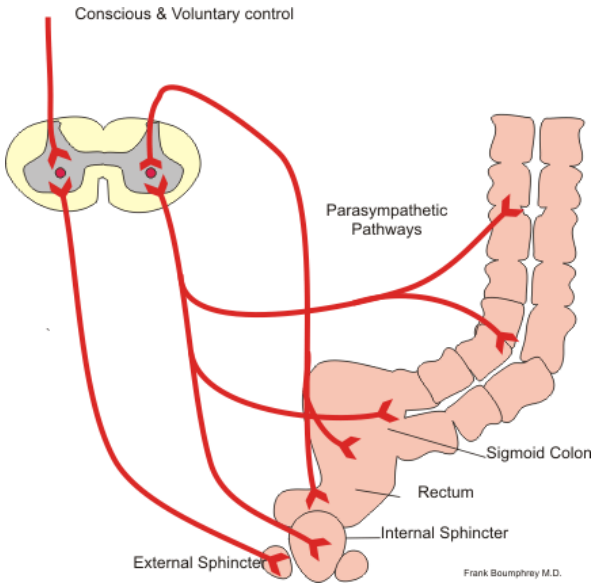


Figure 12.8.1: **Neural Control of Defecation.** The spinal cord coordinates the defecation reflex. Parasympathetic pathways stimulate contraction of the sigmoid colon and rectum and relax the internal anal sphincter. At the same time, higher brain centers provide voluntary control over the external anal sphincter, allowing you to delay or permit defecation.

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12.9: Lactose Intolerance

Lactose intolerance is the inability of the small intestine to digest lactose, a sugar found in milk, due to a lack of the enzyme lactase.

Master this section and you'll be able to:

- Explain what causes lactose intolerance and how undigested lactose leads to GI symptoms.
- Distinguish lactose intolerance from milk allergy and describe basic diagnostic and dietary management options.

Food intolerance occurs when a person has difficulty digesting a specific food or nutrient, causing unpleasant GI symptoms such as gas, bloating, flatulence, cramping, and diarrhea. Food intolerances are commonly caused by the body not producing enough of a particular digestive enzyme, so the symptoms generally involve the digestive system, and the severity of symptoms usually correlates with how much of the food was eaten. Unlike food allergies, the immune system does not play a role in food intolerance, and while the symptoms are unpleasant, they are generally not dangerous and will subside once the food passes out of the GI tract. People with food intolerances can also often consume small amounts of the offending food without symptoms.

The most common food intolerances in the US, affecting a significant portion of the population, are **lactose, wheat, and shellfish** sensitivities. Let's take a closer look at the first one.

Cause of Lactose Intolerance

In people with lactose intolerance, the absorptive enterocytes of the small intestine do not produce enough of the enzyme lactase, which is responsible for digesting the **milk sugar lactose** into single sugar molecules (glucose and galactose) that can be absorbed in the small intestine.

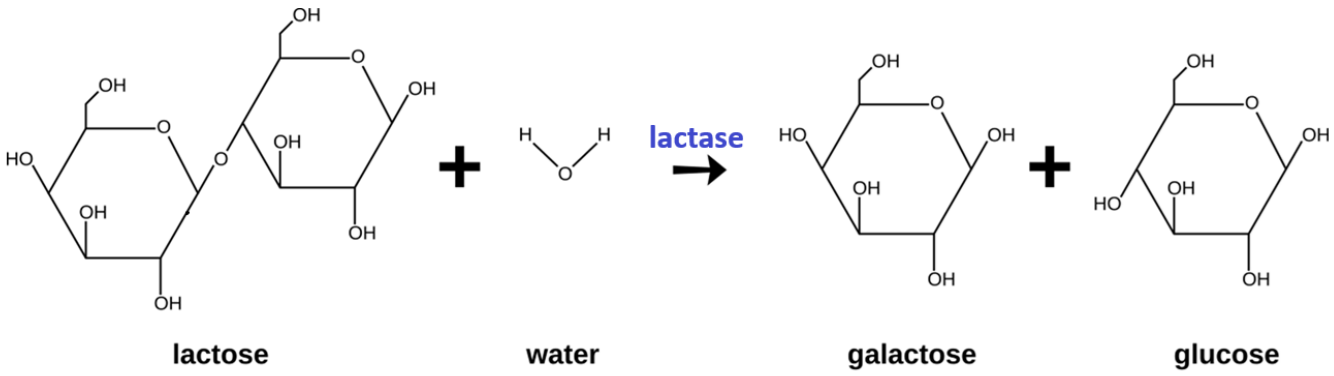


Figure 12.9.1: **Lactase and the Breakdown of Lactose.** The brush border enzyme **lactase**, located on the apical surface of small-intestinal enterocytes, splits the disaccharide **lactose** into its two absorbable monosaccharides, **glucose** and **galactose**. Lactase sits in the microvilli of the small intestine and performs the final step of carbohydrate digestion before these simple sugars are transported into the bloodstream. When lactase levels are low, undigested lactose moves into the large intestine and may cause gas, bloating, and diarrhea.

Undigested lactose can't be absorbed, so it continues on to the large intestine. There, it draws more water into the large intestine, and bacteria metabolize the lactose, resulting in gas and acid production. These conditions cause the uncomfortable symptoms of gas, bloating, and diarrhea within about 30 minutes to two hours of consuming dairy foods.

Primary lactase deficiency is genetic, only affects adults, and is caused by the **absence of a lactase persistence allele**. It is the most common cause of lactose intolerance as a majority of the world's population lacks these alleles. Secondary, acquired, or transient lactase deficiency is caused by an injury to the small intestine, usually during infancy, from acute gastroenteritis, diarrhea, chemotherapy, intestinal parasites, or other environmental causes. Congenital lactase deficiency is a

very rare, autosomal recessive genetic disorder that prevents lactase expression from birth. It is particularly common in Finland. People with congenital lactase deficiency who are unable to digest lactose from birth are unable to digest breast milk.

As with most food intolerances, people with lactose intolerance can often consume some amount of lactose without discomfort, although this varies from person to person. Aged hard cheese, buttermilk, and yogurt (as long as it doesn't include added milk solids) are often well-tolerated because they are low in lactose, which is consumed by bacteria during fermentation and aging. In addition, lactose-free milk and lactase enzyme supplements are available. Dairy products are some of the main dietary sources of calcium and vitamin D, so people who avoid dairy need to take special care to include other sources of these nutrients in their diets.[2]

The vast majority of humans are born with the ability to digest lactose. All mammalian milk, including human milk, contains lactose, so historically, infants with lactose intolerance wouldn't have survived. (Today, infants with lactose intolerance can consume soy-based infant formula.) Beyond infancy, lactose intolerance depends on your genes. In much of the world, it's common for the activity of the lactase gene to decline with age, resulting in less lactase production and more lactose intolerance. Worldwide, 65% of the human population has some degree of lactose intolerance in adulthood. On the other hand, **lactose tolerance** is common in cultures where early domestication of dairy animals provided an important source of nutrition. In the U.S., adults of European descent can often tolerate lactose, whereas lactose intolerance is common among Asian Americans, African Americans, Mexican Americans, and Native Americans.



Figure 12.9.2: **Lactase Enzyme Supplement.** Taking a lactase enzyme supplement allows many people with lactose intolerance to eat dairy products without suffering symptoms. ("Home-breakfast (lactaid photo)" by Ernesto Andrade is licensed under CC BY-ND 2.0)

Symptoms of Lactose Intolerance

Since in people with lactose intolerance, the lactose in chyme is not digested, **bacteria in the large intestine ferment the undigested lactose**, a process that produces gas. In addition to gas, symptoms include abdominal cramps, bloating, and diarrhea, and/or vomiting after consuming significant amounts of lactose.

Since individuals may be lactose intolerant to varying degrees, symptom severity ranges from mild discomfort to severe pain. All symptoms resolve once the lactose is eliminated in feces.

Assessment and Treatment of Lactose Intolerance

To assess lactose intolerance, intestinal function is challenged by ingesting more dairy products than can be readily digested.

Clinical symptoms typically appear within 30 minutes, but may take up to two hours, depending on other foods and activities. Substantial variability in response (symptoms of nausea, cramping, bloating, diarrhea, and flatulence) is to be expected, as the extent and severity of lactose intolerance varies among individuals.

It is important to distinguish lactose intolerance from milk allergy, an abnormal immune response (usually) to milk proteins. This may be done in diagnosis by giving lactose-free milk, producing no symptoms in the case of lactose intolerance, but the same reaction as to normal milk if it is a milk allergy. An intermediate result might suggest that the person has both conditions. Since lactose intolerance is the normal state for most adults worldwide, it is not considered a disease and a medical diagnosis is not normally required, although tests are available if confirmation is necessary.

Lactose intolerance is not considered a condition that requires treatment in societies where the diet contains relatively little dairy. However, those living among societies that are largely lactose-tolerant may find lactose intolerance troublesome. Although there are still no methodologies to reinstate lactase production, some individuals have reported that their intolerance varies over time, depending on health status and pregnancy. About 44% of lactose intolerant women regain the ability to digest lactose during pregnancy. This might be caused by slow intestinal transit and intestinal flora changes during pregnancy.

The **hydrogen breath test** is used to help diagnose lactose intolerance. Lactose-tolerant people have very little hydrogen in their breath. Those with lactose intolerance exhale hydrogen, which is one of the gases produced by the bacterial fermentation of lactose in the colon. After the hydrogen is absorbed from the intestine, it is transported through blood vessels into the lungs. There are a number of lactose-free dairy products available in grocery stores. In addition, dietary supplements are available. Taken with food, they provide lactase to help digest

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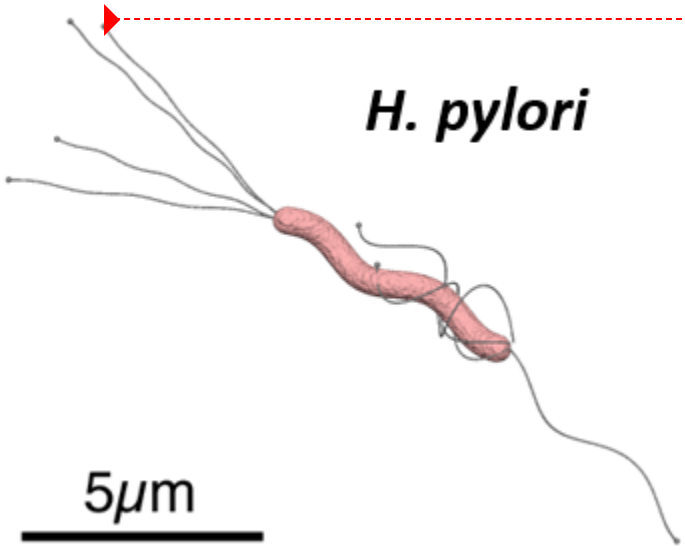
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12.10: Peptic Ulcer Disease

A peptic ulcer, also known as peptic ulcer disease, is an erosion in the wall of the stomach, duodenum, or esophagus.

Master this section and you'll be able to:

- List the causes of and treatments for peptic ulcer disease



Causes

A peptic ulcer, also known as peptic ulcer disease, is an **erosion in the wall of the stomach, duodenum, or esophagus.** The stomach protects itself from its own acidic gastric juice with a mucosal barrier made of mucus, bicarbonate, and tight junctions that seal the epithelial cells together. This barrier is highly effective but not flawless. When it becomes damaged, stomach acid can erode the mucosa. Small, shallow erosions usually heal on their own, but deeper injuries that extend into the tissue are called ulcers.

Helicobacter pylori

About 10% of Americans will develop a peptic ulcer during their lifetime. Contrary to popular belief, ulcers are **not caused by stress or spicy foods.** Most are linked to an infection of the stomach with *Helicobacter pylori*, a bacterium that can survive the acidic environment by neutralizing its immediate environment As many as 70–90% of peptic ulcers are associated with ***Helicobacter pylori*** *(=* ***H. pylori****)*, a spiral-shaped bacterium that can live in the acidic environment of the stomach. (See image on the right.)

Roughly 30 to 40% of Americans carry this organism. People who are **carriers for *H. pylori*** often have no symptoms at all, even though the bacteria slowly thin the protective mucus layer of the stomach and duodenum and slightly inflame the lining. Carriers can unintentionally spread the infection to others, especially in childhood, through contaminated food or water or contact with saliva, vomit, or feces. Most carriers never develop problems, but some may eventually experience chronic gastritis, peptic ulcers, or, over many years, a small increase in gastric cancer risk. Because they feel fine, carriers are usually identified only when a family member tests positive or a clinician investigates unexplained stomach pain or anemia.

Why *H. pylori* Can Live in an Environment as Acidic as the Stomach

Helicobacter pylori survives in the stomach's extreme acidity by creating a **tiny "safe zone" around itself**. It produces an enzyme called **urease**, which breaks down urea (a substance always naturally present in stomach fluid) into **ammonia**.

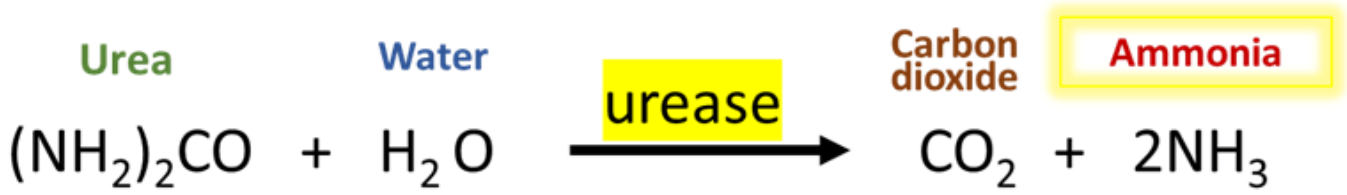


Figure 12.10.1: ***H. pylori* Breaking Down Urea.** Urease is an enzyme that breaks urea by adding water. The reaction releases **one molecule of carbon dioxide** and **two molecules of ammonia**.

Ammonia is basic, so it neutralizes the acid immediately surrounding the bacteria. With this protective cloud, *H. pylori* can nestle into the mucus layer that coats the stomach wall, where the environment is less acidic than the stomach lumen. It also uses its spiral shape and flagella to burrow deeper into the mucus and avoid direct exposure to gastric acid. Together, these strategies allow *H. pylori* to survive and thrive in one of the harshest environments in the body.

H. pylori weakens the protective mucus layer that normally shields the stomach and duodenum from gastric acid. As the mucus thins, acid can damage the underlying tissue, leading to inflammation and ulcer formation. The exact route of transmission is still unclear, but the bacterium may spread through contaminated food or water, or through contact with the saliva, vomit, or feces of an infected person.

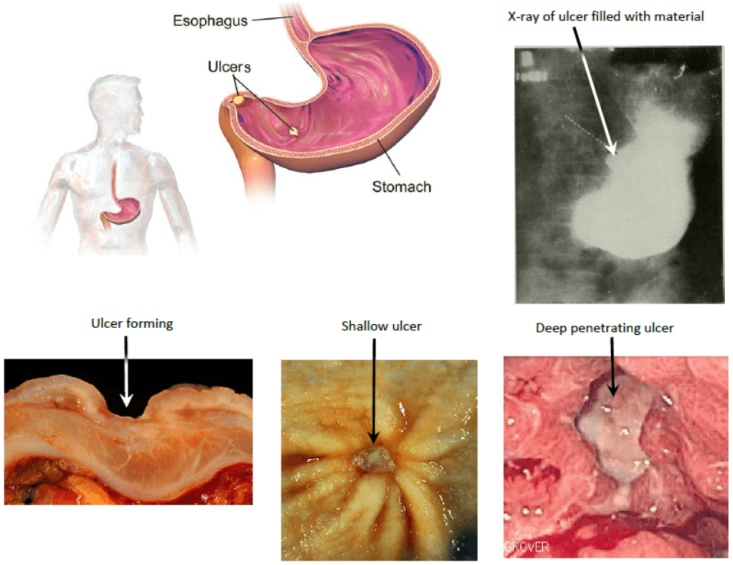


Figure 12.10.2: **Peptic Ulcer Progression.** Ulcers form when the stomach's protective mucus layer is weakened, allowing acid to damage the underlying tissue. (Copyright 2020: Augustine G. DiGiovanna, Ph.D., Salisbury University, Maryland. Used with permission.)

NSAIDs (Non-Steroidal Anti--Inflammatory Drugs)

NSAIDs such as **aspirin**, **ibuprofen**, and **naproxen** can also cause or worsen peptic ulcers because they **reduce the production of protective mucus.** Normally, the stomach is shielded from its own acid by a thick layer of mucus and bicarbonate, both of which are produced in response to **prostaglandins**. Prostaglandins are short-lived, hormone-like chemicals made from fatty acids that act locally in tissues to regulate inflammation, pain, blood flow, amongst much more.

NSAIDs block the enzyme (COX) that the body uses to make prostaglandins. When prostaglandin levels drop, three problems occur at the same time:

1. **Less protective mucus is produced.**
   The stomach surface becomes more exposed to acid.

2. **Less bicarbonate is secreted.**
   Acid is not neutralized as effectively.

3. **Blood flow to the mucosa decreases.**
   This slows healing and makes the tissue more vulnerable to damage.

With these defenses weakened, normal stomach acid can begin to injure the mucosa. Small erosions can progress into deeper ulcers, especially wit

h continued NSAID use. Over time, these ulcers may bleed or, in rare cases, perforate the stomach wall.

This is why long-term NSAID use is one of the leading causes of peptic ulcers, even in people without *H. pylori* infection.

Symptoms

Peptic ulcers can cause a range of symptoms. The most common is abdominal pain, especially near the stomach, often linked to mealtimes and sometimes appearing a few hours after eating. Other symptoms may include bloating, a sense of abdominal fullness, nausea, loss of appetite, weight loss, and sometimes heavy vomiting. If bleeding occurs, a person may vomit blood or pass melena, which are dark, tarry stools created when iron in hemoglobin is oxidized during digestion. In rare cases, an ulcer may perforate the stomach or duodenum and spill contents into the abdominal cavity, causing acute peritonitis, a medical emergency that requires immediate surgery.

Diagnosis

Doctors usually begin making a diagnosis based on the characteristic symptoms, especially stomach pain, which is often the first warning sign. In some cases, treatment is started right away without specific tests. If the symptoms improve within a few weeks, that improvement helps confirm that the initial diagnosis was correct.

If symptoms do not improve with treatment, or if they first appear in someone over age 45 or in a person with concerning signs such as unexplained weight loss, doctors may order diagnostic tests such as an **endoscopy** or a **barium contrast x-ray.** These tests help rule out other conditions, including stomach cancer, which can mimic ulcer symptoms. Doctors may also test further when ulcers are unusually resistant to treatment, unusually located, or when there is concern that the stomach is producing too much acid due to an underlying disorder.

An **esophagogastroduodenoscopy** (EGD) — often called an **upper endoscopy or gastroscopy** — is the most direct way to evaluate a suspected ulcer. With this procedure, the clinician can see the ulcer, determine its exact location and severity, and, if no ulcer is present, often identify another cause for the symptoms.

If a peptic ulcer **perforates**, air from inside the gastrointestinal tract can leak into the peritoneal cavity, which normally contains no air. This escaped air rises and collects under the diaphragm when the patient is standing, making it visible on an erect chest x-ray. The presence of this “free gas” on imaging is a classic sign of a perforated ulcer and requires immediate medical attention.

Treatment

Younger patients with ulcer-like symptoms are often treated first with antacids. These medications help neutralize stomach acid by raising the pH or by blocking acid secretion from gastric cells, which reduces irritation of the stomach lining. Patients who use NSAIDs may also be prescribed a prostaglandin analogue to replace the protective prostaglandins that NSAIDs suppress, helping prevent peptic ulcers from forming.

When *H. pylori* infection is present, the most effective therapy is “triple therapy,” which combines two antibiotics (such as clarithromycin, amoxicillin, tetracycline, or metronidazole) with a proton pump inhibitor. Antacids may also be added. In more severe or resistant cases, a third antibiotic can be included. Clearing the *H. pylori* infection usually relieves symptoms and allows

ulcers to heal, although some patients may require retreatment if the infection returns.

A perforated peptic ulcer is a medical emergency and requires immediate surgical repair. Most actively bleeding ulcers require urgent endoscopy so the bleeding vessel can be treated by cautery, injection, or clipping.

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13: GENITOURINARY (A.K.A. UROGENITAL) SYSTEM

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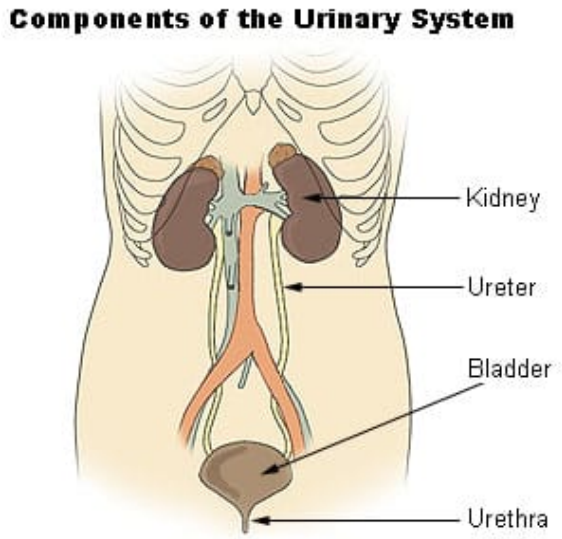
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13.1: Overview of the Renal (Urinary) System

The renal (urinary) system filters the blood, removes wastes, and helps maintain fluid and chemical balance in the body.

Master this section and you'll be able to

- List the organs of the renal system and state their primary roles.
- Describe how the renal system helps maintain a stable internal environment.



Structural Overview of the Renal System

The renal system — also commonly called the urinary system — is a group of o**nly four organs:**

- **two kidneys**,
- **two ureters**,
- **one urinary bladder**, and
- **one urethra.**

(See image on the right.)

Functional Overview of the Renal System

Beyond **forming urine,** the **kidneys** carry out **several essential homeostatic roles** that influence nearly every other body system:

1. **Removal of Metabolic Wastes and Toxins**
   The kidneys filter the blood to eliminate nitrogenous wastes, drugs, and other toxins that the body cannot use or must keep at very low levels.

2. **Regulation of Blood Volume and Blood Pressure**
   By adjusting how much water and sodium are returned to the bloodstream, the kidneys help determine blood volume. Through the renin-angiotensin-aldosterone system (RAAS), they also influence vascular resistance. Together, these processes are central to maintaining stable blood pressure.

3. **Maintenance of Electrolyte and Metabolite Balance**
   Electrolytes such as sodium, potassium, calcium, and bicarbonate are constantly filtered and then selectively reabsorbed or excreted. This careful regulation supports nerve signaling, muscle contraction, and normal cellular metabolism.

4. **Control of Blood pH**
   The kidneys help stabilize the body's acid-base balance by excreting hydrogen ions and reabsorbing bicarbonate. This complements the work of the respiratory system and chemical buffers in the blood.

5. **Stimulation of Red Blood Cell Production**
   When oxygen levels drop, special peritubular cells in the renal cortex and outer medulla release **erythropoietin** (**EPO**), a hormone that signals the bone marrow to increase red blood cell production, improving the blood's ability to carry oxygen.

6. **Activation of Vitamin D**
   The kidneys convert calcidiol into calcitriol, the active form of vitamin D. **Calcitriol is required for calcium absorption** in the intestines and plays a major role in bone health.

Although we often think of the kidneys as simple urine producers, it is more accurate to view them as **regulators of plasma composition**. By adjusting how much water and which solutes are returned to or removed from the bloodstream, the kidneys help maintain homeostasis and indirectly influence the function of every other body system.

Once urine is formed in the kidneys, the two **ureters** carry it from the kidneys to the urinary bladder through **peristaltic movements**. The urinary bladder stores urine until **stretch receptors** signal that it is time to empty. When the appropriate sphincters relax, urine flows out of the bladder and exits the body through the **urethra**.

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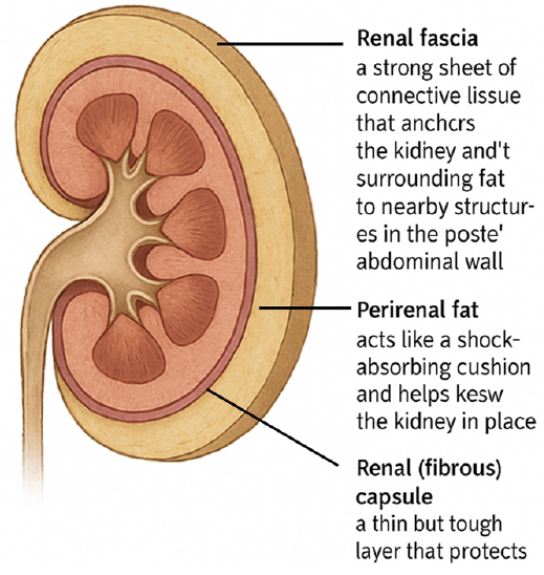
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13.2: The Kidneys — Exterior and Interior Structures

The kidneys' location, protective layers, and internal organization into cortex and medulla provides the foundation for learning how they carry out filtration and maintain homeostasis.

Master this section and you'll be able to:

- Identify the major external and internal structures of the kidney, including its protective layers, cortical and medullary regions, hilum, and renal pelvis.



The Kidneys — External Gross Anatomy

Anatomically, the kidneys lie on either side of the spine in the **retroperitoneal space**, not within the abdominal cavity. The kidneys are the primary organs of the renal system and — as you saw in the previous section — carry out essential homeostatic functions. They are a **pair of bean-shaped, brown organs** about the size of your fist.

Each kidney is wrapped in **three protective layers** that help cushion and stabilize it in the body:

1. Closest to the surface of the kidney is the **renal (fibrous) capsule,** a thin but tough layer that protects against injury and infection.
2. Surrounding this is a **thick layer of perirenal fat** that acts like a shock-absorbing cushion and helps keep the kidney in place.
3. The outermost layer is the **renal fascia**, a strong sheet of connective tissue that anchors the kidney and its surrounding fat to nearby structures in the posterior abdominal wall.

The kidneys are highly vascular organs, **receiving about one quarter (25%) of the resting cardiac output,** which supports their continuous role in filtering and regulating the composition of the blood.

The asymmetry within the abdominal cavity caused by the liver typically results in the right kidney being slightly lower than the left, and left kidney being located slightly more medial than the right. The right kidney sits just below the diaphragm and posterior to the liver, the left below the diaphragm and posterior to the spleen.

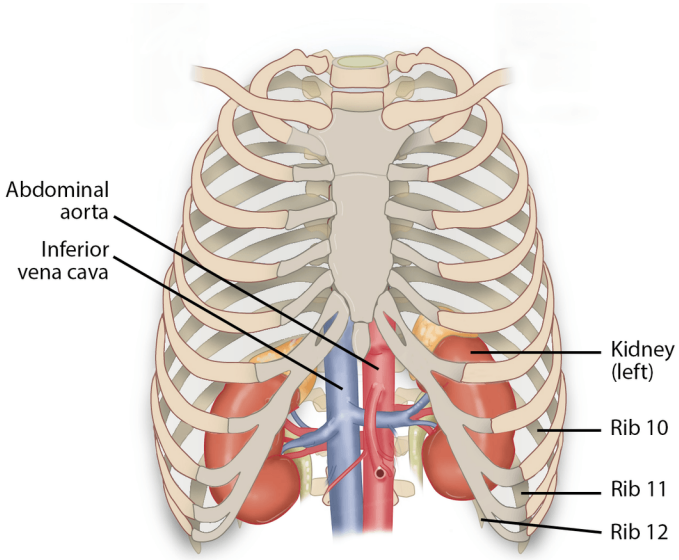


Figure 13.2.1: **Kidney Position.** The kidneys are located deep to the floating ribs, which provide protection for the kidneys. *(Image credit: "Kidney Position Relative to the Thoracic Cage" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; modification of "Slagter - Drawing and Chest X-ray of the ribs and clavicula - no labels" by Ron Slagter, and "Slagter - Drawing Anatomy of the kidney, adrenal glands and bladder - no labels" by Ron Slagter.)*

Resting on top of each kidney is an **adrenal gland** (adrenal meaning on top of renal), primarily endocrine organ. The upper parts of the kidneys are partially protected by lower ribs, and each whole kidney and adrenal gland are **surrounded by two layers of fat (the perirenal and pararenal fat)** and the renal fascia.

Internal Gross Anatomy of the Kidneys

The **renal hilum** (see image below) is the medial-facing, concave entry and exit site for structures servicing the kidneys: **blood vessels, nerves,** lymphatics**,** and **ureters**. The **renal arteries** branch directly from the abdominal aorta, whereas the **renal veins** return blood directly to the inferior vena cava. The vein, artery, and ureter are arranged in an anterior-to-posterior order.

The ureters are structures that come out of the kidneys, bringing urine downward into the bladder.

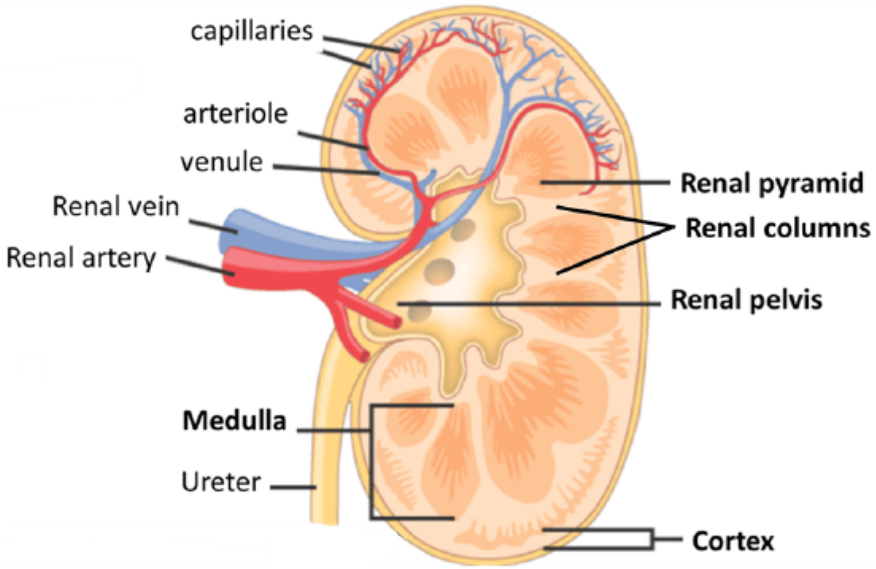


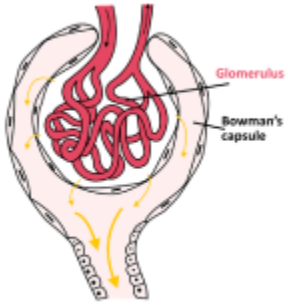
Figure 13.2.2: **Internal Anatomy of the Kidney.** This coronal section of a kidney shows the major regions and structures involved in filtering the blood and producing urine. The **cortex**, the outer region, contains most of the glomeruli. The **medulla** forms the deeper, triangular **renal pyramids**, which contain the loops and collecting ducts that help concentrate urine. Between the pyramids are **renal columns**, extensions of cortical tissue that carry blood vessels into the medulla. Filtered urine drains from the pyramids into the **renal pelvis**, which funnels it into the **ureter**. Shown also are branches of the **renal artery** and **renal vein**, along with **arterioles**, **venules**, and **capillaries** that support the high rates of filtration and reabsorption within the nephron.

Renal Cortex & Medulla

As you saw above, the kidneys are enclosed by three protective layers: the renal capsule (a tough fibrous covering), the adipose capsule (a layer of fat that cushions the organ), and the renal fascia (connective tissue that anchors the kidney in place).

Beneath these coverings lies the **renal cortex**, the outer region of the kidney that appears granular because it contains the superficial portions of the nephrons (more details below), the kidney's functional units.
The renal cortex extends deep into the medulla in the form of **renal columns.** These columns appear as vertical "bands" of cortical tissue that separate the cone-shaped renal pyramids (which are part of the medulla). Their function is to provide an anchor for the cortex and to provide a corridor for the kidney's blood vessels and nerves.

Special cells in the renal cortex also produce the hormone erythropoietin.



The **renal medulla** is the inner region of the kidney's parenchyma (functional tissue). It contains several triangular structures called **renal pyramids**. Each pyramid is packed with parts of nephrons and associated blood vessels that help concentrate the urine.

A nephron begins in the cortex with a cup-shaped structure called the **Bowman's capsule**. This capsule surrounds a tuft of capillaries known as the **glomerulus**. (*See image on the right.*) Blood arrives in the glomerulus from branches of the renal arteries, and plasma is filtered across the capillary walls into the Bowman's capsule.

Once the filtrate has entered the capsule, it flows through the nephron in a specific sequence: first the proximal convoluted tubule, then the loop of Henle, then the distal convoluted tubule, and finally the collecting ducts. The collecting ducts carry the processed filtrate toward the renal pelvis and into the ureter. Each segment of the nephron has unique permeability properties that allow the kidneys to regulate water balance, electrolyte levels, and overall homeostasis in the body. For more details see the next page\

Renal Pelvis

The renal pelvis is a funnel-shaped cavity in the center of the kidney that collects urine from the major calyces and represents the expanded upper end of the ureter. It sits within the renal sinus at the hilum and channels urine out of the kidney into the ureter for transport to the bladder.

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- 24.2B: Internal Anatomy of the Kidneys by Boundless (now LumenLearning) is licensed CC BY-SA 4.0.

13.3: Nephron — The Functional Unit of the Kidneys

The nephron is the kidney's microscopic working unit, and is responsible for the regulation of water and soluble substances in blood.

Master this section and you'll be able to:

- Describe the major structural regions of a nephron.
- Trace the movement of filtrate and blood from the renal corpuscle through the nephron.
- Explain what ADH is and its effect on the kidneys.

Structure of a Nephron

Within the kidneys are the microscopic **functional units of the kidneys**, called **nephrons**. Each kidney contains about **one million nephrons**, a number established by birth that does not increase throughout life. Each nephron filters the blood, adjusts the amounts of water and solutes that are reabsorbed or excreted, and ultimately produces urine.

As each nephron begins to filter the blood, It allows water, electrolytes, and small solutes to enter a tubular system while keeping cells and large proteins in the bloodstream. This so called **filtrate** flows through the nephron's winding tubules, the kidneys have ample opportunity to fine-tune its composition by **reabsorbing** substances the body needs, such as water, glucose, and amino acids, and by **secreting** additional wastes or excess ions that must be eliminated.

Each nephron has *two major regions:* the **renal corpuscle** and the **renal tubule**:

1. The renal corpuscle includes the **glomerulus,** a capillary bed where filtration begins, and the **Bowman's capsule**, which collects the filtered fluid.

2. The renal tubules make up the remainder of the nephron and include three main segments: the **proximal convoluted tubule**, the **loop of Henle** (with descending and ascending limbs), and the **distal convoluted tubule**. These winding tubules allow the kidneys to adjust the filtrate by reabsorbing needed substances and secreting additional wastes.

Overall, the nephron's job is to filter the blood, reclaim essential water and solutes, and form urine from what the body does not need. Nephron activity helps regulate blood volume, blood pressure, and plasma osmolarity, and is influenced by hormones such as antidiuretic hormone, aldosterone, and parathyroid hormone.

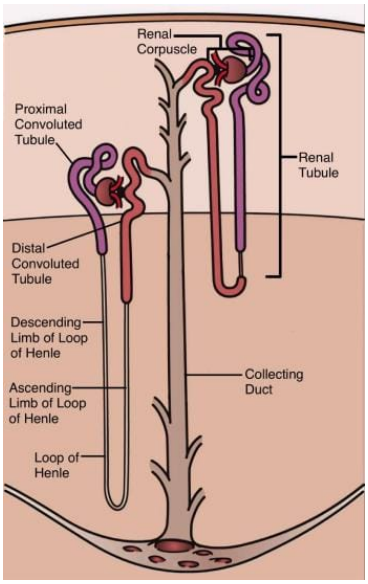
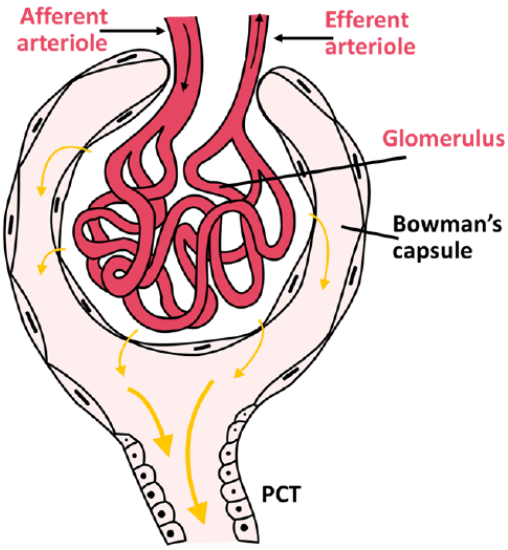


Figure 13.3.1: **Structure of a Nephron.** Shown is the structure of a Juxtamedullary Nephron (left) and a Cortical Nephron (right). Nephrons are the functional units of the kidney. Filtration begins in the renal corpuscle, where blood is filtered into the start of the renal tubule. The filtrate then moves through the proximal convoluted tubule, descends and ascends through the loop of Henle, and continues into the distal convoluted tubule. These segments adjust the amounts of water and solutes that are reabsorbed or secreted. Multiple nephrons empty their final filtrate into a collecting duct, which carries forming urine toward the renal pelvis.

The Glomerulus



The glomerulus is a tuft of **fenestrated capillaries**, which means the capillary walls contain tiny pores that allow water and many small solutes to pass through quickly. Fenestrated capillaries are found in places where rapid filtration or exchange is essential, such as the kidneys, intestines, and endocrine glands.

Unlike other capillary beds, glomerular capillaries begin at an **afferent arteriole** and drain into an **efferent arteriole**, rather than into a venule. Because the efferent arteriole is narrower, pressure inside the glomerulus stays high. The body can adjust this pressure by changing the diameter of the afferent and efferent arterioles. The fluid and solutes filtered out of the glomerulus collect in **Bowman's capsule**, beginning their journey through the nephron.

The Bowman's capsule — also called the **glomerular capsule** — surrounds the glomerulus. It is composed of visceral (simple squamous epithelial cells; inner) and parietal (simple squamous epithelial cells; outer) layers. The visceral layer lies just beneath the thickened glomerular basement membrane and only allows fluid and small molecules like glucose and ions like sodium to

pass through into the nephron.

Red blood cells and large proteins, such as serum albumins, cannot pass through the glomerulus under normal circumstances. However, in some injuries they may be able to pass through and can cause blood and protein content to enter the urine, which is a sign of problems in the kidney.

Proximal Convoluted Tubule (PCT)

The proximal convoluted tubule (PCT) is a significant component of the nephron. Starting at the Bowman's capsule in the renal cortex, the PCT plays a vital role in reabsorbing essential substances and regulating urine composition. It is a convoluted tube with a **simple cuboidal epithelium** lined by a brush border of **microvilli** on its luminal (apical) surface. The microvilli dramatically increases the surface area for absorption.

The PCT is the first site of **water reabsorption into the bloodstream**, and the site where the majority of water and salt reabsorption takes place. Water reabsorption in the proximal convoluted tubule occurs due to both passive diffusion and active transport from Na^+/K^+/ATPase pumps that actively transports sodium back into the blood.

Water and glucose follow sodium in a process called **co-transport.** Approximately **65% of water** and — under normal conditions — **100% of the glucose** in the nephron are reabsorbed by cotransport in the PCT. Various other essential solutes like amino acids, vitamins, and ions (e.g., sodium, potassium, calcium, and bicarbonate) are also reabsorbed in the PCT. Unfortunately, the PCT is highly susceptible to damage from various toxins and medications, which can disrupt its reabsorptive functions, a consideration in clinical settings where drug-induced kidney damage may occur.

The PCT also participates in the secretion of specific organic molecules and waste products, such as **drugs and hydrogen ions.** The reabsorption of bicarbonate ions and the secretion of hydrogen ions help **regulate the pH of the blood and**, consequently, the body's overall acid-base balance.

Filtrate leaving this tubule generally is unchanged due to **the equivalent water and ion reabsorption**, with an osmolarity (ion concentration) of 300 mOSm/L, which is the same osmolarity as normal plasma.

Nephron Loop or Loop of Henle

The Loop of Henle is a U-shaped section of the nephron that carries filtrate from the PCT to the distal convoluted tubule (DCT). It is divided into two segments: the **descending** and **ascending limbs**. Its two limbs have opposite jobs that help concentrate and then dilute the filtrate.

- The **descending limb** *lets water leave* but *does not let ions leave*. Because the medulla around it is very salty, water moves out of the LOH, making the filtrate more concentrated as it travels downward.
- The **ascending limb** does the **opposite**. It *lets ions leave* (especially sodium and chloride) but *does not let water leave*. As ions are pumped out, the filtrate becomes more dilute as it heads toward the distal tubule.

Distal Convoluted Tubule (DCT) and Collecting Duct (CD)

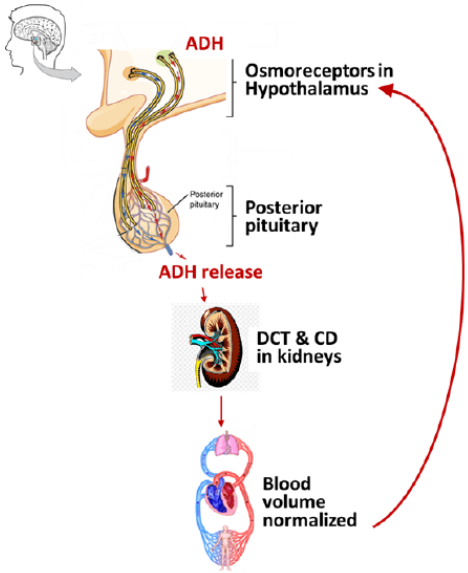
The **distal convoluted tubule (DCT)** and the collecting duct are the last places where the nephron can adjust what stays in the body and what becomes urine. Their permeability to water and ions is not fixed. Instead, their permeability changes depending on hormones, allowing the kidneys to help control blood osmolarity, volume, blood pressure, and pH.

The DCT also secretes substances into the filtrate, including potassium ions and certain drugs or toxins.

Multiple DCTs drain into a shared collecting duct, which is not considered part of any one nephron but is continuous with them. Each collecting duct receives filtrate from many nephrons and carries it downward through the cortex and into the medulla for final adjustments. As these ducts descend, they merge to form larger terminal ducts that open at the renal papilla.

The **collecting duct (CD)** functions much like the DCT, especially in its response to the antidiuretic hormone. When ADH is present, the walls of the collecting duct become more permeable to water, allowing additional water to be reabsorbed into the bloodstream. By the time the fluid finishes its passage through the collecting duct and enters the renal pelvis on its way to the ureter, all processing is complete and the filtrate is now considered **urine**.

Anti-Diuretic Hormone Feedback



One of the hormones that acts on the distal convoluted tubule (DCT) and especially the collecting duct is **ADH (antidiuretic hormone)**. **Antidiuretic means "against making urine."** An antidiuretic substance reduces the amount of urine the body produces. The main antidiuretic in the human body is the antidiuretic hormone. When your body needs to save water, ADH tells the kidneys to reabsorb more water and release less of it as urine. As a result, urine volume goes down and the body conserves water.

ADH is released from the **posterior pituitary** gland when plasma osmolarity increases, meaning the blood has become too concentrated. This usually happens when plasma volume drops or when ion concentration rises relative to the amount of water in the blood.

Osmoreceptors in the hypothalamus detect this increase in osmolarity and **signal the posterior pituitary to release ADH.** Once released, ADH travels to the kidneys and **acts on the nephrons** to retain water, lower plasma osmolarity, and produce urine that is more concentrated.

ADH works by increasing the water permeability of the **DCT and** the **collecting duct**, which are normally impermeable to water. With ADH present, more water is reabsorbed back into the bloodstream. This reabsorption increases blood volume and reduces the volume of urine produced.

When plasma volume goes up and therefore osmolarity returns to normal, the hypothalamic osmoreceptors stop sending signals, ADH release decreases, and the system returns to baseline. This makes ADH regulation a clear example of negative feedback.

Many substances that we ingest can act as diuretics or antidiuretics, albeit with different mechanisms.

A common example is **alcohol** and **water ingestion**, which directly **inhibit ADH secretion in the pituitary gland**.

Alternatively **caffeine is a diuretic** because it interferes with sodium reabsorption (reducing the amount of water reabsorbed by sodium cotransport) and increases the glomerular filtration rate by temporarily increasing blood pressure. Also, many medications act as diuretics because they slow water reabsorption.

Peritubular Capillaries

After blood leaves the glomerulus through the efferent arteriole, it does not return directly to the veins. Instead, it enters a second capillary network called the **peritubular capillaries**, which wrap closely around the proximal and distal convoluted tubules. These capillaries are low-pressure vessels that allow easy movement of water, ions, glucose, and other useful solutes back into the bloodstream. They also provide a route for the secretion of additional wastes from the blood into the nephron. In this way, the peritubular capillaries work hand-in-hand with the nephron tubules to fine-tune the composition of the filtrate and maintain homeostasis.

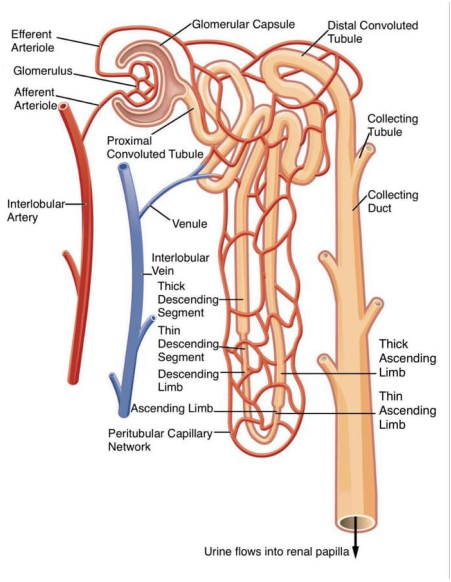


Figure 13.3.2: **The Nephron and Its Associated Blood Vessels.** Filtrate moves through the nephron while interacting closely with the kidney's blood supply. Filtration starts in the glomerulus within the glomerular capsule, where water and small solutes enter the nephron. The filtrate then flows through the PCT for major reabsorption, continues through the descending and ascending limbs of the nephron loop , and reaches the DCT for further ion regulation. It then enters the collecting duct, where water reabsorption is hormonally controlled. The peritubular capillary network, return reabsorbed substances to the bloodstream.

Do the Kidneys Have a Portal System?

You have previously learned that a *portal system* is a special circulatory pathway in which blood flows through **two consecutive capillary beds before returning to the heart**. Instead of going straight from one capillary bed back to the venous system, the blood is routed into a second capillary network. This arrangement allows substances picked up or released in the first capillary bed to be modified, filtered, or adjusted in the second. You learned about the **hypophyseal portal system** and the **hepatic portal system** in previous modules.

The kidneys do indeed have two capillary beds in a row, but they are *not* considered a portal system. A true portal system requires a **vein** connecting one capillary bed to the next. In the kidneys, the first capillary bed (the glomerulus) drains into an **efferent arteriole**, which then leads to the second capillary bed (the peritubular capillaries). Because an **arteriole**, not a vein, connects the two, the kidneys do not meet the definition of a portal system.

Nevertheless, the kidney's design is still unusual and highly specialized. The two capillary beds in the kidneys are the

1. **Glomerular capillaries**, located inside the renal corpuscle. These capillaries are uniquely specialized for **filtration**. They are high-pressure, fenestrated capillaries that push plasma out of the blood to form the initial filtrate.

2. **Peritubular capillaries**, surrounding parts of the nephron, they are designed for **reabsorption and secretion**. Their job is

to reclaim water, ions, glucose, and other useful materials from the filtrate and return them to the blood.

In Summary

A portal system requires: capillary bed → **vein** → second capillary bed.

But in the kidneys, the connection is: capillary bed → **arteriole** → second capillary bed.

Therefore, the kidneys do not have a portal system. Their very specialized vessel set-up, however, matters greatly, because arterioles can change diameter and therefore regulate pressure entering the second capillary bed. This regulation is essential for kidney function.

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13.4: Formation and Analysis of Urine

Urine formation is a three-step process that allows the kidneys to regulate blood composition while removing wastes and excess water from the body.

Master this section and you'll be able to

- Summarize the steps in urine formation
- Describe physical and chemical characteristics of urine
- Identify key urine test findings.

Urine Formation

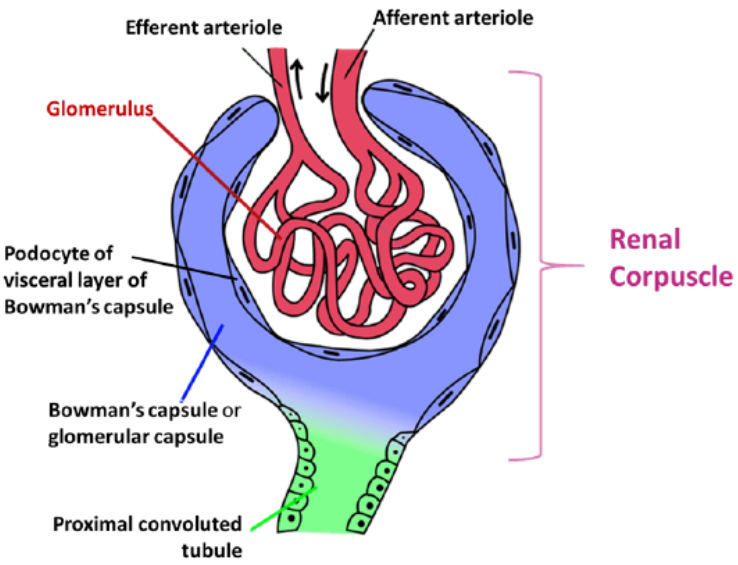
Urine is a waste byproduct that forms when the kidneys remove excess water and metabolic waste molecules from the blood. Although we often think of urine as the main output, the primary function of the renal system is actually to regulate blood volume and plasma osmolarity. Making urine is simply the most efficient way for the body to adjust water and solute levels while also removing wastes.

Urine formation relies on three key steps:

1. **Filtration**: Blood pressure forces water and small solutes out of the glomerulus and into the nephron.
2. **Reabsorption**: Useful substances such as water, glucose, amino acids, and ions move from the tubular fluid back into the bloodstream.
3. **Secretion**: Additional wastes, drugs, and excess ions are actively transported from the blood into the tubular fluid.

The three processes work together to maintain homeostasis and produce the final urine that leaves the body.

1) Filtration



Filtration begins when blood enters the afferent arteriole and flows into the glomerulus, a tuft of intertwined, fenestrated capillaries enclosed by the Bowman's (glomerular) capsule. About 20% of the cardiac output becomes the filtration fraction,

meaning this portion of the blood is routed to the kidneys for filtration while the remaining 80% continues through the systemic circulation.

The **Bowman's capsule** surrounds the **glomerulus** and consists of **two layers of simple squamous epithelium**. The parietal layer forms the outer wall of the capsule, while the **visceral layer** lies directly on the glomerular capillaries and is composed of specialized cells called **podocytes**. Podocytes extend foot-like processes that create narrow filtration slits. As blood flows through the glomerulus, water and small solutes such as nitrogenous wastes pass through these slits to form the **glomerular filtrate.**

Selectivity of the **filtration barrier** is maintained by three components working together: **the fenestrated capillary endothelium, the negatively charged basement membrane, and the podocyte filtration slits.** This combination prevents large molecules (such as albumin), negatively charged proteins, and all blood cells from entering the filtrate. These non-filterable components remain in the bloodstream and exit the glomerulus through the efferent arteriole, which then branches into peritubular capillary network that supports oxygen delivery to kidney tissues and participates in reabsorption and secretion before draining into the venous system.

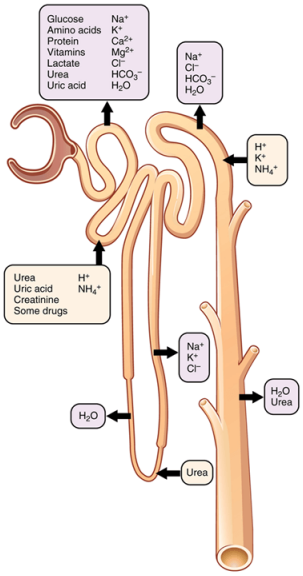
The Mechanisms of Filtration

Filtration at the glomerulus is driven mainly by pressure differences. The most important of these is **glomerular hydrostatic pressure**, which is the **blood pressure inside the glomerular capillaries**. This pressure pushes water and small solutes out of the capillaries and through the filtration slits of the Bowman's capsule.

Working against this pushing force is the osmotic pressure created by plasma proteins such as albumin. Because albumin stays in the blood, it pulls water back toward the capillaries. In other words, hydrostatic pressure pushes fluid out, and osmotic pressure pulls fluid in.

The balance between these two pressures determines the net filtration pressure, which is the actual force that drives filtration. When the pushing force of hydrostatic pressure is greater than the pulling force of osmotic pressure, filtrate moves into the glomerular capsule. These pressures, along with a few additional factors such as the resistance in the afferent and efferent arterioles, help determine the **glomerular filtration rate (GFR)**

The **GFR is the amount of filtrate the kidneys produce each minute**. Out of the roughly 5 liters of blood the heart pumps each minute, about 20% enters the kidneys for filtration. This produces about 125 mL of filtrate per minute in males and about 105 mL per minute in females (with normal ranges around these values). **Over a full day**, this adds up to about **180 liters of filtrate in males and 150 liters in females.** This seems like a huge amount, and — luckily — we do not produce anywhere near that much urine. In fact, as the filtrate travels through the nephron's tubules, the kidneys reabsorb almost all of it. Reabsorption is carefully regulated to help maintain stable blood volume, blood pressure, plasma osmolarity, and blood pH. Water, ions, and useful molecules move out of the tubules and back into the bloodstream through the peritubular capillaries, so they are not lost from the body. Because about 99% of the filtrate is reclaimed, only about 1 to 2 liters exit the body as urine each day.



2) Reabsorption

Reabsorption is the step in urine formation where the nephron takes back useful water, ions, and molecules into the bloodstream. As the filtrate flows through the PCT, loop of Henle, DCT, and CD, its composition changes because different parts of the nephron remove different substances. By the time the fluid reaches the collecting duct, most needed materials have been reclaimed, and a bit more secretion occurs before the final fluid leaves the kidney as urine.

Reabsorption happens in several ways, depending on the substance and the nephron segment:

- **Passive diffusion**: molecules move from a higher concentration to a lower concentration across the cell membrane without using energy.
- **Active transport**: membrane pumps use ATP to move substances like sodium ions against their concentration gradients.
- **Cotransport**: substances move together across the membrane, such as sodium pulling glucose or water with it. This helps water follow solutes that are actively reabsorbed.

The overall goal is simple: the nephron reabsorbs what the body needs and leaves behind what will become urine.

3) Secretion

Secretion is the final adjustment step in urine formation. During this step, certain substances leave the blood in the peritubular capillaries and enter the nephron's tubules so they can be eliminated from the body. This process works in the opposite direction of reabsorption and allows the kidneys to fine tune the composition of the blood by removing excess ions, wastes, and some medications.

Most secretion uses active transport, and some substances can also move by passive diffusion. Only a limited number of substances are normally secreted, and they are mainly wastes the body needs to remove. These include potassium ions, hydrogen ions, ammonium ions, creatinine, urea, some hormones, and certain drugs such as penicillin.

As an example, the kidneys help regulate the body's pH by secreting hydrogen ions (H^+) and ammonium ions (NH_4^+) from the blood into the tubular fluid. Removing these acidic ions helps prevent the blood from becoming too acidic. This process also helps the body conserve sodium bicarbonate ($NaHCO_3$), an important buffer that stabilizes blood pH.

Blood pH is normally kept between 7.35 and 7.45, while **urine is usually more acidic, with a typical pH around 6.0.** This difference reflects the kidneys' role in removing excess acid from the body.

Although the respiratory system is the main regulator of pH by adjusting CO_2 levels, the kidneys provide an important secondary line of defense. By secreting H^+ and NH_4^+, the kidneys fine-tune pH balance and help maintain homeostasis.

Once reabsorption and secretion are complete, the remaining fluid in the collecting duct becomes urine. Urine contains water that has not been reabsorbed and therefore represents a way for the body to lower blood volume by allowing more water to leave in the urine. Urea is the other major component of urine and provides a safe way for the body to remove nitrogen, which comes from protein metabolism. Urine also contains various ions and other waste products. Red blood cells and glucose are not normally present in urine, and their presence may indicate problems such as injury to the glomerulus or diabetes mellitus.

Because its composition reflects many internal body processes, urine is often used in diagnosing disease conditions. Physical and chemical features of urine can reveal important information about health, and these are commonly evaluated through urinalysis, a routine clinical test.

Basic Physical Characteristics of Urine.

Characteristic	Normal Findings	What Influences It	Possible Abnormal Causes
Color	Yellow to amber	Hydration level, diet	Dehydration, blood in urine (kidney damage or disease)
Smell	Mild odor when fresh	Time since voiding, diet	Sweet or fruity smell in diabetes, strong ammonia smell in aged urine
pH	4.6 to 8 (average about 6)	Diet, acid base balance	Persistent high or low pH may indicate metabolic imbalance or disease
Density (Specific Gravity)	1.001 to 1.035	Hydration, solute concentration	Very high values may reflect dehydration or excess solutes; very low values may indicate kidney problems
Turbidity	Clear or slightly cloudy	Time since voiding	Cloudiness due to infection, increased cells, or obstruction

Changes in any of these physical characteristics may indicate disease or metabolic imbalance. Although these changes may appear minor on their own, they can be early signs of conditions such as diabetes mellitus or glomerular damage.

Normal Chemical Composition of Urine

Urine is an aqueous solution of greater than 95% water, with a minimum of these remaining constituents, in order of decreasing concentration:

- Urea 9.3 g/L.
- Chloride 1.87 g/L.
- Sodium 1.17 g/L.
- Potassium 0.750 g/L.
- Creatinine 0.670 g/L.
- Other dissolved ions, inorganic and organic compounds (proteins, hormones, metabolites).

Formed in the **kidneys** and stored in the **bladder, urine** is **sterile** (free of harmful microbe). As it **passes through the urethra,** however, it picks up bacteria that live on the epithelial lining. Many of these bacteria are normal residents of the lower urinary tract and are usually harmless.

Urea is the main nitrogenous waste in urine. It is produced in the liver from ammonia and carbon dioxide. Ammonia is highly toxic to cells, so converting it to urea makes it much safer to transport in the blood and to eliminate from the body.

Abnormal Types of Urine

There are several conditions that can cause abnormal substances to appear in urine or cause urine to have abnormal characteristics. Many of these are named with the suffix **-uria**, which means “related to urine.” Some common examples are:

- **Proteinuria**: Protein in the urine, often due to leaky or damaged glomeruli in the kidneys.
- **Oliguria**: An abnormally small volume of urine, often caused by shock or kidney damage.
- **Polyuria**: An abnormally large volume of urine, often seen in diabetes and some other hormonal or kidney disorders.
- **Dysuria**: Painful or uncomfortable urination, often caused by urinary tract infections or inflammation.
- **Hematuria**: Red blood cells in the urine, which can result from infection, kidney stones, or other injury to the urinary tract.
- **Glycosuria**: Glucose (sugar) in the urine, usually due to high blood glucose in diabetes that exceeds the kidneys’ ability to reabsorb it in the proximal convoluted tubule.

Urinalysis

A urinalysis (UA) is a common diagnostic test that examines the physical, chemical, and microscopic characteristics of urine. It helps identify many medical conditions because urine contains measurable clues about how the body is functioning.

A standard urinalysis may **evaluate** substances such as **glucose**, **proteins**, **ketones**, and **red or white blood cells**, as well as properties like **pH** and **specific gravity**. Some parts of the test use **urine dipsticks,** which change color to indicate the presence or concentration of certain substances. Other parts require examining a small urine sample under a **light microscope.**

Clinicians typically order either a **routine urinalysis** or a **routine and microscopy (R&M)** urinalysis. A routine urinalysis includes the physical and chemical tests only. An R&M urinalysis adds microscopic analysis and may include culturing bacteria found in the urine. Because of this, R&M is particularly useful when evaluating possible urinary tract infections (UTIs).



Test Strip Urinalysis

Test strip urinalysis uses small reagent strips that change color when they come into contact with specific substances in urine. It is the most common method used in routine urinalysis because it is fast, inexpensive, and easy to interpret. A single strip can screen for several important findings, including:

• **Leukocytes** – White blood cells in the urine, called **leukocyturia**, often suggest inflammation or infection in the urinary tract.

• **Nitrites** – Certain bacteria convert nitrates into nitrites, so nitrituria is another indicator of a possible urinary tract infection.

• **Proteins** – Protein in the urine is called **proteinuria** (or albuminuria/microalbuminuria). This may point to increased permeability of the glomeruli or early kidney damage.

• **Blood** – The presence of red blood cells, called **hematuria**, can occur with infection, kidney stones, or injury.

• **pH** – Test strips can quickly determine urine acidity or alkalinity. Abnormal urine pH can help identify metabolic acidosis, alkalosis, or certain types of infections.

Urine Microscopy

The numbers and types of cells and/or material, such as urinary casts, can yield a great detail of information and may suggest a specific diagnosis. A urinary cast is any tiny structure found in urine that consists of multiple molecules or cells bound together.

Casts form within the nephron when abnormal cells and molecules are filtered from blood, and are excreted as the bound structures in urine. Microscopy can identify casts in urine and use them to diagnose kidney diseases, by characterizing symptoms such as:

- Red blood cell casts are associated with glomerulonephritis, vasculitis, or malignant hypertension.
- White blood cell casts are associated with acute interstitial nephritis, exudative glomerulonephritis, or severe pyelonephritis.
- Epithelial cell casts are associated with toxin-induced, acute tubular necrosis, hepatitis, and cytomegalovirus.
- (Heme) granular casts are associated with acute tubular necrosis, and are often composed of proteins, especially antibodies.
- Hyaline casts are associated with dehydration; it is the most common type of cast.
- Bacterial casts are associated with urinary tract infection; the cast may be cultured in order to identify the causative organism of the cast.

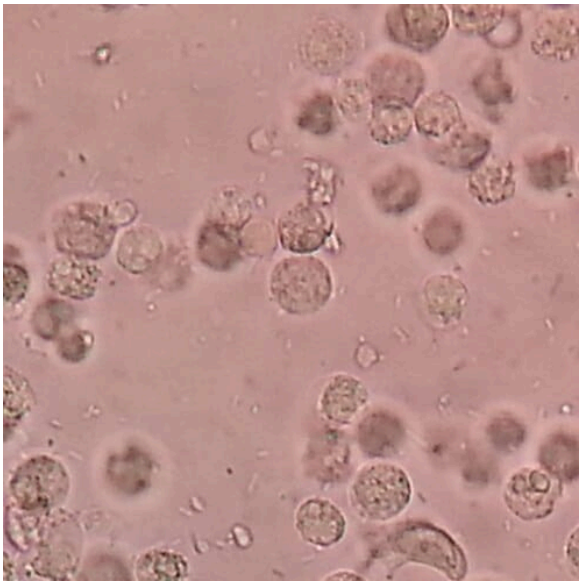


Figure 13.4.1: **Light-Microscope View of Urine Sediment.** This sample is from a patient with a urinary tract infection. Numerous white blood cells (WBCs) appear as round, granular cells scattered throughout the field, indicating inflammation within the urinary tract. Small bacterial clusters are also present, confirming active infection. Together, the high WBC count and visible bacteria are characteristic findings in a UTI.

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13.5: Urine Transport and Elimination

The urinary tract transports, stores, and releases urine through a coordinated system of tubes, muscles, and reflexes.

Master this section and you'll be able to

- Describe the path of urine flow from the renal pelvis to the exit from the body.
- Explain how the structure of the ureters, bladder, and urethra supports one-way transport, storage, and controlled release of urine.
- Summarize how the micturition reflex and sphincters regulate urination and how these processes relate to common clinical situations.

Besides the all important kidneys, the urinary system also includes the **urinary tract**, a set of tubular structures — the ureters, urinary bladder, and urethra — through which urine travels. This section follows urine as it leaves the kidneys, moving from the renal pelvis into the ureters, then the bladder, and finally the urethra. Although urine varies in composition, it must be removed safely and efficiently, so the body uses specialized structures to transport and store it. Blood is filtered continuously, and the resulting filtrate is processed into urine at a fairly steady rate. The urine is then stored until it can be excreted at an appropriate time. All organs that transport or store urine are visible to the naked eye, and together they not only move and hold this waste fluid but also protect tissues from damage, help prevent infection, and in males contribute to reproductive function.

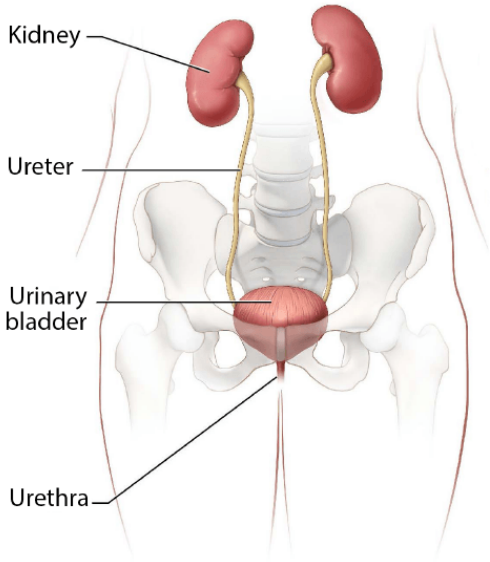


Figure 13.5.1: **Urinary Tract Organs.** The organs of the urinary tract transport, store, and void urine. *(Image credit: "Organs of the Urinary System" by NIH Medial Arts is licensed under CC-BY-NC 2.0.)*

Ureters

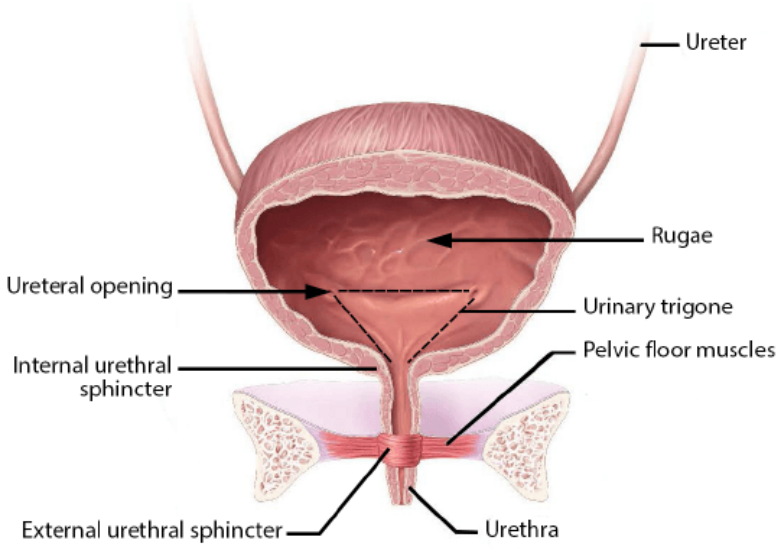
As urine is produced, it first drains into the minor and major calyces of the kidney, which merge to form the funnel-shaped **renal pelvis located in the hilum**. The ureters are two narrow tubes, about 30 cm long. They are made of **smooth muscle** and lined with **transitional epithelium**, a special tissue that can appear columnar when stretched and squamous when relaxed. Each kidney has its own ureter, and these tubes carry urine from the renal pelvis down to the urinary bladder.

Along their length, ureters have a few natural points of narrowing where kidney stones or other obstructions are more likely to lodge. Urine does not simply drip into the bladder. Instead, **peristaltic waves move urine along the ureters**.

The smooth muscle in the ureter wall contracts rhythmically. These waves of contraction — just like in the GI tract called **peristalsis** — push urine toward the bladder in small spurts rather than allowing it to simply drain by gravity. When urine enters

the bladder, small transverse folds of the bladder mucosa act as one-way valves (the ureteral valves) and prevent urine from flowing backward into the ureters. Pregnancy can increase the chance of urine flowing backward (reflux) into the ureters, which raises the risk of a **UTI**. As the uterus grows, it can press on the ureters and partially block the normal flow of urine into the bladder. When urine cannot drain easily, it may back up toward the kidneys, creating conditions where bacteria can grow more easily and cause infection.

Urinary Bladder



The urinary bladder collects urine arriving from the two ureters. Each ureter enters the bladder on the inferior posterior wall, one on each side of the urethral opening. These three openings define the **trigone**, a smooth triangular region that lacks the folds found in the rest of the bladder's mucosal lining (Greek tri = "three," as in "trigonometry").

In females, the bladder lies anterior to the uterus, posterior to the pubic bone, and anterior to the rectum. Late in pregnancy, the enlarging uterus compresses the bladder and reduces its capacity, which increases urinary frequency. In males, the bladder is positioned similarly but without the uterus and with the **prostate gland** located just inferior to it. The bladder is **partially retroperitoneal**, and its dome is covered by peritoneum, which allows the dome to rise into the abdominal cavity when the bladder becomes full.

The wall of the bladder is highly distensible because its middle layer is composed of the **detrusor muscle**, a thick layer of smooth muscle arranged in irregular, crisscrossing bundles. When stimulated during the micturition reflex, the detrusor muscle contracts to generate the force needed to expel urine. The interior surface of the bladder is lined with **transitional epithelium**, which changes shape depending on bladder volume. When the bladder is empty, these epithelial cells appear more cuboidal or columnar; when stretched, they become squamous and allow the lumen to expand. Most of the bladder's mucosa contains rugae that flatten out during filling, similar to the stomach. Adult bladder capacity varies but generally ranges from nearly zero when empty to about 500 to 600 mL when full. Although bladder muscle tone decreases with age, contraction of abdominal skeletal muscles can increase intra-abdominal pressure and assist with more forceful bladder emptying.

Micturition Reflex

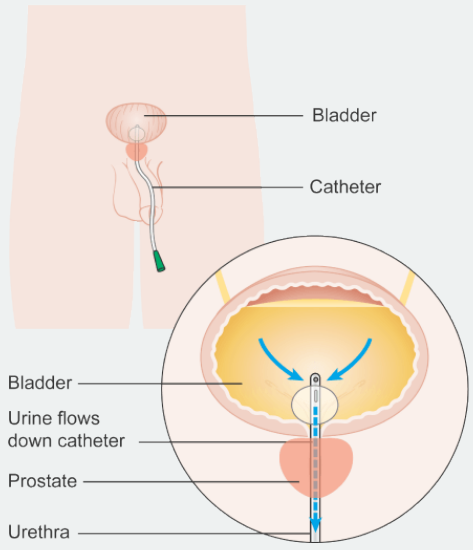
Micturition is a technical term for urination or voiding. It depends on both involuntary and voluntary control of two sphincters: the smooth-muscle internal urethral sphincter and the skeletal-muscle external urethral sphincter. **As the bladder fills to about 150 mL, stretch receptors begin sending signals that create the first urge to urinate**, but this urge can be consciously suppressed by keeping the external sphincter contracted. As bladder volume increases, the sensation becomes stronger and more difficult to ignore. Once the bladder reaches roughly 300 to 400 mL, voluntary control may fail, and involuntary leakage (incontinence) can occur.

The basic mechanism of micturition is a **spinal reflex.**

Stretch receptors in the bladder wall send signals to the sacral spinal cord, which responds with **parasympathetic output** that **contracts the detrusor muscle and relaxes the internal sphincter.** At the same time, **somatic motor neurons to the external sphincter are inhibited**, causing that sphincter to relax. In infants, this spinal reflex operates without conscious control, which is why urination is automatic early in life. As the nervous system matures, children learn to override the reflex by keeping the external sphincter contracted until an appropriate time to void.

In certain spinal cord injuries, the micturition reflex may remain intact even though voluntary control is lost. In these cases, the bladder may still contract reflexively, but the person may not be able to relax the external sphincter voluntarily. When coordinated emptying is not possible, intermittent catheterization may be required to remove urine safely from the bladder.

Catherization



Difficulties voiding may require catheterization so that urine does not back up into the urinary tract and potentially damage the kidneys. A urinary catheter is a flexible tube inserted through the urethra into the bladder to allow urine to drain into a collection bag. Catheter placement is usually performed by a trained health professional, although some individuals with chronic conditions learn to self-catheterize. A catheter may remain in place for extended periods (indwelling catheter) or be inserted and removed each time it is needed (intermittent catheterization).

The most common type of indwelling catheter is the Foley catheter, which is held in place by a small balloon at the tip. For removal, the balloon is simply deflated. Intermittent catheters do not have a balloon and therefore cannot be anchored; they are designed for temporary, single-use drainage.

Common reasons for urinary catheterization include:

- Urethral obstruction, such as scarring or prostate enlargement, that prevents normal urine flow
- Bladder weakness or nerve injury that interferes with voluntary voiding
- Bladder drainage during childbirth when an epidural anesthetic reduces bladder sensation
- Bladder drainage before, during, or after certain surgeries

Figure 13.5.2: **Foley Catheter.** A urinary catheter is placed in the bladder to provide passage for urine. Foley catheters have a balloon below the intake opening that is inflated to keep the catheter in place within the urinary tract. *(Image credit: "Urinary Catheter" by Cancer Research UK is licensed under CC BY-SA 4.0, via Wikimedia Commons.)*

Urethra

The urethra transports urine from the bladder to the outside of the body for disposal. It is the only structure in the urinary tract that differs significantly between males and females; all other urine-transport structures are essentially identical. The most noticeable

difference between the two urethras is **length**, but their **course** and **function** also differ in ways that have important clinical consequences.

In males, the urethra is long, about 18 to 20 cm. It passes through the **prostate gland**, the pelvic floor, and the **penis**, and its course is curved. It has a **dual role** because it carries both **urine** from the bladder **and semen** from the reproductive tract.

In females, the urethra is much shorter, about 3 to 5 cm. It follows a relatively straight path from the bladder to its opening in the vulva, just anterior to the vaginal opening, and its only function is to conduct urine.

Clinical Implications

Because the **female** urethra is short and its opening lies close to the vagina and anus, **bacteria** have a shorter and more direct route to the bladder. This helps explain the higher incidence of **urinary tract infections (UTIs)** in people with female anatomy.

In contrast, the **male** urethra is longer and its opening is more distant from potential sources of bacteria. UTIs are therefore less common in males, but other conditions such as **urethral strictures or obstruction from prostate enlargement** are more common concerns.

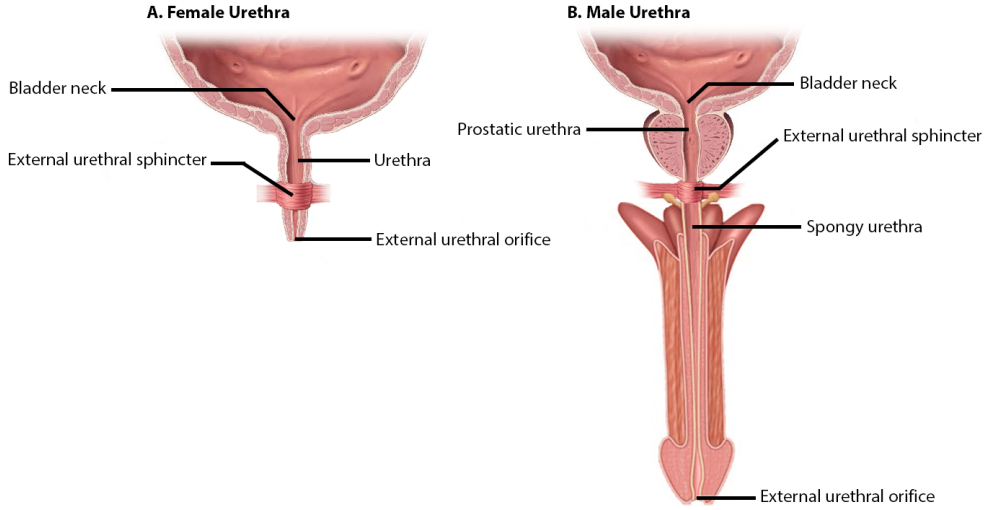


Figure 13.5.3: **Comparison of the Female and Male Urethra.** The urethra transports urine from the urinary bladder to the outside of the body. The female urethra (A) is short, as it only passes through the pelvic floor before reaching the external surface. The majority of the male urethra (B) is shared by the urinary and reproductive systems and, thus, is longer because it passes through both the prostate gland and the penis. *(Image credit: "Urethra Comparison - Male and Female" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Modification of originals "Organs of the Urinary System" by NIH Medial Arts and "Cenveo - Drawing Male and female urinary tract - English labels" by Cenveo.)*

In both males and females, the **proximal (upper)** part of the urethra is lined with **transitional epithelium**, the same stretchable tissue found in the bladder. As the urethra approaches the body's exterior, this changes to a **nonkeratinized, stratified squamous epithelium**, which is better suited to protect against friction at the urethral opening.

Voiding is controlled by **two sphincters** stacked vertically:

• The **internal urinary sphincter** sits at the bladder–urethra junction. It is made of **smooth muscle** and is regulated **involuntarily** by the autonomic nervous system.

• Just below it is the **external urinary sphincter**, made of **skeletal muscle**. This sphincter is **under voluntary control**, allowing a person to consciously delay urination.

Can you assign the appropriate terminology to each number?

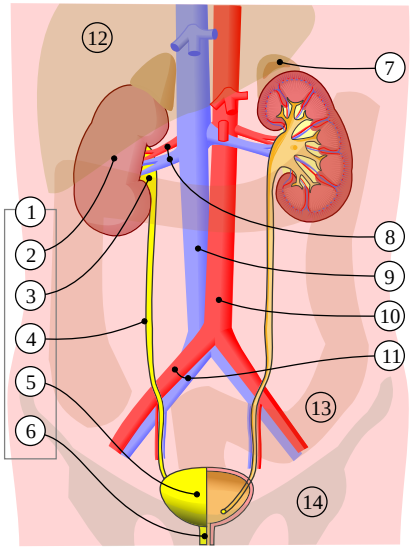


Figure 13.5.4: **Labeling Practice.** Can You Assign a Name to All of these Numbers?

1) Human urinary system. 2) Kidney. 3) Renal pelvis. 4) Ureter. 5) Urinary bladder. 6) Urethra. 7) Adrenal gland. 8) Renal artery and vein. 9) Inferior vena cava. 10) Abdominal aorta. 11) Common iliac artery and vein. 12) Liver. 13) Large intestine (colon);14) Pelvis.

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13.6: Kidney Stones

Kidney stones form when crystals build up, and while many remain silent in the kidney, they often become painful and symptomatic when they move into and obstruct the ureters.

Master this section and you'll be able to:

- Describe what kidney stones are, how they form, and list common risk factors for developing them.
- Explain why stones cause pain when they move into the ureters and identify common symptoms of a urinary tract stone.
- Recognize how kidney stones are diagnosed and treated.

Nephrolithiasis

Nephrolithiasis (pronunciation) is the medical condition marked by the presence of **renal calculi** (pronunciation), commonly known as **kidney stones.** It refers to solid pieces of material that form in the kidneys when certain substances in the urine, such as **calcium** or **uric acid**, crystallize. Renal calculi — plural for one renal calcul**us** — may be as small as a grain of sand or as large as a pearl.



Most kidney stones pass out of the body on their own, but some become lodged in the ureters. The most common locations are where the **renal pelvis narrows to become the ureter,** and where **the ureter enters the urinary bladder.** When this happens, the stone can block the flow of urine and cause intense **pain**. The pain is usually felt in the **flank** (the side of the body — **posterolateral region** — between the ribs and the hip.) Additional symptoms may include **hematuria** (blood in the urine), fever and chills, vomiting, foul-smelling urine that may appear cloudy, or **dysuria** (painful urination).
Note: Blood in urine supports the diagnosis but **absence of blood does not rule it out**.

Common Types of Kidney Stones

Kidney stones come in several types, each named for the crystals that form them.

- **Calcium stones** (most common): **calcium-oxalate or calcium-phosphate stones.** They develop when a person is not drinking enough fluids or consumes too many high-oxalate foods.
- **Uric acid stones** appear more often in people who eat large amounts of animal protein.
- **Struvite stones** often form in response to urinary tract infections (UTIs) and can grow into very large “staghorn” stones.

- **Cystine stones** are a **rare type of kidney stone** caused by a **genetic disorder called cystinuria**. In people with cystinuria, the kidneys do not properly reabsorb **cystine**, an amino acid that normally stays dissolved in the blood. As a result, **too much cystine enters the urine**. Cystine does not dissolve well in urine. When its concentration becomes too high, it **crystallizes and forms stones**.

Many factors increase the risk of developing kidney stones. These include **dehydration, a high intake of meat, sodium,** or **sugars**, certain medications, and a family history of stones. Previous stomach or intestinal surgery or specific medical conditions such as cystic fibrosis, diabetes, gout, obesity, inflammatory bowel disease, osteoporosis, parathyroid disorders, and conditions that elevate calcium or oxalate levels in the urine can also increase the risk.

Kidney stones may lead to several complications if they obstruct urine flow or irritate the urinary tract. A blockage can cause **hydronephrosis**, where the kidney swells with trapped urine, and stones can also lead to kidney infections, repeated UTIs, or acute kidney injury. Over time, recurrent stones may contribute to chronic kidney disease, highlighting the importance of early diagnosis and prevention.

Most stones **form in the kidneys**, but they often do not cause symptoms until they **leave the kidney and enter the ureter**. Inside the kidney, stones may sit quietly for months or years without being noticed. Once a stone drops into the ureter, the narrow muscular tube, the body reacts strongly. The ureter tries to push the stone toward the bladder with waves of peristalsis, which is why people feel sudden, severe flank pain.

So, in terms of location:

- **More stones exist in the kidneys**, because that is where they actually form.
- **More symptomatic or "detected" stones are found in the ureters**, because that is where they get stuck and cause pain, obstruction, or hematuria.

Clinically, stones in the kidney may be found incidentally on imaging, but stones in the ureter are far more likely to bring a patient to the ER.

The single best diagnostic evidence for kidney stones is a non-contrast **CT scan of the abdomen and pelvis.** The reason why CT-scans are the gold standard in the diagnosis of nephrolithiasis is that they detect >95% of kidney and ureteral stones. CT scans (unlike regular X-rays) can also visualize the size and exact location of **all stone types** (calcium, uric acid, cystine, and struvite), and finally, this method can identify complications such as complete obstruction or hydronephrosis.

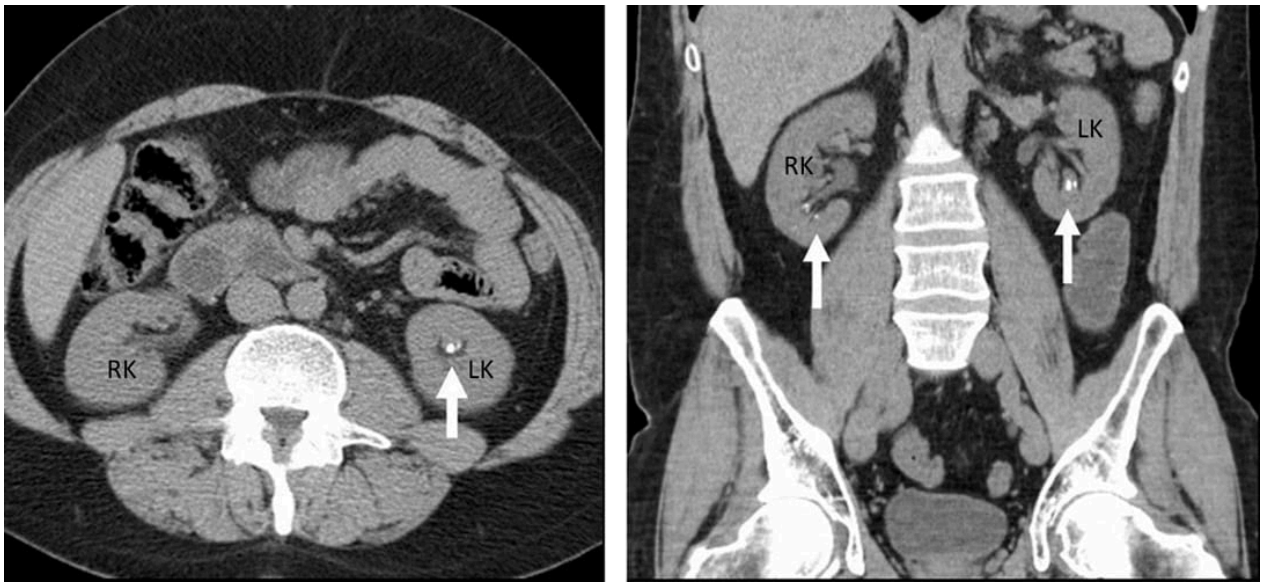


Figure 13.6.1: **CT Scan of the Abdomen with Multiple Renal Calculi.** Note in the axial cross-section image on the left that axial CT images are displayed as if you are standing at the patient's feet and looking up toward their head. Because you are facing the patient, the patient's right side appears on the left side of the image, and the patient's left side appears on the right side of the image.

The bright structures are bone, since osseous tissue is very dense. Surrounding fat appears dark, which helps outline abdominal organs. This image shows multiple renal calculi. (https://commons.wikimedia.org/wiki/F...al_calculi.jpg)

Case Study: Sudden Flank Pain in the Emergency Department



Patient Presentation

A 54-year-old woman arrives at the emergency department complaining of **severe pain in her left flank**. She describes the pain as intense and cramp-like, coming in waves rather than remaining constant. At times, the pain becomes so strong that she almost doubles over and cannot find a comfortable position.

She also reports that earlier in the day she noticed what looked like **blood in her urine**, and as the day progressed, the pain began to radiate from her lower back around to the **left groin**.

Questions

1. Where is the flank located anatomically? Use some of the anatomical terminology that you learned in Module 1.

2. Why might pain that radiates from the flank to the groin suggest involvement of the ureter rather than the kidney alone?

3. Why do you think this pain comes in waves instead of being constant?

Medical History

The patient has a history of **uterine fibroids**, also called leiomyomas. These are noncancerous growths of smooth muscle that develop in the wall of the uterus and are very common in women.

Although fibroids can cause pelvic pain or abnormal bleeding, they usually do not cause flank pain or blood in the urine.

Questions

4. Which body system is primarily affected by uterine fibroids?

5. Why is it important to consider a patient's medical history even when it may not directly explain the current symptoms?

6. Based on the symptoms so far, do uterine fibroids seem like the most likely cause of this patient's pain? Why or why not?

Physical Examination and Laboratory Findings

On physical examination, the health care provider notes **left costovertebral angle tenderness**. This means that pressing on the area overlying the kidney causes pain.

A urine sample shows visible blood.

Urinalysis confirmed **hematuria.**

Question

7. List two possible causes of hematuria and how could a solid object inside the ureter lead to blood appearing in the urine?

Differential Diagnoses

Before imaging, several conditions are considered:

- Urinary tract calculus
- Urinary tract infection
- Renal mass
- Ovarian torsion

Questions

8. Which of these conditions is most consistent with sudden, severe pain that comes in waves?

9. Which condition on the list is most likely to be associated with fever?

Imaging

The **noncontrast CT scan of the abdomen and pelvis** came back as follows:



Figure 13.6.2: **CT Imaging of the Patient's Abdomen.** Visible in this coronal (frontal) CT image, which displays the kidneys, ureters, and surrounding abdominal structures is the fact that the left kidney is mildly **hydronephrotic** (swollen) and there is mild inflammation of the surrounding fat. A dense, small (5mm), calcification is seen in the left ureter. Interpretation: *Left ureteric calculus*

Questions

10. Why is CT imaging preferred over plain X-ray for detecting kidney stones?

11. Why is correct image orientation especially important in cases involving paired organs like the kidneys?

12. What does hydronephrosis indicate about urine flow and why does the ureter appear dilated above the stone?

Diagnosis: Left Ureteric Calculus

The question now is: will the stone pass on its own? As it turns out:

- Stones **5 mm or smaller** often pass spontaneously
- Larger stones are more likely to require intervention (see below).

Treatment



Extracorporeal Shock Wave Lithotripsy (ESWL)

ESWL is a **noninvasive** procedure used to treat some of the kidney and ureter stones **without surgery**. A machine outside the body sends focused, **high-energy shock waves** through the skin and soft tissues until they reach the stone. The repeated shock waves create tiny fractures that break the stone apart, eventually reducing it to pieces as small as grains of sand. These small fragments can then move through the ureter more easily and pass out of the body in the urine. ESWL works best for stones that are not extremely large and are located where the shock waves can be accurately targeted.

YouTube Video

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Percutaneous Nephrolithotomy

This technique is used for **large**, **irregularly shaped**, or **difficult-to-reach** kidney stones, especially when ESWL has not worked or when the patient is not a good candidate for other minimally invasive procedures. In this technique, the surgeon makes a small incision in the back directly over the kidney and inserts a nephroscope, which is a slender instrument equipped with a fiberoptic camera. Through this tract, the surgeon can visualize the stone and use specialized tools to break it apart and remove it. This method is more invasive than ESWL but very effective for stones that would otherwise be impossible to pass.

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13.7: Water Balance

Water balance is essential and disruptions from dehydration, overhydration, or environmental stresses can quickly impair normal body function.

Master this section and you'll be able to:

- Explain how the kidneys, thirst mechanism, and ADH work together to regulate water balance.
- Describe the effects of dehydration and overhydration on blood volume, temperature regulation, and brain function.
- Apply water balance concepts to situations such as aging, exercise, heat exposure, and alcohol consumption.

Water Balance and Why It Matters

Water balance means that the amount of water we take in matches the amount we lose. The kidneys and the thirst center in the brain work together to keep this balance steady. When we have not taken in enough water, we feel thirsty and the kidneys produce more concentrated urine. When we have more water than we need, we do not feel thirsty and the kidneys produce dilute urine.

In **older adults**, the **thirst mechanism is not as reliable**. They may not feel thirsty even when their body needs water, so they need to drink regularly throughout the day. Thirst is also not a good indicator when the body is losing water very quickly, such as with **severe diarrhea, vomiting, fever, or heavy sweating during intense exercise.** In these situations, dehydration can develop faster than the body's normal control systems can respond.

Many body functions depend on water, so the balance between intake and loss must stay within a fairly narrow range. There is only a limited amount of flexibility before dehydration begins to interfere with normal function.

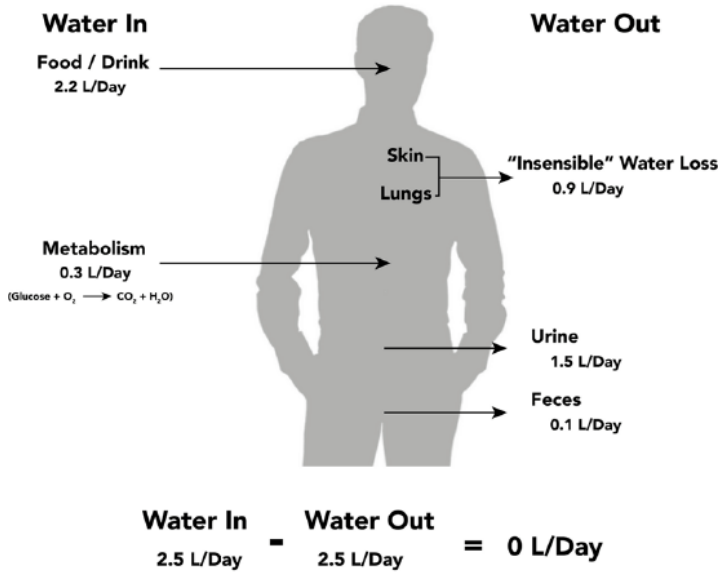


Figure 13.7.1: **Daily Water Balance in the Human Body.** The body maintains water balance by matching daily water intake with water loss. Most water comes from food and drink, while a smaller amount is produced during metabolism. Water leaves the body through several routes, including "insensible losses" from the skin and lungs, urine produced by the kidneys, and a small amount in feces. In a healthy adult, total water in (about 2.5 L per day) equals total water out (about 2.5 L per day), keeping body fluid levels stable.

Dehydration

As dehydration develops, the body protects the organs and systems that are essential for survival. Maintaining blood volume is one of the highest priorities because circulation depends on it. To preserve blood volume, the body will reduce water loss in areas that are less immediately critical, such as sweating. This is why the body may allow only a certain amount of water to be used for cooling when conditions are hot and dry.

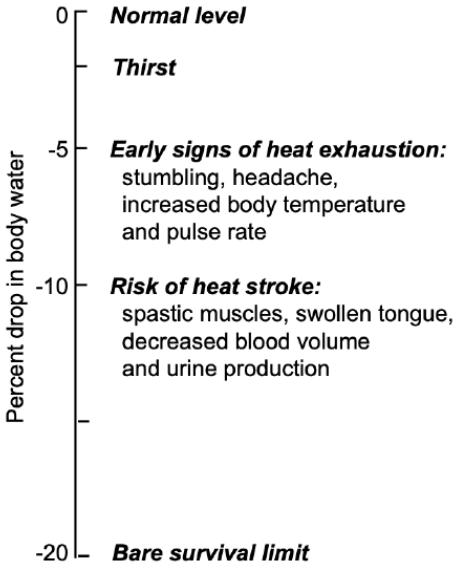
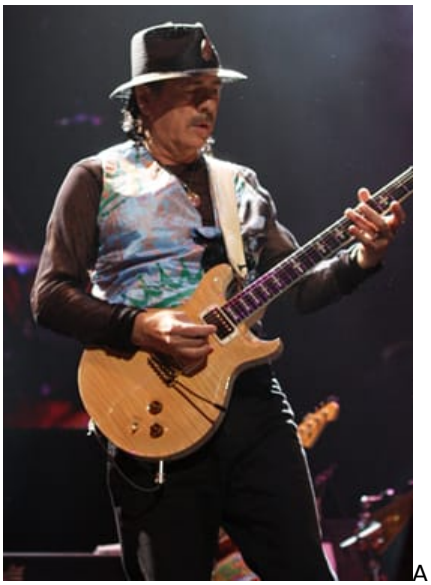


Figure 13.7.2: **Effects of Progressive Dehydration on the Human Body.**

Limits of the Body's Water-Saving Response

The body can conserve water for only a short time. Holding back sweat helps preserve fluid, but it also allows body temperature to climb.

- Normal core temperature is about **37 °C** (98.6 °F).
- An increase of **6–7 °C** means a core temperature of **43–44 °C** (about 109–111 °F), which is incompatible with survival for more than a very short time.

 A real-world example occurred in April 2025, when 77-year-old guitarist **Carlos Santana (musician, age 77)** was getting ready for a concert in San Antonio, Texas. He developed a medical problem during preparations and had to be taken to the hospital. His manager later explained that he had been hospitalized for dehydration, and the show was postponed while he was monitored and rehydrated. He recovered and planned to resume his tour once stable.where doctors determined that he was dehydrated. The show was postponed while he was monitored and rehydrated, but after treatment and rest he resumed his Oneness Tour later that week.

A loss of only about five percent of body water may trigger early heat-exhaustion symptoms such as weakness, headache, and a rapid, weak pulse. When body water falls to around ten percent below normal, the risk of heat stroke becomes high. Heat stroke is a medical emergency and can be fatal if not treated quickly.

Even without heat exposure, dehydration lowers total blood volume. Reduced blood volume leads to lower blood pressure and a weak, fast pulse, as the heart works harder to maintain circulation. If the problem continues, decreased circulation can cause dangerous complications, including the inability to produce urine.

Can You Drink Too Much Water?

Although we often worry about drinking too little, there is also a condition in which people drink far too much and develop **water intoxication**. In some cases, compulsive water drinking is part of a psychological disturbance, leading a person to consume such large volumes of water that the kidneys cannot eliminate the excess quickly enough. This causes the body's fluids to become overly diluted, allowing water to move into tissues and make them swell. The brain is especially vulnerable because it is enclosed within the skull and cannot expand safely.

Early symptoms include headache and vomiting. These can also occur with dehydration, which shows how headaches often serve as a general signal that something in the body is amiss.

Cases of water intoxication have occurred when **fraternity pledges** were forced to drink large quantities of water during **hazing**, sometimes with fatal outcomes. Your study guide mentions Matthew Carrington, who died in 2005 after a water-drinking hazing ritual at Chico State University. In spite of stronger laws meant to prevent this dangerous behavior, it is astonishing that such hazing tragedies continue. Not with water, but with alcohol and other noxious methods. In fact, **alcohol-related hazing is the most common and most deadly form of hazing**.

Unfortunately there are **other documented cases of water intoxication** besides hazing deaths in college fraternities. So, while water intoxication is rare, it has been documented in several settings:

1. **Radio contest: "Hold Your Wee for a Wii":** In 2007, Jennifer Strange, a 28-year-old mother of three, died after a radio contest in which participants drank large amounts of water without urinating. She consumed nearly two gallons in a few hours and later died of water intoxication.

2. **Military training and endurance sports:** Some military trainees and endurance athletes have developed fatal hyponatremia after drinking extreme amounts of water to prevent dehydration, overwhelming the kidneys' ability to excrete the excess.

3. **Psychiatric conditions** (**psychogenic polydipsia**): Certain psychiatric disorders, such as schizophrenia or bipolar disorder, can lead to compulsive water drinking. In severe cases, this can cause hyponatremia, brain swelling, and even death.

Alcohol and Dehydration

Drinking alcohol leads to dehydration. If that seems strange, consider what alcohol does inside your body:

Alcohol readily crosses the blood–brain barrier, because ethanol is a small and lipid-soluble molecule. In the brain, ethanol acts on the hypothalamic nuclei that normally synthesize **antidiuretic hormone** (ADH). As you have learned, these neurons send their axons to the **posterior pituitary, where ADH is stored** and then released into the bloodstream. ADH's role is to increase water reabsorption in the kidney DCTs and collecting ducts, helping the body conserve water. When alcohol suppresses the activity of these hypothalamic neurons, less ADH is released from the posterior pituitary, so the collecting ducts become less permeable to water and reabsorb less of it, leading the kidneys to produce a larger volume of relatively dilute urine.

This extra urination pulls water out of the body more quickly than usual, decreasing total body water and lowering blood volume. The result is dehydration, which contributes to thirst, dizziness, fatigue, and the famous "morning-after" headache. In fact, a portion of a hangover is simply your body reacting to water loss. Drinking water during or after consuming alcohol helps replace some of the fluid your kidneys are rapidly sending out of the body.

In hot conditions, your body is already losing water through sweat. With less water available, alcohol becomes a larger proportion of your blood, so it will affect you more quickly. A beer, which has more water relative to alcohol, is usually a better choice in hot weather than a strong cocktail.

Add Exercise or High Altitude, and the Effect Intensifies. Heavy exercise and high altitude both increase water loss. At high altitude, the air is dry and thinner, so you lose more water when you breathe. After a tough tennis match in the sun or while on a mountain vacation, even a small amount of alcohol can feel stronger because there is less circulating blood volume to dilute it.



The same thing happens on airplanes. Cabin air is very dry, similar to high-altitude conditions on land. Dehydration contributes to jet lag, so staying hydrated and limiting alcohol makes a real difference during air travel.

What Controls Your Body's Need for Water?

Adults need roughly 2 quarts of water each day to replace normal losses. About one quart is lost as urine, and the rest leaves the body through sweat, breathing, and feces. A general guideline is about one quart of water for every 1,000 calories consumed, while infants need about one and a half quarts per 1,000 calories. Daily needs rise in hot or dry climates or during strenuous activity because evaporation from the skin and lungs is a major cooling mechanism. Under extreme heat and exertion, such as in soldiers working in the desert, water loss can reach one quart per hour.

There are many misconceptions about water and sports. Some coaches still tell young athletes to limit drinking during a hot, intense game. In truth, unless someone drinks extreme amounts very quickly, water will not cause cramps or other problems. The real danger is poor performance or even serious illness when players do not drink enough. Thirst is usually a reliable warning that the body needs water, although the absence of thirst does not necessarily mean the body is fully hydrated.

Hot, strenuous activity creates special risks because athletes can lose water faster than they can drink it. During long events, athletes cannot rely on thirst alone and often cannot replace water losses quickly enough. This is why athletes should drink plenty of water before, during, and after activity lasting more than thirty minutes, even if they do not feel thirsty. Cold water may be absorbed slightly faster and helps cool the body, but room-temperature water works as well.

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13.8: Overview of the Human Reproductive System

The reproductive system produces gametes, supports fertilization and pregnancy, and enables the development and birth of a new individual.

Master this section and youi'll be able to:

- Describe the major structures and functions of the male and female reproductive systems.
- Distinguish diploid and haploid cells by chromosome number and explain why haploid gametes are necessary.
- Compare mitosis and meiosis.

Understanding the Language of Biological Sex in Anatomy and Physiology

When you study Anatomy and Physiology, you will often encounter descriptions of how structures and processes differ between the biological sexes. In everyday language, the words “female” and “male” may refer either to gender identity or to biological sex. In science, however, these terms refer specifically to biological sex, which is determined by chromosomes, hormones, and reproductive anatomy. Gender identity is a separate concept related to how a person experiences and identifies themselves, and it may or may not align with the sex assigned at birth.

In this course, the terms *female* and *male* refer only to biological sex and to the typical anatomy and physiology associated with XX (female) and XY (male) chromosomal patterns.

The Role of the Reproductive System

The reproductive system enables the production of offspring and supports the biological processes required for **fertilization**, **pregnancy**, and **birth**. It includes sets of paired or complementary organs in biological males and females, and its functions are coordinated by **multiple hormones.** In humans, reproduction occurs through **internal fertilization:** sperm enter the female reproductive tract and may unite with an ovum, forming a **zygote** that begins development into an **embryo** and eventually a **fetus**.

Major Structures of the Male and Female Reproductive Systems

In this section, you will explore the structures and functions of the male and female reproductive systems and discover how healthy coordination between these systems can culminate in the powerful sound of a newborn’s first cry.

Before diving into the details, let's cover some basic common terms. Unique for its role in human reproduction, a **gamete** is a specialized sex cell carrying **23 chromosomes** — one half the number found in other body cells. **Gonads** are the organs that make the gametes. Once the gametes are made, they travel in tubular structures. These structures are often the site for permanent sterilization procedures because if the gametes of the opposite sex cannot meet, then fertilization will not be possible. Comparing the midsagittal view of the female and male pelvis, there are multiple differences *(See figures below)*. We will first start with the discussions on the male reproductive system, then move to the female.

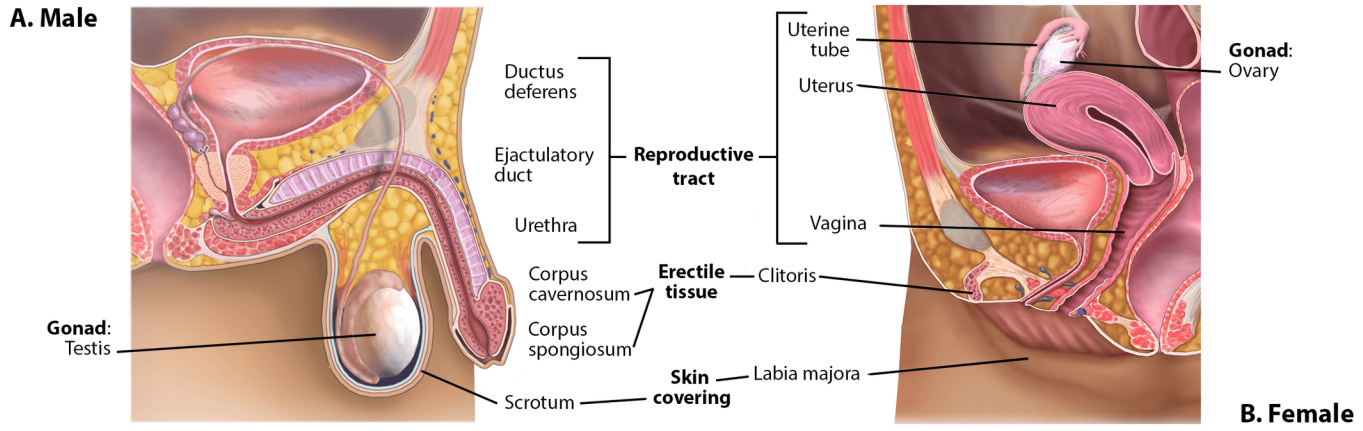


Figure 13.8.1: **Male and Female Homologous Structures in the Reproductive System.** Because they develop from common structures (primordial tissues) and serve a common function in adults, many of the reproductive organs are homologous between the male and the female. *Homologous* means that two structures share a **common developmental origin**, even if they end up looking different or performing different functions in adults. *(Image credit: "Reproductive System Homologues - Male and Female" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of "Varicocele" by BruceBlaus and of "Female Reproductive System - Midsagittal" by Blausen.com staff (2014), from the Medical gallery of Blausen Medical 2014, WikiJournal of Medicine.)*

Comparison of Male and Female Reproductive Structures

Term	Male	Female
Gonads	Testes	Ovaries
Gametes	Sperm	Ova (ovum, singular, also known as eggs)
Tract Organs	Ductus deferens (or vas deferens), ejaculatory duct, urethra	Uterine tubes (or Fallopian tubes), uterus, vagina
Permanent Sterilization Procedure	Vasectomy	Tubal ligation, hysterectomy
Copulatory organ	Penis	Vagina

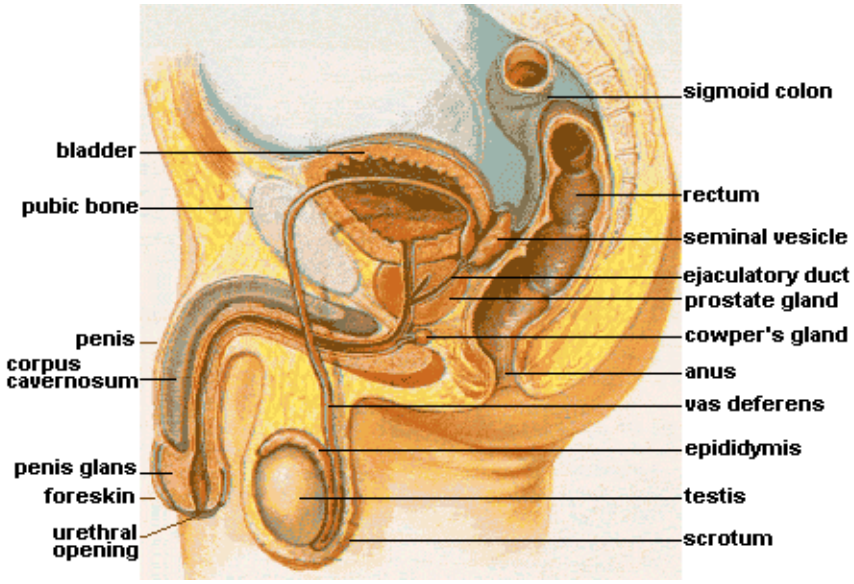
Sexual maturity begins with **puberty**, when the reproductive organs start producing gametes.

Male Reproductive System

The human male reproductive system consists of internal and external organs located in and around the pelvic region. Its primary biological function is to produce, store, and deliver sperm for potential fertilization of an ovum. The organs can be grouped into three functional categories:

Sperm Production and Storage

- **Spermatogenesis** occurs in the seminiferous tubules of the **testes**. The testes produce both **sperm** (**male gametes**) and **testosterone**.
- **Epididymis**: A long, coiled tube where sperm mature and are stored until ejaculation.



Accessory Glands

The accessory glands produce the fluids that support and transport sperm. **Semen** is the combination of these fluids with sperm. Specifically, these glands produce fluids that:

- protect sperm from the acidic environment of the urethra and vagina
- provide nutrients that help sperm survive and function
- supply the bulk of the liquid that carries sperm through the male reproductive tract
- help sperm move more easily by reducing friction and thickening or thinning the fluid as needed.

The three accessory glands are the

- **Seminal vesicles:** produce a thick, nutrient-rich fluid that makes up most of the semen and helps energize sperm.
- **Prostate gland:** adds a thin, slightly alkaline fluid that protects sperm and helps them move more easily through the female reproductive tract.
- **Bulbourethral (Cowper's) glands:** release a small amount of clear, slippery fluid that lubricates the urethra and helps neutralize any leftover acidity before sperm pass through.

Structures for Sperm Transport

- **Vas deferens**: Transports sperm from the epididymis toward the urethra.
- **Urethra**: Passageway for semen during ejaculation; also part of the urinary system.
- **Penis**: External organ that delivers sperm (in the form of semen) into the female reproductive tract. It contains erectile tissues that fill with blood during sexual arousal.

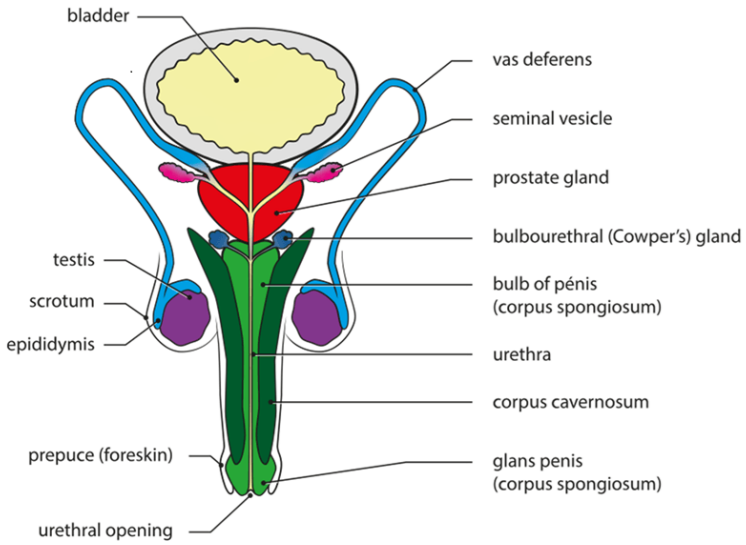
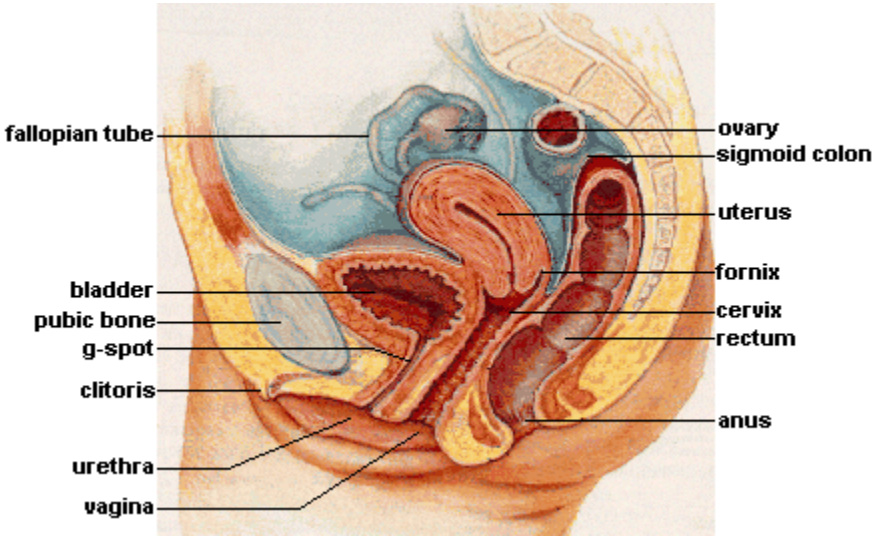


Figure 13.8.2: **Anatomy of the Male Reproductive System.** Major structures of the male reproductive system include the testes and epididymides within the scrotum for sperm production and maturation, the vas deferens for transport, and the seminal vesicles, prostate, and bulbourethral glands for adding fluids to semen. The urethra passes through the penis, which contains erectile tissues (corpus cavernosum and corpus spongiosum) and ends at the glans and urethral opening. The bladder sits superior to the reproductive organs.

Female Reproductive System



The human female reproductive system includes a set of internal organs in the pelvic cavity and external structures at the vulva. The external opening leads into the **vagina**, a muscular canal that receives semen during intercourse. It also functions as the birth canal during delivery and provides the passageway for menstrual flow. Mucus from the Bartholin's glands helps lubricate this area.

The vagina leads to the **cervix**, the lower, narrow portion of the **uterus** that opens into the vagina. The uterus is a muscular organ that houses and supports a developing fetus during pregnancy.

Ovum Production and Transport

On each side of the uterus lie the **ovaries**, the organs responsible for producing the female gametes. This process, called **oogenesis**, is the female equivalent of spermatogenesis in males. Oogenesis begins before birth, pauses, and then resumes at puberty, continuing across the reproductive lifespan. The mature **ovum**, like a sperm cell, is **haploid**, meaning it carries only one

set of chromosomes.

Besides producing the **ova (eggs),** the ovaries also produce the hormones **estrogen** and **progesterone**. Each month, an ovary typically releases one ovum. The ovum enters a **Fallopian tube**, where fertilization commonly occurs if sperm are present.

If a sperm fertilizes the ovum, the resulting **zygote** begins dividing as it travels to the **uterus**, where a fertilized egg **implants in the endometrium** and **pregnancy** begins with embryonic development.

If fertilization does not occur, the thickened endometrium is not needed, so it breaks down and is shed along with the unfertilized ovum during **menstruation**, the monthly cycle.

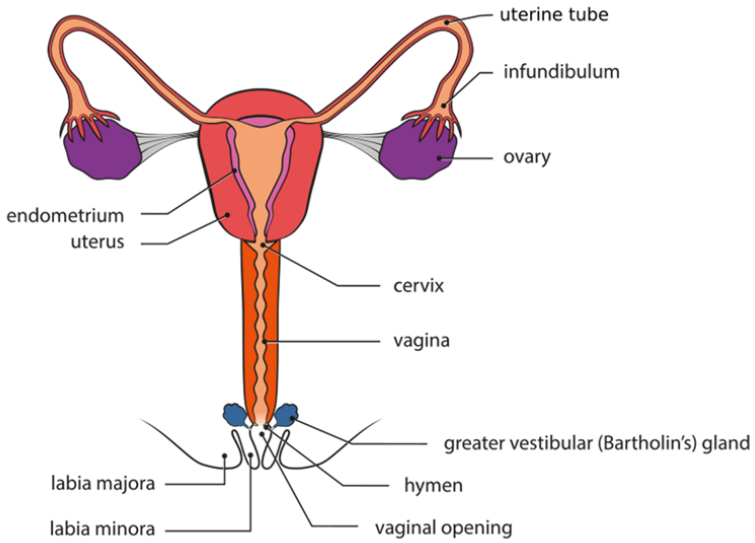


Figure 13.8.3: **Anatomy of the Female Reproductive System.** Major structures of the female reproductive organs. The ovaries produce oocytes and hormones, and the uterine tubes receive and transport the oocyte toward the uterus. The uterus contains the endometrium, which supports implantation and pregnancy. The cervix forms the opening to the vagina, which serves as the passageway for intercourse, childbirth, and menstrual flow. External structures include the labia majora and labia minora, the vaginal opening, the hymen, and the greater vestibular (Bartholin's) glands, which provide lubrication.

Diploid and Haploid: Understanding Chromosome Count

Chromosomes are long, tightly coiled strands of **DNA** that organize and store the **genetic information** inside each cell.

Humans normally have **46 chromosomes** arranged in **23 pairs**, with one chromosome in each pair inherited from the mother and the other from the father. Along the length of each chromosome are thousands of genes, which are small segments of DNA that function like individual instructions for building proteins and guiding the body's development and activities.

The **somatic cells** in the human body contain **46 chromosomes** — the **full diploid number** — meaning they have **two sets of chromosomes.** Diploid cells include skin cells, liver cells, muscle cells, nerve cells, and all the other cells that make up the body.

Alternatively, **gametes** — specifically, the sperm and egg cells — contain only **23 chromosomes**. This reduced **haploid number** allows fertilization to restore the complete set of 46 chromosomes in the zygote, keeping the chromosome number stable from one generation to the next.

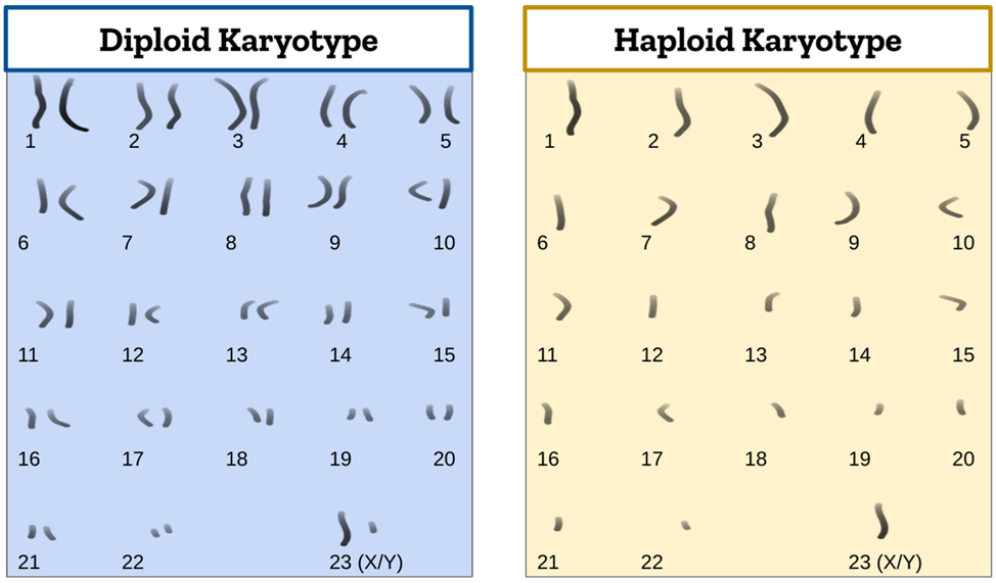


Figure 13.8.4: **Diploid vs. Haploid Karyotype.** A side-by-side comparison of human chromosome organization. The diploid karyotype (left) contains 46 chromosomes arranged in 23 homologous pairs, including one pair of sex chromosomes (X/Y). The haploid karyotype (right) shows 23 single chromosomes—the set found in gametes—illustrating how meiosis reduces the chromosome number by half to prepare for fertilization.

Why Does This Matter?

Mitosis and **meiosis** are the two major ways cells divide in the human body.

Mitosis is the type of cell division used for growth, repair, and everyday maintenance, producing two genetically identical diploid cells.

Meiosis is different because it is used only to make gametes; it involves two rounds of division and produces four genetically unique haploid cells.

In short, mitosis makes identical body cells, while meiosis creates specialized sex cells with half the usual chromosome number. Keeping chromosome numbers consistent from generation to generation is critical as it prevents cells from gaining too much DNA. **Meiosis**, the **special cell division that makes gametes**, cuts the chromosome number in half so that fertilization can restore it to the normal diploid number.

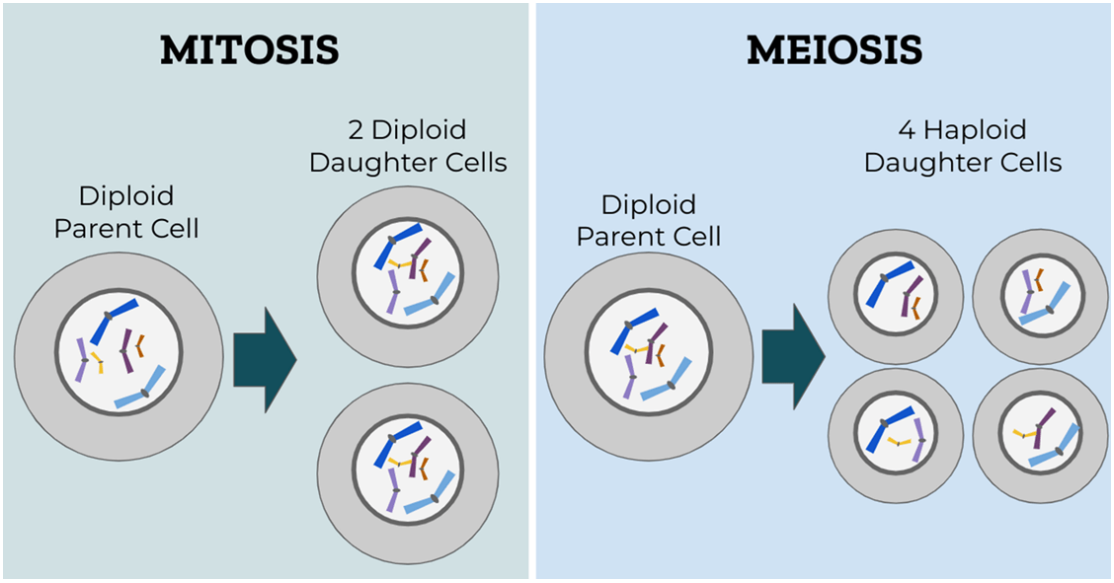


Figure 13.8.5: **Comparison of mitosis and meiosis.** Both processes begin with a diploid parent cell, but mitosis produces two genetically identical diploid daughter cells for growth and tissue repair, whereas meiosis produces four genetically unique haploid daughter cells for use as gametes in sexual reproduction. The diagram highlights how chromosome number is maintained in mitosis and halved in meiosis.

Fertilization and Early Development

Fertilization occurs when a paternal sperm nucleus fuses with a maternal egg nucleus to form the first cell of a new individual: the **zygote**.

- The zygote is **diploid (2n)**, containing **46 chromosomes** again, one set of 23 chromosomes from each parent.
- After fertilization, the zygote undergoes **rapid mitotic divisions and cell differentiation**, forming an **embryo** during the **first 8 weeks of development.**
- After 8 weeks, the developing human is considered a **fetus**, which continues growing until birth at approximately **40 weeks of gestation**.

This entire sequence, beginning from a single microscopic zygote, highlights why gametes must be haploid: combining two half-sets of chromosomes ensures that the species maintains a consistent chromosome number.

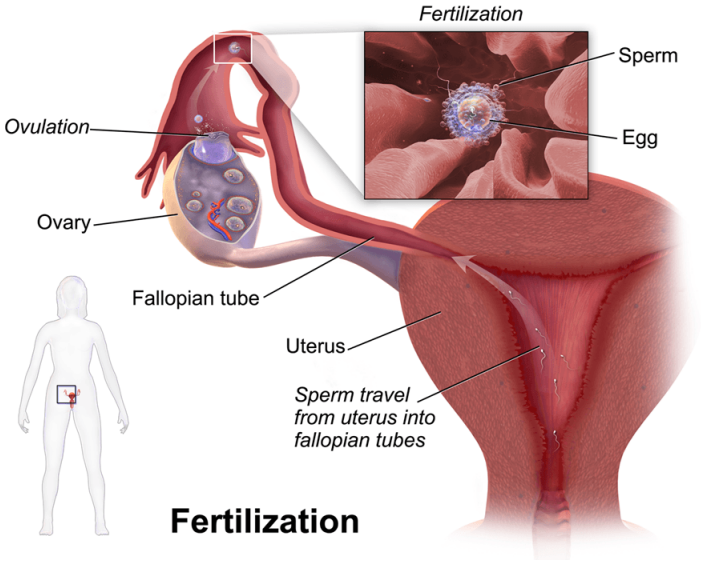


Figure 13.8.6: **Fertilization.** Fertilization occurs when sperm that have traveled through the uterus enter a Fallopian tube and encounter an ovulated egg. The ovary releases the mature oocyte during ovulation, and the egg is then moved along the tube where fertilization commonly takes place. The inset highlights the moment a sperm reaches and fuses with the egg, beginning the formation of a zygote.

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13.9: Testes and Male Gamete Production

The testes are the male gonads that produce sperm and secrete the hormones essential for male reproductive function.

Master this section and you'll be able to:

- Explain how the scrotum and its muscles regulate testicular temperature for proper sperm production.
- Identify the major structures of the testes and describe their roles in producing and supporting sperm.
- Summarize the stages of spermatogenesis from spermatogonia to mature sperm and the functions of Leydig and Sertoli cells.

The testes are located in a skin-covered, highly pigmented, muscular sac called the **scrotum**, which hangs behind the penis. This position is important because sperm production inside the testes works best when they are kept about **2 to 4°C below core body temperature.**

The **dartos muscle** forms the subcutaneous muscle layer of the scrotum and continues inward to create the scrotal septum, which divides the scrotum into two compartments. Each testis is also surrounded by a **cremaster muscle**, which descends from the internal oblique muscle of the abdominal wall. Working together, the dartos and cremaster muscles can lift the testes in cold conditions, reducing heat loss, or relax in warm conditions, allowing the testes to move farther from the body and release heat. On the outside, the scrotum shows a raised midline ridge called the raphe.

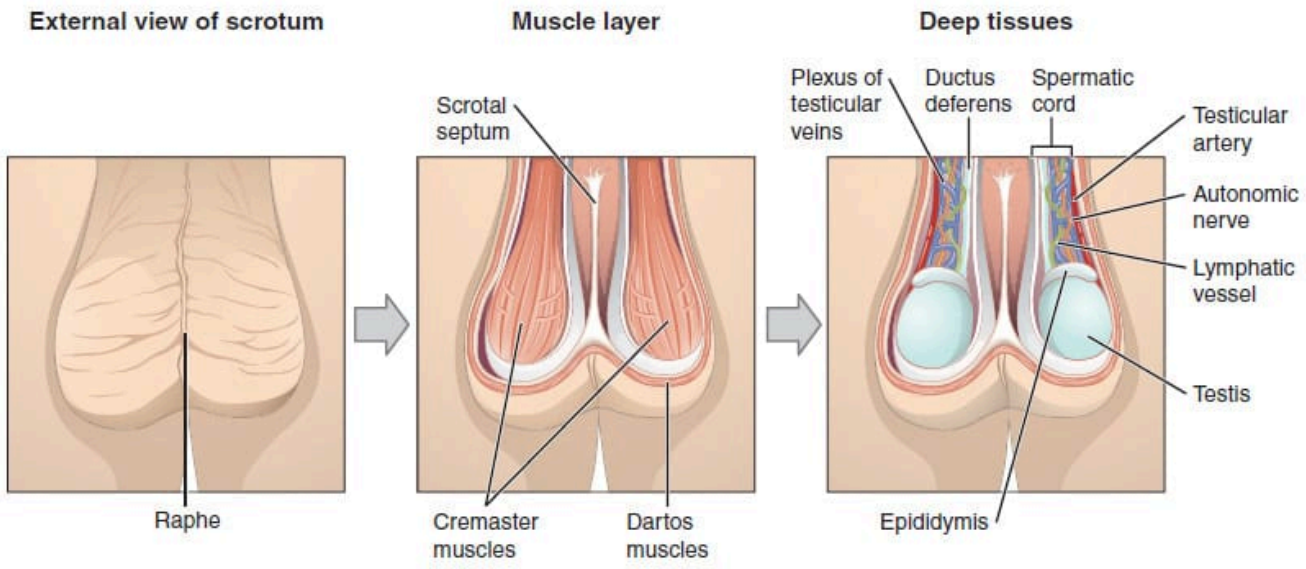


Figure 13.9.1: **The Scrotum and Testes.** This anterior view shows the different layers surrounding the scrotum and testes. *(Image credit: "Scrotum and Internal Structures" by OpenStax is licensed under CC BY 4.0)*

Testes

The **testes** (singular, **testis**) are the male gonads, meaning the **primary reproductive organs**. They **produce sperm** and **secrete androgens such as testosterone**, and they remain active throughout the male reproductive lifespan.

Each testis is an oval structure about 4 to 5 centimeters long and is housed within the scrotum *(see Figure above)*. Two protective connective tissue layers surround each testis. Just deep to the cremaster muscle lies the tunica vaginalis, a serous membrane with parietal and thin visceral layers. Beneath this is the **tunica albuginea, a tough, white, dense connective tissue layer** that not only covers the testis but also folds inward to form **septa**. These septa divide the interior into **300 to 400 lobules.**

Inside the lobules are the **seminiferous tubules**, where sperm develop. During fetal development, the testes normally descend

from the abdomen into the scrotum around the seventh month. This process is called the descent of the testis. When one or both testes fail to descend before birth, the condition is known as **cryptorchidism**.

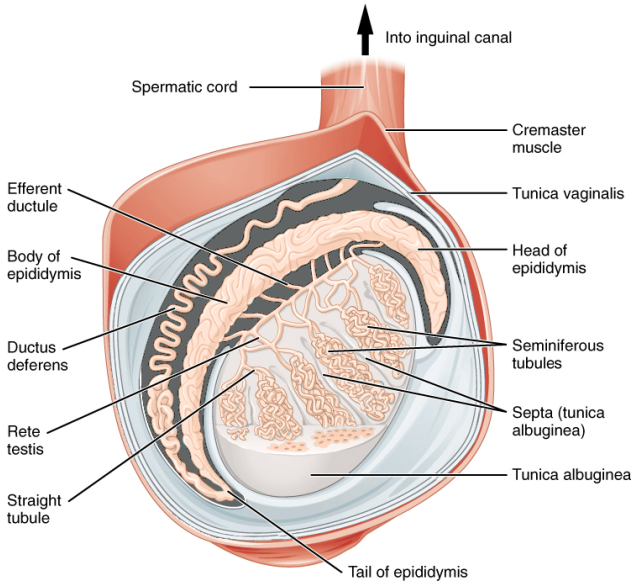


Figure 13.9.2: **Cross-Section of the Testis and Epididymis.** Internal structures of the testis are organized into lobules filled with seminiferous tubules, where sperm are produced before passing into the straight tubules, rete testis, and efferent ductules. The sperm then enter the epididymis for maturation and storage. Surrounding layers, including the tunica albuginea, tunica vaginalis, and cremaster muscle, protect the testis and help regulate its temperature, while the spermatic cord carries vessels and the ductus deferens toward the inguinal canal. *(Image credit: "Anatomy of the Testis" by OpenStax is licensed under CC BY 4.0, modifications by Jennifer Lange.)*

Seminiferous Tubules for Sperm Production

The seminiferous tubules make up most of each testis. These tightly coiled tubes contain **developing sperm cells** that mature as they move toward the central lumen. Once released into the lumen as **spermatozoa** (or simply "**sperm**"), they enter the testicular duct system. From there, sperm flow into the straight tubules, then into the rete testis, and finally leave the testis through 15 to 20 efferent ductules that pass through the tunica albuginea.

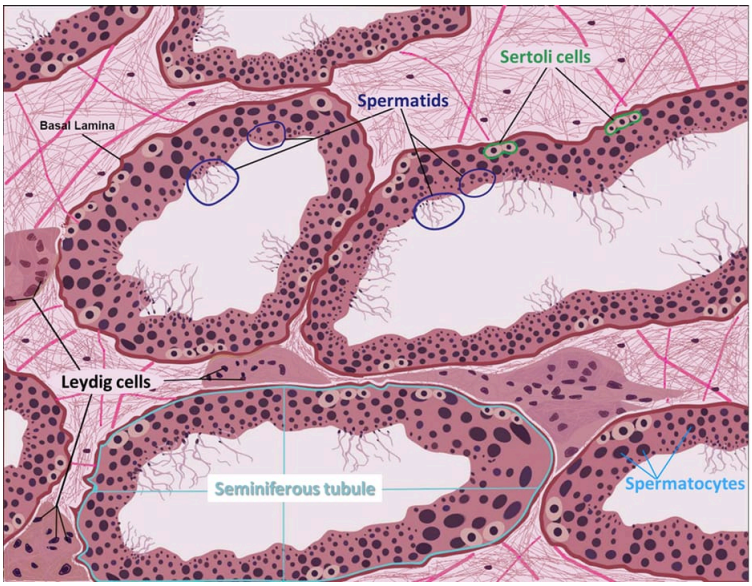


Figure 13.9.3: **Seminiferous Tubules with Developing Sperm Cells.** Cross-sections of seminiferous tubules display the layers of developing germ cells arranged from the basal lamina toward the lumen. **Spermatocytes** lie deeper in the wall, while

spermatids appear closer to the lumen as they near maturation and eventually will be released as spermatozoa. Large **sustentacular (Sertoli) cells** support developing sperm. Between the tubules, **interstitial (Leydig) cells** occupy the connective tissue and secrete testosterone.

The Two Testicular Supporting Cells

Leydig cells and Sertoli cells are the two main supporting cell types inside the testis. They perform distinct, complementary roles that enable male fertility and proper hormone balance. Without the coordinated actions of both cell types, normal sperm production and male fertility would not be possible.

Interstitial (Leydig) cells

Leydig cells are interstitial cells nestled **between the seminiferous tubules** in the testis. Their primary function is to produce **testosterone**, especially in response to l**uteinizing hormone (LH)** from the anterior pituitary gland. Testosterone supports the development of male secondary sexual characteristics and drives spermatogenesis in conjunction with the sustentacular (or Sertoli) cells. These cells are named after Franz Leydig, the German anatomist who first described them in the mid-1800s.

Sustentacular (or Sertoli) Cells

Sertoli cells provide structural and nutritional **support for developing sperm** by creating the scaffold of the seminiferous tubules, regulating spermatogenesis, forming the blood-testis barrier, secreting signals and nutrients, and clearing away leftover cytoplasm via phagocytosis. Because they support and organize every stage of germ cell development, they are often called supporting or sustentacular cells. The name comes from Enrico Sertoli, the Italian physiologist who first described these big cells “nurse cells” in 1865. *Note that both cell names start with an* "S".

The Main Players Inside the Testes: The Germ Cells

The least mature germ cells, the **spermatogonia** sit along the basement membrane of the seminiferous tubules. These cells **act as stem cells** and continuously divide, with some remaining as spermatogonia and others becoming primary spermatocytes. Primary spermatocytes move inward and undergo meiosis to form secondary spermatocytes, which then divide again to produce haploid spermatids. As development continues, spermatids begin transforming their shape and internal structures until they become mature sperm. The full sequence of cell divisions and maturation is called **spermatogenesis.** Let us take a closer look at this topic:

Male Gamete Production: Spermatogenesis

As you just learned, **spermatogenesis** takes place inside the seminiferous tubules, which make up most of each testis. The process begins at puberty and continues throughout adult life. One full production cycle takes about 64 days, and new cycles begin roughly every 16 days, although different tubules are not synchronized. Sperm counts tend to decline slowly after about age 35, and smoking is associated with lower counts at any age.

The process starts with **mitosis of the diploid spermatogonia** at the outer edge of the tubule. Each spermatogonium divides to form two **primary spermatocytes**, which still contain the full diploid set of 46 chromosomes. These primary spermatocytes then enter **meiosis**. **Meiosis I** produces **secondary spermatocytes**, and **meiosis II** produces **spermatids**, all of which are haploid cells containing 23 chromosomes. Because mature gametes must be haploid, the second round of cellular division is essential. Spermatids then undergo **spermiogenesis**, the **final maturation** that transforms them into streamlined **spermatozoa (sperm cells)**. In a cross section of a seminiferous tubule, the youngest cells lie along the outer basement membrane, while the

increasingly mature cells are found closer to the central lumen, where sperm are eventually released.

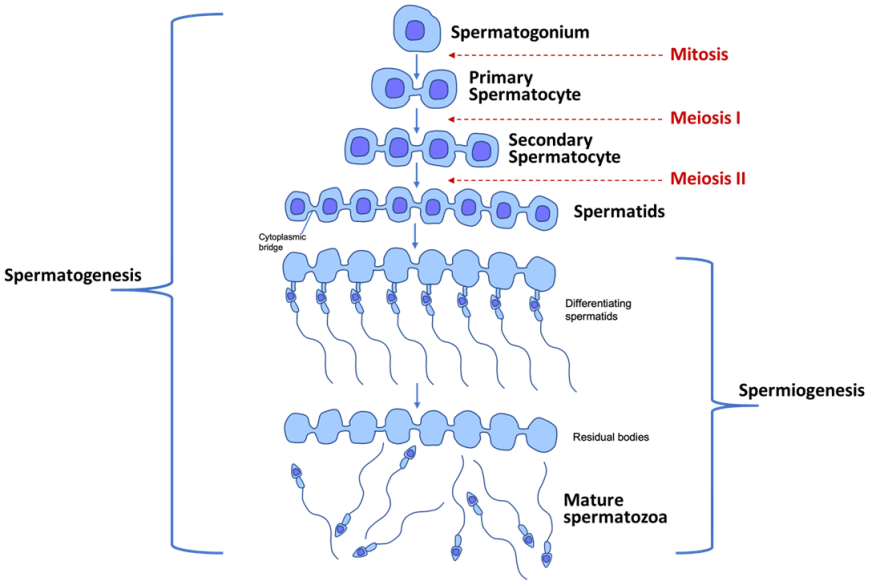


Figure 13.9.4: **Progression of Male Germ Cells from Stem Cell to Mature Spermatozoon.** A spermatogonium at the basement membrane divides by mitosis to produce primary spermatocytes. These enter meiosis, forming secondary spermatocytes after meiosis I and then haploid spermatids after meiosis II. Spermatogenesis refers to all stages up to the formation of spermatids. Spermiogenesis is the final differentiation step in which spermatids elongate, condense their nucleus, form an acrosome and a flagellum, and become mature spermatozoa that are eventually released into the lumen for transport to the epididymis.

Building a Sperm, One Step at a Time

Mitosis of a spermatogonium produces **two identical diploid cells**. One of these new cells stays behind as a spermatogonium so that the process can continue throughout life. The other becomes a **primary spermatocyte**. This primary spermatocyte is the cell that will begin the long **journey through meiosis,** the special type of cell division that creates gametes.

Before a **primary spermatocyte** divides, **it copies its DNA,** just as cells do before mitosis. It then enters **meiosis I,** the first stage of meiosis. During this division, the cell separates its pairs of replicated chromosomes and produces two **secondary spermatocytes.** These two cells still have duplicated chromosomes, but each now holds only one member of each chromosome pair.

Next, **both secondary spermatocytes enter meiosis II.** This second division separates the duplicated chromosomes into single copies. By the end of meiosis II, each secondary spermatocyte produces **two haploid daughter cells**, giving a total of four haploid cells. These cells are called **spermatids**. Even though spermatids have the correct haploid chromosome number, they do not yet look or function like sperm. Early spermatids are round cells with a central nucleus and a fairly large amount of cytoplasm, very different from the streamlined shape of a mature sperm cell.

Spermiogenesis is the **remodeling process** that turns these round spermatids into recognizable sperm. During spermiogenesis, most of the cytoplasm is removed, the nucleus becomes tightly packed, the acrosome begins to form over the nucleus, mitochondria gather in the midpiece, and a long tail develops for movement. None of this changes the chromosome number; it simply transforms the cell's structure so that it can function as a gamete.

The final product of this transformation is the **spermatozoon** (one spermatozoon, two or more spermatozoa) — the formed sperm cell. These mature-shaped sperm cells appear in the region of the seminiferous tubule closest to the lumen. Once they reach this point, the sperm are released into the lumen and carried away through a series of tiny ducts toward the epididymis. There, they will undergo further maturation and eventually gain the ability to swim on their own.

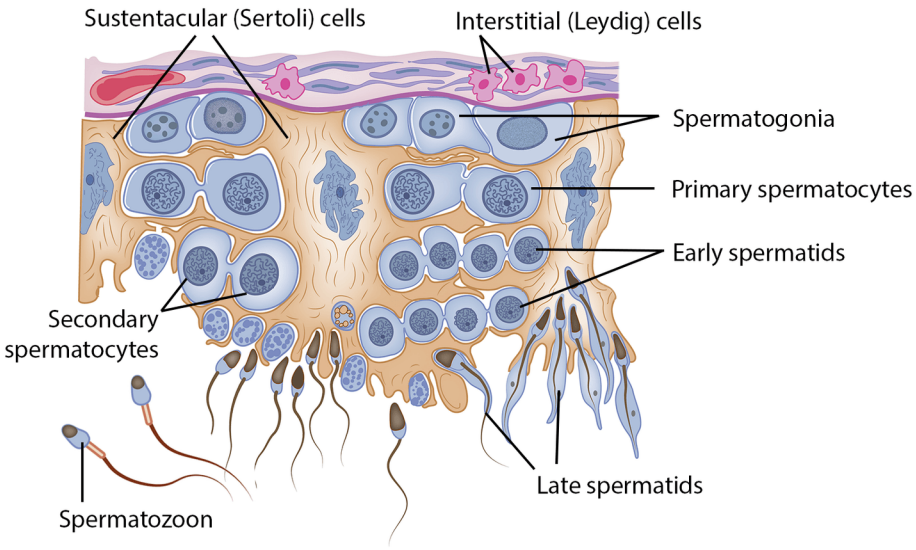


Figure 13.9.5: **Progression of Spermatogenesis in a Seminiferous Tubule.** Developing germ cells are shown progressing from the outer edge of the seminiferous tubule toward the central lumen. Spermatogonia line the basement membrane, where stem cells divide to produce primary spermatocytes. As these cells move inward, they undergo meiosis to form secondary spermatocytes and then early spermatids. Late spermatids elongate and begin shaping into spermatozoa during spermiogenesis. Fully formed spermatozoa are released into the lumen for transport toward the epididymis. Sertoli cells support and nourish the developing cells, while interstitial (Leydig) cells in the surrounding tissue produce testosterone, which drives this entire process. *(Image credits: "Slagter - Drawing Human spermatogenesis diagram - English labels" by Ron Slagter, O. Paul Gobée, LUMC, Hope Wicks, LUMC et al, license: CC BY-NC-SA. "Slagter - Drawing Spermatogenesis in seminiferous tubules of testis - no labels" by Ron Slagter, Jill P.J.M. Hikspoors, MUMC+, Hope Wicks, LUMC et al, license: CC BY-NC-SA; modified by Jennifer Lange.)*

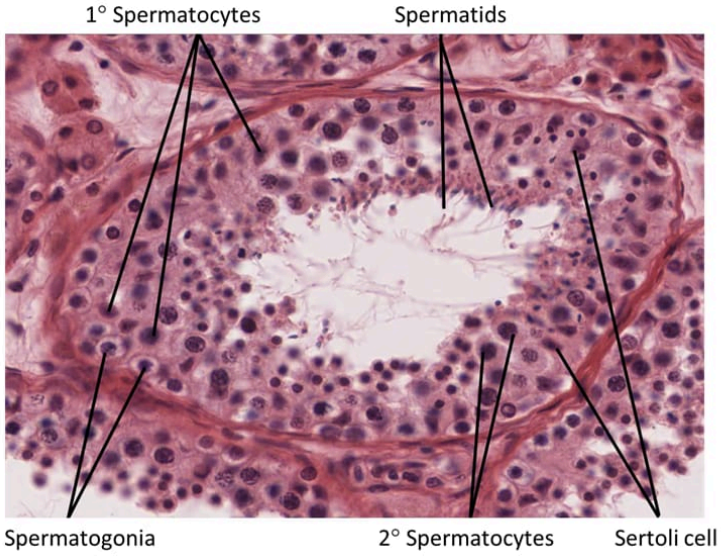
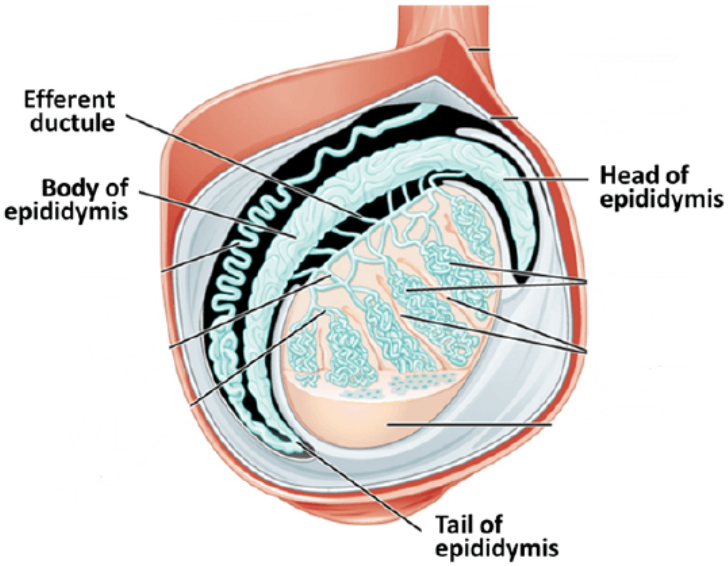


Figure 13.9.6: **Cross-section of a Seminiferous Tubule Under High Power.** Germ cell development progresses from the outer edge of the tubule toward the central lumen. Along the basement membrane lie the spermatogonia, the least mature germ cells. Moving inward, larger primary spermatocytes and then smaller secondary spermatocytes mark the two stages of meiotic division. Closer to the lumen, early spermatids appear as small, round haploid cells beginning their transformation into sperm. Elongated Sertoli cells extend across the entire thickness of the tubule, providing structural and nutritional support to each stage of germ cell development. *Image provided by the Regents of the University of Michigan under a BY-SA-NC 4.0. Illustration by Sofia Elizondo and Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*



Sperm Maturation in the Epididymis

After sperm are released into the lumen of the seminiferous tubules, they are carried in testicular fluid toward the epididymis (plural = epididymides). The epididymis is a long, tightly coiled tube attached to each testis, and it is where sperm complete much of their maturation.

Although it appears small from the outside, the epididymis would measure about 6 meters (20 feet) if stretched out. Sperm take an average of 12 days to travel through these coils, although the fastest recorded transit in humans is about one day. Sperm enter at the head of the epididymis and are gently moved forward by rhythmic contractions of smooth muscle in the tube walls.

As they progress, sperm continue to mature, gaining characteristics needed for future motility and fertilization. The most mature sperm are stored in the tail of the epididymis, where they remain until ejaculation.

Sperm Structure

Sperm are much smaller than most cells in the body. Their volume is roughly **85,000 times less** than that of the female gamete. Males produce **100 to 300 million sperm per day**, whereas females typically ovulate just **one oocyte per month**. As with many highly specialized cells, the structure of a sperm reflects its job.

The **head** contains the tightly packed **haploid nucleus** with almost no cytoplasm, which helps keep the sperm small and streamlined. Covering most of the head is the **acrosome**, a cap filled with enzymes that help the sperm penetrate the outer layers of the oocyte during fertilization.

The **midpiece** is packed with mitochondria that produce **ATP**, the energy needed for movement. This energy powers the **flagellum**, which extends from the midpiece into the tail and propels the sperm forward. At the core of the flagellum is the **axial filament**, a structural strand formed from a centriole during the final stages of spermatogenesis.

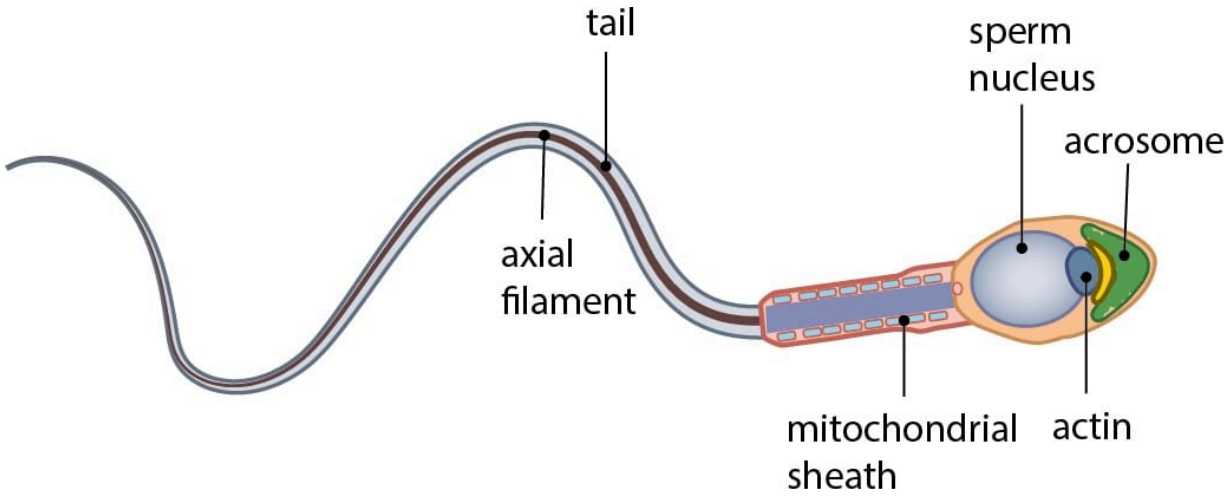


Figure 13.9.7: **Structural Features of a Sperm Cell.** A streamlined spermatozoon is organized into three main regions that support its role in reaching and fertilizing an oocyte. The **head** contains the tightly packed haploid nucleus and is capped by the acrosome, which stores enzymes that help the sperm penetrate the egg's outer layers. Just behind the head, the **midpiece** houses a dense mitochondrial sheath that supplies ATP to power movement. Extending from this region, the long **tail** contains a central axial filament whose rhythmic beating propels the sperm forward through the reproductive tract. *(Image credit: Cropped version of "Slagter - Drawing Penetration of oocyte wall at fertilisation - English labels" by Ron Slagter, Cindy J.M. Hulsman, MUMC+, Jill P.J.M. Hikspoors, MUMC+ et al, license: CC BY-NC-SA.)*

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13.10: Duct System and Accessory Glands

Sperm begin in the seminiferous tubules, mature in the epididymis, and travel through the duct system with support from accessory gland secretions for successful transport out of the body.

Master this section and you'll be able to:

- Explain the role of the epididymis in supporting sperm.
- Identify how the male accessory glands contribute to seminal fluid and why this is essential.
- Describe the path of sperm from their site of production to their exit from the body.

From the Seminiferous Tubules to the Epididymis

In the previous section, you have learned that sperm are produced inside the seminiferous tubules of the testes, where Sertoli (sustentacular) cells support them as they develop. As they mature, the young sperm move toward the center of the testis and then enter small passageways that guide them out of the testis and toward the epididymis. During this short transition, the surrounding fluid is modified and some water is removed, helping to concentrate the sperm.

From there, sperm enter the long, coiled epididymis. Their journey through this tube takes about 12 days, during which they continue to mature, gradually gaining the ability to swim. The most fully developed sperm are stored in the tail of the epididymis, where they remain until ejaculation.

From Testes to Exit and the Role of Seminal Fluid

The testes provide the environment needed for sperm formation, from external temperature control to the highly organized seminiferous tubules inside. The scrotum and its muscles keep the testes slightly cooler than body temperature, allowing normal sperm production. Within each testis, the seminiferous tubules, Sertoli cells, Leydig cells, and surrounding tissues support the ongoing development of sperm from stem cells to nearly mature spermatozoa. After leaving the testes, these sperm still require final maturation in the epididymis before they are ready to leave the male body and look for that rare ovum.

However, sperm alone cannot accomplish fertilization. They require a specialized fluid environment that nourishes them, protects them, and allows them to move effectively through the male and female reproductive tracts. This crucial support comes from the **accessory male glands**, which add the components that transform sperm into semen. In this section, we will explore how the **seminal vesicles**, **prostate gland**, and **bulbourethral glands** each contribute to creating a fluid medium that enables sperm survival and successful transport.

Accessory Glands and Seminal Fluid Production

Sperm make up only about 5 percent of the total volume of **semen**, the thick, milky fluid released during ejaculation. Most of the semen comes from three important accessory glands of the male reproductive system: the seminal vesicles, the prostate gland, and the bulbourethral glands. Together, their secretions form the **seminal fluid,** which supports, nourishes, and transports the sperm.

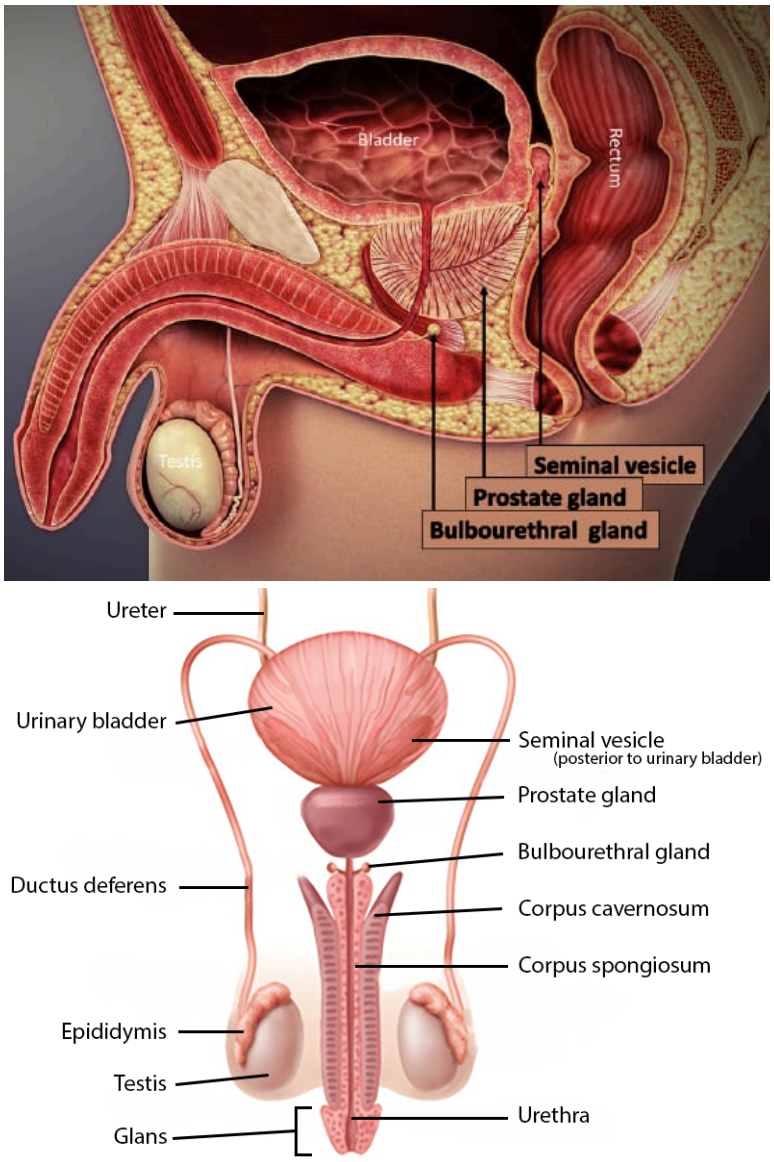


Figure 13.10.1: **Male Accessory Glands and Their Position.** In the sagittal section on the left, the three major accessory glands that contribute to seminal fluid are pointed out by arrows. The paired seminal vesicles sit behind the bladder and add a fructose-rich secretion that fuels sperm. Just below them, the prostate gland surrounds the proximal urethra and contributes a slightly alkaline fluid that supports sperm survival in the acidic female reproductive tract. The bulbourethral glands lie inferior to the prostate and release a small amount of mucus that lubricates and neutralizes the urethra before ejaculation.
The diagram on the right provides an anterior view of the three male accessory glands shown in context with nearby ducts and reproductive structures. *(Image on the right credits: "Male Reproductive Organs - Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by StacyRed-Wiki via Wikimedia Commons; "Leiden - Drawing Male bladder and urethra from posterior - no labels" by Bas (S) Blankevoort, LUMC and Marco C DeRuiter, LUMC, is licensed under CC BY-NC-SA, modifications and labeling by Jennifer Lange.)*

Seminal Vesicles

The paired seminal vesicles contribute most of the fluid in semen, producing an **alkaline secretion that makes up about 60 percent of the total volume.** As sperm enter the ampulla of the ductus deferens during ejaculation, they mix with this fluid, which supplies **fructose** for ATP production and helps activate their movement. The alkaline pH helps neutralize the acidic environment of the vagina, improving sperm survival. Seminal vesicle fluid also contains prostaglandins, hormone-like molecules that encourage the cervical opening to dilate so sperm can more easily pass from the vagina into the uterus.

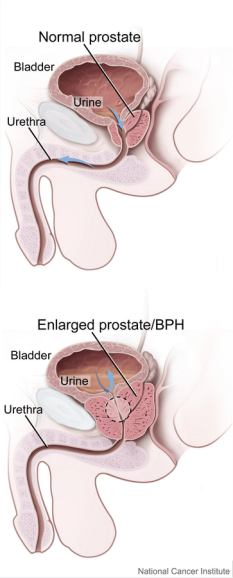
Prostate Gland

The prostate gland sits just **below the urinary bladder** and surrounds the first portion of the urethra, as shown in the figure above. About the size of a walnut, it contains both glandular and muscular tissue. The prostate adds a milky, slightly acidic fluid rich in citric acid to the semen. This fluid briefly thickens semen after ejaculation, helping it remain in the female reproductive tract while sperm begin using the fructose supplied by the seminal vesicles. An enzyme called prostate-specific antigen (PSA) then liquefies the semen, allowing sperm to move farther into the reproductive tract. Prostatic secretions also include seminalplasmin, an antimicrobial substance that helps limit bacterial growth.

Bulbourethral (Cowper's) Glands

The final addition to the seminal fluid comes from the two bulbourethral glands. They produce a thick, slippery mucus that is released early in sexual arousal, before ejaculation. This mucus lubricates the urethra and vagina and helps wash away traces of acidic urine from the urethra. Because this "pre-ejaculate" can pick up sperm left in the urethra from earlier ejaculation, it *can* occasionally contain sperm and may still lead to pregnancy.

Disorders of the Prostate Gland



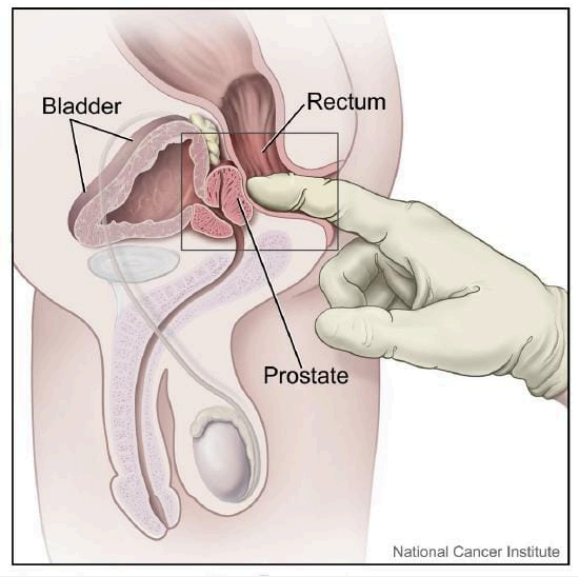
Prostate Specific Antigen (PSA) is an enzyme made almost entirely by the cells of the prostate gland. Its main job is to help liquefy semen after ejaculation, allowing sperm to move more easily through the female reproductive tract.

Although PSA is mostly found in semen, a small amount normally enters the bloodstream. Because the prostate releases PSA, a blood test for PSA can give information about prostate health.

Higher-than-expected blood PSA levels can occur for several reasons, including prostate enlargement, inflammation or infection of the prostate, and prostate cancer. The PSA test is therefore used as part of screening and evaluation for prostate disorders, but the results always need to be interpreted in context because many non-cancerous conditions can raise PSA levels.

The prostate normally doubles in size during puberty. At approximately age 25, it gradually begins to enlarge again. This enlargement does not usually cause problems; however, abnormal growth of the prostate, or **benign prostatic hyperplasia (BPH),** can cause **constriction of the urethra** as it passes through the middle of the prostate gland, leading to a number of lower urinary tract symptoms, such as a frequent and intense urge to urinate, a weak stream, and a sensation that the bladder has not emptied completely.

By age 60, approximately 40 percent of men have some degree of BPH. By age 80, the number of affected individuals has jumped to as many as 80 percent. Treatments for BPH attempt to relieve the pressure on the urethra so that urine can flow more normally. Mild to moderate symptoms are treated with medication, whereas severe enlargement of the prostate is treated by surgery in which a portion of the prostate tissue is removed.



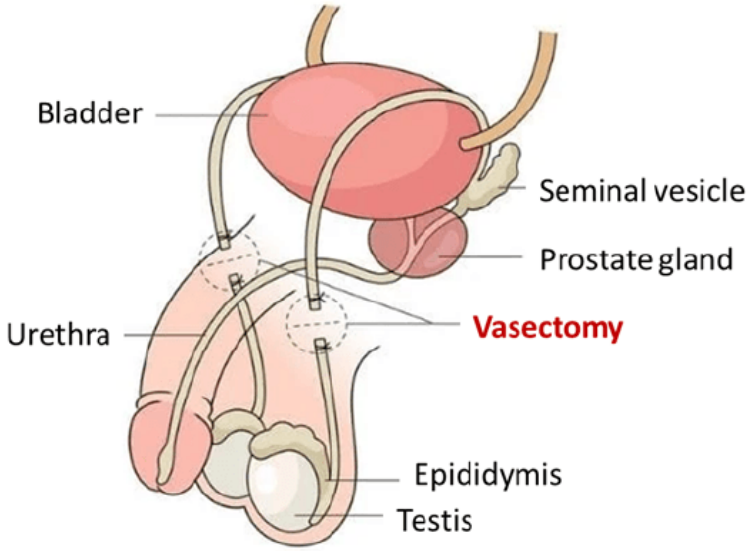
Prostate cancer is the second most common cancer in men, and while some forms grow very slowly and may never need treatment, aggressive forms can spread to organs such as the lymph nodes, lungs, and brain. There is no link between benign prostatic hyperplasia (BPH) and prostate cancer, although both can cause similar urinary symptoms.

Diagnosis typically includes taking a medical history, measuring prostate-specific antigen (PSA) levels in the blood, and performing a digital rectal exam. Because the prostate sits just in front of the rectal wall and below the bladder, a clinician can easily palpate its posterior surface by inserting a gloved, lubricated finger into the rectum to check for enlargement, tenderness, or abnormal nodules. If a suspicious mass is found, a biopsy confirms the diagnosis. Treatment options depend on how advanced the cancer is and may include active surveillance, hormone therapy, surgery, chemotherapy, or radiation therapy. For additional details, readers can visit the National Cancer Institute's page on prostate cancer.

Image credits: Top right - "Prostate (Normal and Enlarged)" by Alan Hoofring for the National Cancer institute is in the public domain. Bottom left: "Exam, Digital Rectal" by the National Cancer Institute is in the public domain.

Ductal System

During ejaculation, mature sperm leave the tail of the epididymis and are propelled by smooth muscle contractions (peristalsis) into the **ductus deferens (vas deferens)**, a thick, muscular tube bundled with blood vessels and nerves **inside the spermatic cord.** The ductus deferens travels upward through the inguinal canal into the pelvic cavity and curves around the bladder.



Because the vas deference is easily accessed within the scrotum, male sterilization can be achieved by cutting and sealing it in a **vasectomy.** *(See image on the right)*. Although reversal is sometimes possible, vasectomies are considered permanent and are recommended only for individuals who are certain they no longer wish to father children.

Mature sperm leave the tail of the epididymis and enter the vas deferens that propels them forward with peristaltic contractions. The vas deferens travels within the spermatic cord, loops into the pelvic cavity, and **joins the duct of the seminal vesicle to form the ejaculatory duct.** This short duct passes through the prostate gland and **empties into the prostatic urethra,** where additional fluid from the prostate mixes in.

As sperm move along this route, the key glandular contributions they receive converts the fluid into **semen**.

The bulbourethral glands release a small amount of clear mucus **early in arousal that lubricates the urethra.**

During ejaculation, the combined fluid is pushed through the urethra and exits the body through the penis. Because the urethra carries both urine and semen, the nervous system coordinates ejaculation so that urine flow is temporarily blocked. This one-way routing ensures that semen can pass efficiently to the outside of the body. The urethra is subdivided into three regions: the **prostatic urethra** (within the prostate gland), the **membranous urethra** (passing through the pelvic floor), and the **spongy urethra** (within the penis).

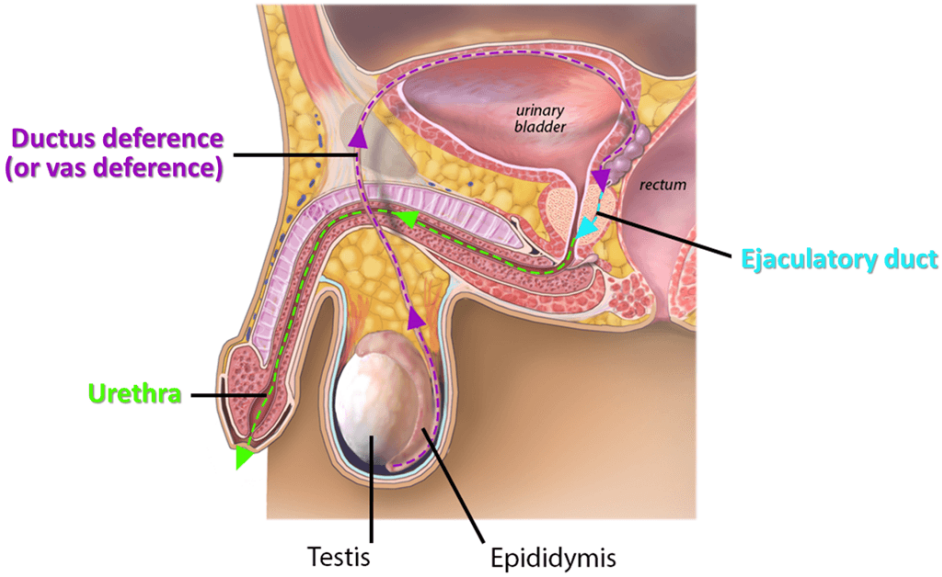


Figure 13.10.2: **Male Duct System Pathway from the Testis to the Urethral Opening.** Sagittal section showing sperm being ejaculated from the epididymis and pass through the ductus deferens, which travels from the scrotum and into the pelvic cavity. Each ductus deferens loops around the urinary bladder to join with a duct of the seminal vesicle and become the ejaculatory duct. The two ejaculatory ducts empty into the urethra, which carries the sperm to the outside. *(Image credit: "Varicocele" by BruceBlaus is licensed under CC BY-SA 4.0, modifications and labeling by Jennifer Lange.)*

Watch this video to learn about vasectomy

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

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13.11: Hormonal Regulation of the Male Reproductive System

Male reproductive function is controlled by hormonal signaling between the hypothalamus, pituitary gland, and testes.

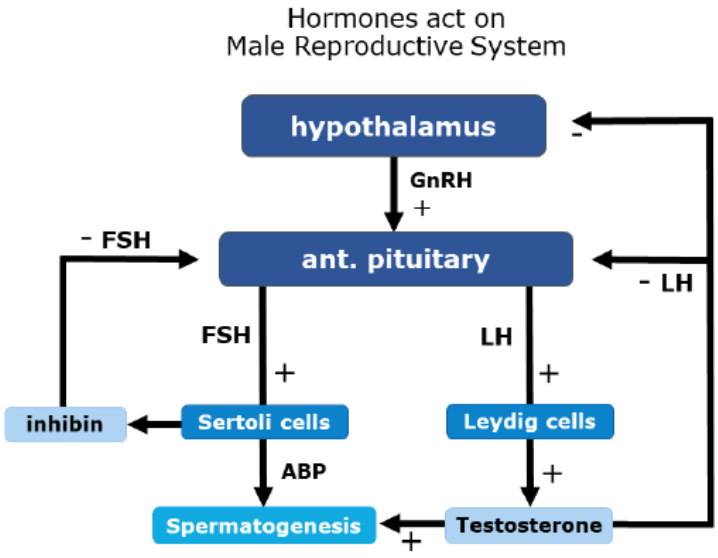
Master this section and you'll be able to:

- Explain how the hypothalamus, anterior pituitary, and testes interact to regulate testosterone production and spermatogenesis.
- Differentiate the roles of LH and FSH in the male reproductive system.

Gonadotropin-Releasing Hormone (GnRH), Follicle Stimulating Hormone (FSH), and Luteinizing Hormone (LH)

Hormonal regulation of the male reproductive system is controlled largely by the hypothalamus and the anterior pituitary. The **hypothalamus** releases **gonadotropin-releasing hormone (GnRH)**, which stimulates the **anterior pituitary** to synthesize and secrete the **gonadotropins: luteinizing hormone (LH)** and **follicle-stimulating hormone (FSH)**.

These hormones travel through the bloodstream to the testes, where they regulate **testosterone** production and support spermatogenesis.



Are you wondering why the male hormones are called LH and FSH, so clearly related to female reproductive functions?
The names reflect their *initial discovery in female physiology*, not their roles in males. hey were named for the *first* effects scientists observed in females long before their roles in males were understood. Unfortunately, the original names stuck even after researchers discovered they regulate testes function as well.

- **LH** was named because it triggers formation of the corpus luteum in the ovary. In the male LH targets the **Leydig cells** located in the interstitial spaces between seminiferous tubules — (which is why the Leydig cells are also called interstitial cells, remember?). LH promotes these Interstitial cells to produce **testosterone**.

- **FSH** was named so because it stimulates ovarian follicles. In the male, FSH acts on the **Sertoli cells** (sustentacular cells) inside the seminiferous tubules. In response to FSH, Sertoli cells produce **androgen-binding protein (ABP)**, which concentrates testosterone within the tubules. This **high local testosterone level** is essential for stimulating the spermatogenic cells and supporting the full process of **spermatogenesis**.

Figure 13.11.1: **How the Brain Orchestrates Male Reproductive Function.** The hypothalamus releases GnRH to stimulate the anterior pituitary, which secretes FSH and LH. FSH acts on Sertoli cells to support spermatogenesis and triggers the release of **inhibin**, which provides negative feedback to the pituitary. LH stimulates Leydig cells to produce testosterone, which promotes spermatogenesis and provides negative feedback to both the hypothalamus and anterior pituitary.

Testosterone

Testosterone is an **androgen** and a **steroid hormone produced by the Leydig (interstitial) cells** that lie between the seminiferous tubules of the testes. In male embryos, Leydig cells begin secreting testosterone by the seventh week of development, with levels peaking in the second trimester. This early surge drives the **anatomical differentiation** of male reproductive structures. After birth, testosterone levels remain low throughout childhood, then rise sharply during puberty to trigger characteristic physical changes and initiate spermatogenesis.

Functions of Testosterone

Within the testes, very high local concentrations of testosterone support Sertoli cells, maintain the structure and function of the seminiferous tubules, and are essential for ongoing spermatogenesis. Even if blood testosterone levels are normal, a drop in intratesticular testosterone can significantly reduce or halt sperm production.

Once testosterone enters the bloodstream, it acts as a classic hormone influencing a wide range of target tissues. In **skeletal muscle**, testosterone increases protein synthesis, which supports muscle enlargement, strength, and overall growth. It also travels to the **brain**, where it enhances sexual desire and stimulates the production and release of Growth Hormone (GH). GH works together with testosterone to promote **bone** growth, especially during the adolescent growth spurt. In fact, the dramatic rise in testosterone during puberty helps explain why males typically reach greater adult height than females. Beyond contributing to a taller and stronger physique, testosterone is essential for the development and long-term maintenance of male **secondary sexual characteristics**, including facial and body hair, a deeper voice, and increased muscle mass.

Before birth, testosterone plays a key role in forming the male reproductive system. It supports the development of the Wolffian ducts, which mature into structures such as the epididymis, ductus deferens, and seminal vesicles. By guiding both internal and external reproductive anatomy, testosterone helps establish the basic male reproductive pathways well before birth.

In females, small amounts of testosterone are produced by the ovaries (with most converted to estradiol), and the **adrenal glands** of both sexes contribute additional minor amounts.

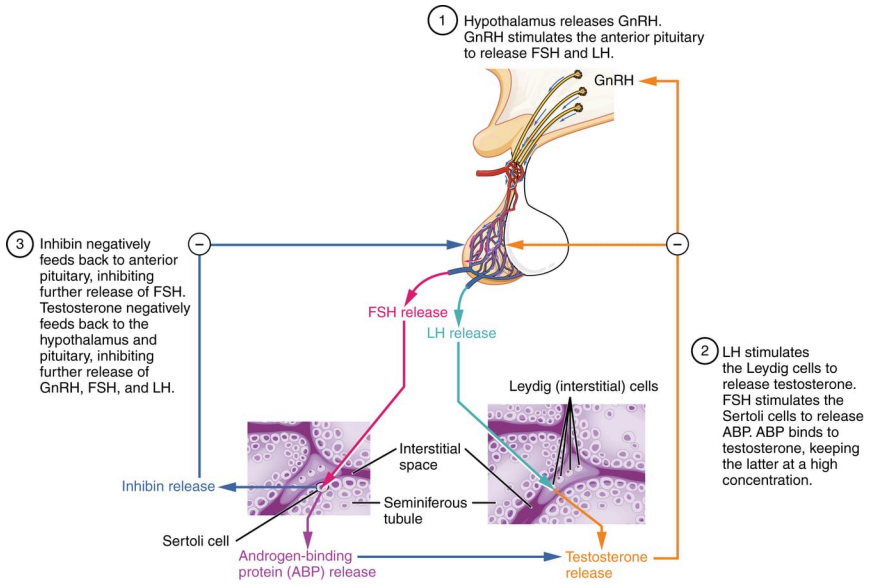
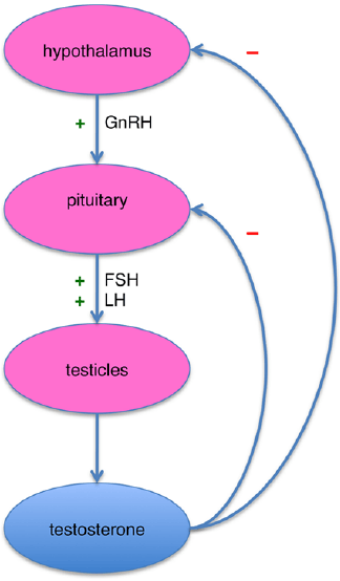


Figure 13.11.2: **Regulation of Testosterone Production.** The hypothalamus and pituitary gland regulate the production of testosterone and the cells that assist in spermatogenesis. GnRH activates the anterior pituitary to produce LH and FSH, which in turn stimulate Leydig cells and Sertoli cells, respectively. The system is a negative feedback loop because the end products of the pathway, testosterone and inhibin, interact with the activity of GnRH to inhibit their own production.



Regulation of Testosterone Production

The body carefully controls testosterone concentrations because normal levels are essential for male reproductive function. This regulation depends on communication between the hypothalamus, the anterior pituitary gland, and the testes.

As you have seen above, the process begins in the hypothalamus, which releases **gonadotropin-releasing hormone (GnRH)** in small pulses. GnRH travels to the anterior pituitary and stimulates the release of two key hormones: **luteinizing hormone (LH)** and **follicle-stimulating hormone (FSH)**. Although they were first discovered in females, LH and FSH are equally important in males.

In the testes, **LH** binds to receptors on **Leydig cells**, stimulating them to produce testosterone. **FSH** acts mainly on **Sertoli cells** inside the seminiferous tubules, supporting spermatogenesis. Sertoli cells also release **inhibin**, a hormone that helps regulate FSH secretion.

Testosterone production is controlled by a **negative feedback loop**. When blood testosterone levels are low, the hypothalamus

increases its release of GnRH, which in turn increases LH secretion and stimulates Leydig cells to produce more testosterone. When testosterone levels rise, the hormone binds to receptors in both the hypothalamus and the anterior pituitary, reducing the release of GnRH and LH. This decrease slows testosterone production until levels fall again and the cycle repeats.

Clinical Correlation

Some athletes use **anabolic steroids** to increase muscle mass and strength. These drugs are synthetic forms of male sex hormones that act like very strong testosterone. When a person takes anabolic steroids, the negative feedback loop causes the hypothalamus to reduce its release of GnRH, and the pituitary gland lowers its secretion of LH and FSH. With less LH and FSH reaching the testes, the Leydig cells produce less natural testosterone inside the testes and the Sertoli cells receive less stimulation to support sperm production. As a result, spermatogenesis can slow down or even stop, sperm counts may drop, and the testes can shrink in size. Over time, this hormonal imbalance can lead to reduced fertility or temporary infertility, and in some cases the effects may last even after steroid use has stopped.

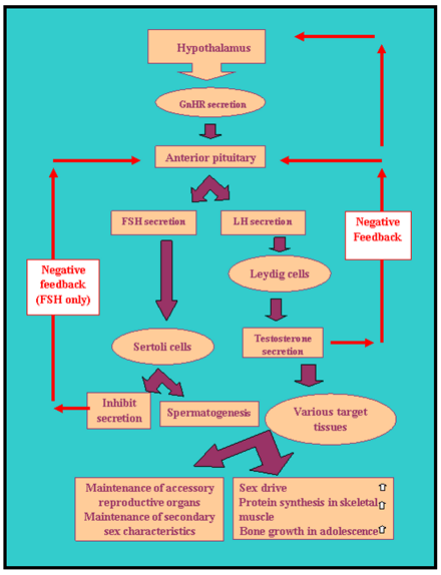


Figure 13.11.3: **And One More Time: Hormonal Regulation at a Glance.** Authored by: Stephaniegreenwood. Provided by: Wikimedia. Located at: commons.wikimedia.org/wiki/Fi...mone_chart.gif. License: *Public Domain: No Known Copyright*.

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13.12: Ovaries and Female Gamete Production

The ovaries produce oocytes and reproductive hormones through coordinated processes that change across the female reproductive lifespan.

Master this section and you'll be able to:

- Describe the location and the function of the ovaries.
- Explain the processes of oogenesis and folliculogenesis.
- List the main three hormones produced by the ovaries and outline their roles.

The female reproductive system functions to produce gametes and reproductive hormones, just like the male reproductive system; however, it also has the additional task of supporting the developing fetus and delivering it to the outside world. Unlike its male counterpart, the female reproductive system is located primarily inside the pelvic cavity. Recall that the **ovaries** are the female gonads. The gamete they produce is called an **oocyte**. We'll discuss the production of oocytes in detail shortly. First, let's look at some of the structures of the female reproductive system.

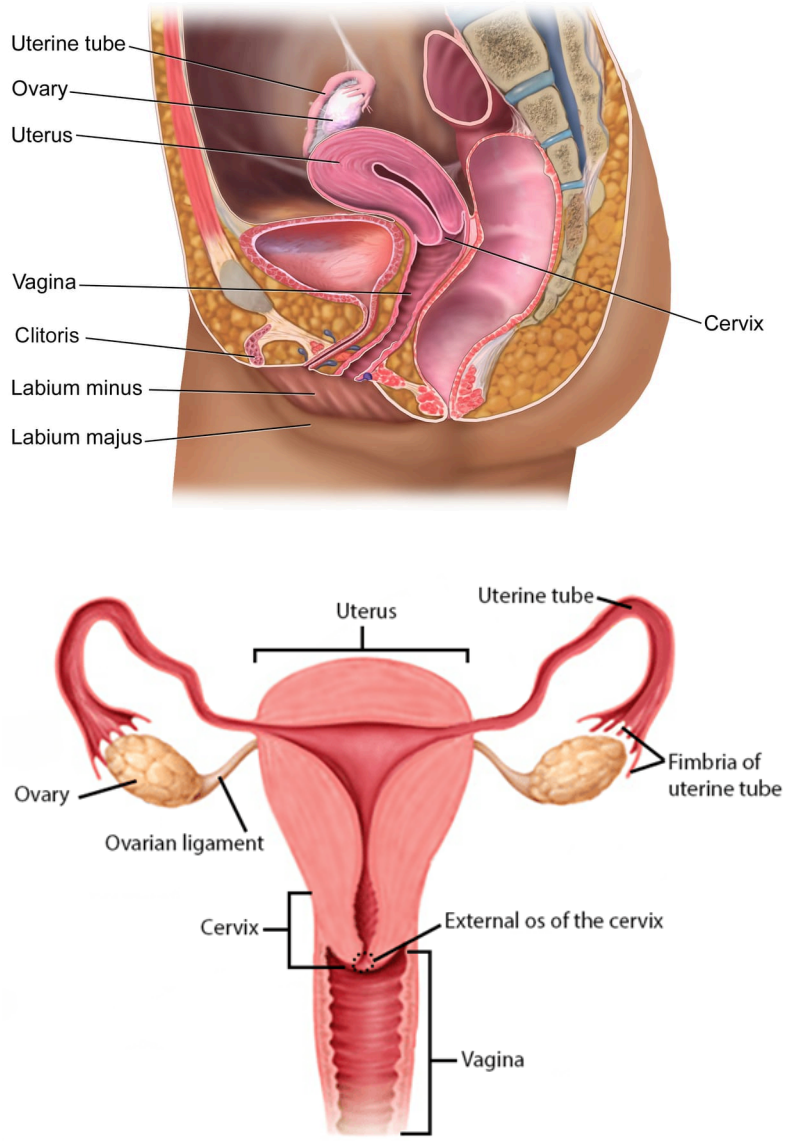


Figure 13.12.1: **Female Reproductive System.** The major organs of the female reproductive system are located inside the pelvic cavity. *(Image credit: "Female Reproductive System - Anterior and Midsagittal" by Blausen.com staff (2014), from the Medical gallery of Blausen Medical 2014, WikiJournal of Medicine, is licensed under CC BY 3.0. Modifications by Jennifer Lange. Image credit: "Female Reproductive Organs - Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by StacyRed-Wiki via Wikimedia Commons.)*

Ovaries and the Ovarian Cycle

The **ovaries** are the female gonads. Each ovary is a small, almond-sized organ (about 2 to 3 cm long) located within the pelvic cavity. The pair sits on either side of the uterus, and each ovary is connected to the uterus by the ovarian ligament.

The ovary is covered by a layer of cuboidal cells called the **germinal epithelium**. Beneath this covering is the **cortex**, the outer region of the ovary where **oocytes** develop. Each oocyte is surrounded by supporting cells to form a **follicle.**

Deep to the cortex lies the **medulla**, which contains the ovary's blood vessels, lymphatic vessels, and nerves.

The **ovarian cycle** refers to the predictable changes that occur in a female's oocytes and ovarian follicles. During the reproductive years, this cycle repeats about every **28 days.** It relates to the menstrual cycle but is not the same process. The **ovarian cycle** describes the monthly events in the **ovaries** that lead to the development and release of an egg, while the **menstrual cycle** describes the coordinated changes in the **uterus** that prepare the uterine lining for possible pregnancy or result in menstruation if pregnancy does not occur.

The ovarian cycle includes two connected events:

- **Oogenesis**, which is the formation of female gametes, and
- **Folliculogenesis**, which is the growth of ovarian follicles.

Oogenesis

Oogenesis is the process of forming an egg cell, or **oocyte**. It begins before birth. During fetal development, **stem cells** in the ovary called **oogonia** divide to form **primary oocytes.** These primary oocytes enter the first stage of meiosis and then pause. They remain in this paused state from before birth until puberty.

At puberty, the beginning of ovulation signals the start of reproductive maturity. From this point on, **ovulation** typically happens about once every 28 days. **Just before ovulation, a surge in luteinizing hormone causes a primary oocyte to resume meiosis.**

The cell divides unevenly. One large cell becomes the **secondary oocyte** that is released during ovulation, and one small cell becomes the first **polar body**. The polar body does not become an egg and eventually breaks down. Even though the division can create up to four cells, only the secondary oocyte survives to continue the cycle.

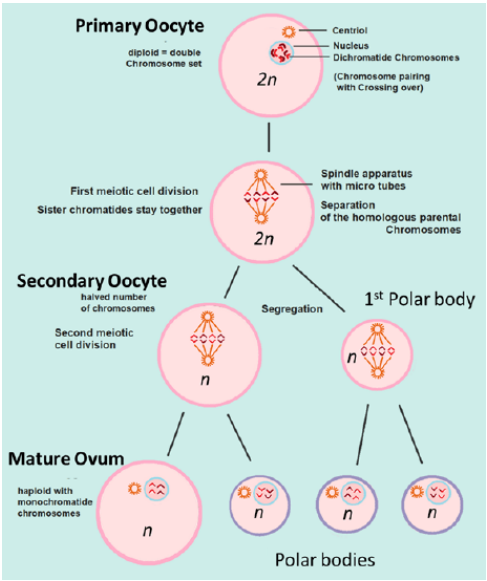
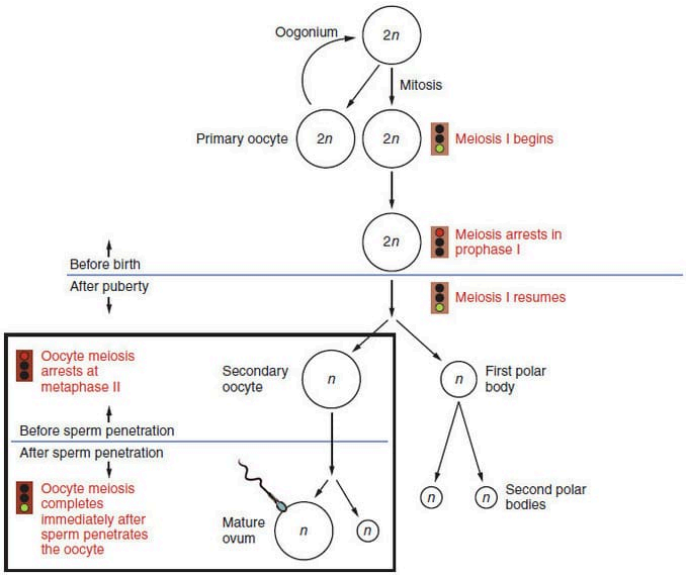


Figure 13.12.2: **Oogenesis and the Formation of Polar Bodies.** A primary oocyte (2n) begins meiosis I and divides unevenly, producing a large secondary oocyte (n) and a much smaller first polar body. The secondary oocyte then starts meiosis II and, if fertilization occurs, completes the division to form one mature ovum (n) and additional polar bodies. Polar bodies contain the excess chromosomes but very little cytoplasm, allowing nearly all available cytoplasm to remain in the single functional ovum.



This second diagram *(see image on the right)* relates oogenesis to the stages of a female's life. To understand what is happening, remember that **meiosis** is a special type of cell division that produces sex cells with half the usual number of chromosomes. It happens in two steps, meiosis I and meiosis II, and it reduces a diploid cell (2n) with paired chromosomes into haploid cells (n) with single chromosome sets.

Oogenesis begins before birth. Early germ cells called **oogonia** (2n) divide normally by mitosis to increase in number. Some of these oogonia prepare to become eggs. They start meiosis I and become primary oocytes. These primary oocytes pause in a very early stage of meiosis I and remain paused throughout childhood.

At puberty, hormones trigger one primary oocyte each month to continue meiosis I. This division is uneven. Most of the cytoplasm stays in one large cell called the secondary oocyte (n). A tiny cell called the first polar body is also formed. The polar body contains chromosomes but almost none of the cytoplasm needed to support development.

The secondary oocyte then starts meiosis II, but it pauses again, this time in metaphase II. This is the stage in which the oocyte is released during ovulation.

Meiosis II of a secondary oocyte is completed only if a sperm succeeds in fertilizing the secondary oocyte, which must occur within 24 hours of ovulation. If fertilization occurs, meiosis II produces the mature ovum (n) and additional polar bodies.

The purpose of polar bodies is to discard extra chromosomes so the developing oocyte keeps almost all of the cytoplasm needed to support early embryonic growth.

If sperm does not penetrate, then the secondary oocyte will break down after 24 hrs.

The larger amount of cytoplasm contained in the female gamete is used to supply the developing zygote with nutrients during the period between fertilization and implantation into the uterus. Interestingly, sperm contribute only DNA at fertilization — no cytoplasm. Therefore, the cytoplasm and all of the cytoplasmic organelles in the developing embryo are of maternal origin. This includes **mitochondria**, which contain their **own DNA**. Scientific research in the 1980s determined that mitochondrial DNA was maternally inherited, meaning that you can trace your mitochondrial DNA directly to your mother, her mother, and so on back through your female ancestors.

The number of primary oocytes decreases over time. A baby girl has one to two million, about four hundred thousand remain at puberty, and none remain by the end of menopause.

To keep the big picture straight, it helps to see oocyte development as a simple timeline:

- Before birth: **primary oocytes (diploid = 2n) form and pause**
- From puberty, each cycle: **one primary oocyte finishes meiosis I and starts meiosis II → secondary oocyte (haploid = n)**

- At fertilization: **secondary oocyte finishes meiosis II → ovum (n)**

Folliculogenesis

Folliculogenesis is the process in which **ovarian follicles (an oocyte plus its supporting cells)** grow and mature. During each roughly 28-day cycle, usually one follicle reaches full maturity and is ovulated, while many others begin to grow but then die. This normal, programmed death of follicles is called **atresia**.

Females are born with about one to two million ovarian follicles, each containing a primary oocyte. This supply is not renewed. Instead, the number of follicles steadily decreases over time. By the time a woman reaches menopause, all follicles have been used up or are lost, and no functional follicles remain.

As follicles develop, they move through several stages: **primordial**, **primary**, **secondary**, and **tertiary (**or **Graafian) follicles**. Even though the follicle grows and changes during these stages, the oocyte inside it remains a **primary oocyte** until just before ovulation, when it finally completes meiosis I.

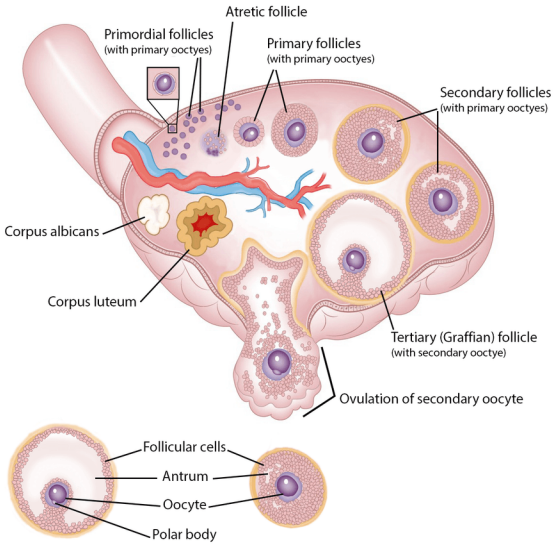


Figure 13.12.3: **Folliculogenesis**. The maturation of a follicle is shown in a clockwise direction proceeding from the smallest, resting primordial follicles to the large, fluid-filled tertiary (Graafian) follicle that releases a secondary oocyte at ovulation. Unlike the previous diagram that focused only on meiotic divisions and polar bodies, this image highlights the **growth of the follicle around the oocyte**: **primordial follicles** with a single layer of cells, **primary and secondary follicles** with expanding layers of follicular cells, and the **tertiary follicle** with a large antrum. It also illustrates **atresia**, the natural degeneration of many follicles, and the **post-ovulation structures** of the corpus luteum and corpus albicans. Once the follicle is mature, **it ruptures and releases the oocyte.** Cells remaining in the follicle then develop into the **corpus luteum.** *(Image credit: "Ovarian Follicles" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of "Slagter - Drawing Ovarium with folliculogenesis and ovulation - English labels" by Ron Slagter, Hope Wicks, LUMC, Cindy J.M. Hulsman, MUMC+ et al.)*

Hormones Produced by the Ovaries

The ovaries make three main hormones: estrogen, progesterone, and small amounts of testosterone.

- **Estrogen** helps create the secondary sex characteristics that appear at puberty, such as breast development and wider hips. It also supports the growth and ongoing health of the female reproductive organs.
- **Progesterone** prepares the uterus for a possible pregnancy by thickening the endometrium, and it helps prepare the mammary glands for milk production. Together with estrogen, it drives the monthly changes of the menstrual cycle.
- **Testosterone** is present in low amounts in women but is still important. It helps support muscle mass, bone strength, energy levels, and contributes to libido.

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13.13: Uterus and Uterine Tubes — Structures That Support Fertilization and Pregnancy

The female reproductive tract supports fertilization, pregnancy, and childbirth through coordinated anatomy and hormone-regulated processes.

Master this section and you'll be able to:

- Identify the main structures of the female reproductive tract, explain their anatomy and state their basic functions.

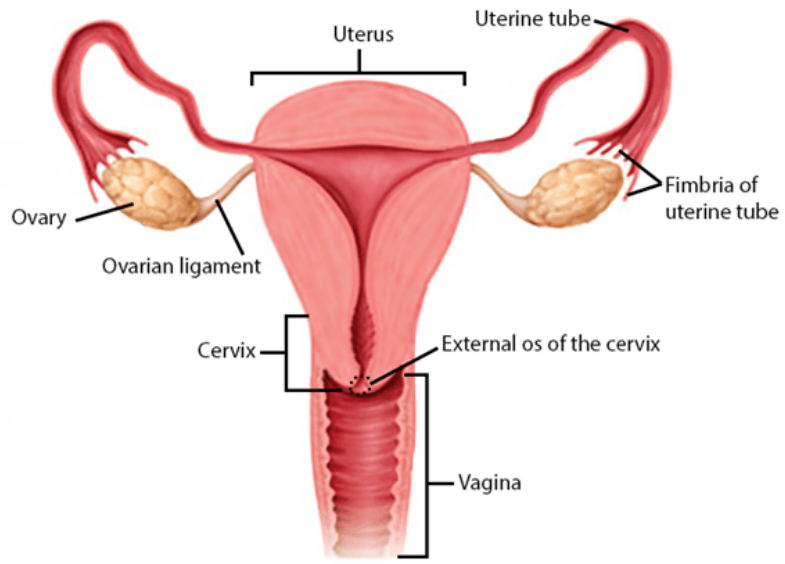


Figure 13.13.1: **Female reproductive tract.** The female reproductive tract includes the uterine tubes, uterus, cervix, and vagina. The uterine tubes extend from the uterus and end in finger-like fimbriae that help guide the oocyte into the tube after ovulation. The uterus is a muscular organ that supports implantation, pregnancy, and childbirth. Inferior to the uterus, the cervix forms a narrow passage that opens into the vagina at the external os. The vagina is a muscular canal that allows menstrual flow to exit the body, receives sperm during intercourse, and serves as the birth canal during delivery.

Uterine Tubes

The uterine tubes, also called **Fallopian tubes** or **oviducts**, serve as the passageway that transports the oocyte from the ovary to the uterus *(see figure13.13.1, above)*. Each uterine tube lies close to an ovary but is not directly attached to it. The widened, distal end of the tube flares outward and forms finger-like projections called **fimbriae**, which sweep over the surface of the ovary and help guide the oocyte into the tube after ovulation. Because the oocyte cannot move on its own, it relies on the uterine tube to transport it. Around ovulation, high estrogen levels cause the smooth muscle of the tube to contract and the cilia to beat more strongly. Together, these actions help sweep the oocyte into the uterine tube and slowly move it toward the uterus.

Watch this video(opens in new window) to observe ovulation and its initiation in response to the release of FSH and LH from the pituitary gland. What specialized structures help guide the oocyte from the ovary into the uterine tube?

If **fertilization** occurs, it usually happens in the ampulla, the **middle region of the uterine tube.** The inner lining of the tube contains **mucus-secreting cells and ciliated columnar cells**. The coordinated beating of the cilia toward the uterus creates a gentle current that moves the oocyte, or a fertilized ovum, from the distal end of the tube toward the uterine cavity.

In case **fertilization occurs,** the resulting **zygote** begins dividing as it travels through the uterine tube toward the uterus. It progresses from two cells to four cells and beyond during this journey. Once it reaches the uterus, the developing embryo implants in the uterine wall and continues to grow. I**f fertilization does not occu**r, the oocyte breaks down either in the uterine tube or in the uterus and is eventually reabsorbed or shed from the body during the next menstrual period.

Pelvic Inflammatory Disease (PID)

When an Infection Travels Upstream

Because the **uterine tubes are open near the ovaries**, they create a potential pathway for infection to spread upward through the female reproductive tract and end up in the pelvic cavity. **Pelvic inflammatory disease (PID)** most often develops when bacteria from a sexually transmitted infection (STI) ascend from the vagina and cervix into the uterus, uterine tubes, and beyond. If not treated promptly, the infection can spread further and, in rare cases, enter the bloodstream, leading to sepsis, a life-threatening condition.

Untreated PID can not only cause inflammation, but also lead to **scarring**, **and adhesions within the reproductive tract.** These structural changes increase the risk of **infertility**, **ectopic pregnancy**, and **chronic pelvic pain**. Early diagnosis and treatment are critical to prevent long-term complications.

Symptoms and Diagnosis

PID does not always cause noticeable symptoms. Many people with evidence of previous PID were unaware they ever had an infection. Even when symptoms are absent, permanent damage to the reproductive tract can still occur.

The risk of PID is also increased when procedures such as abortions are performed under non-sterile conditions, as bacteria that normally live in the vagina can move upward into the uterus and uterine tubes. Co-infections with multiple microorganisms are common.

When symptoms do occur, they may include:

- Lower abdominal or pelvic pain
- Fever
- Unusual vaginal discharge
- Irregular menstrual bleeding
- Pain during sexual intercourse

Diagnosis often involves a combination of clinical evaluation, laboratory testing for STIs, and imaging studies such as pelvic ultrasound.



Infectious Agents

PID can be caused by several different microorganisms, but the most common causes are the sexually transmitted bacteria *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, the causative agents of **chlamydia** and **gonorrhea**. These two infections are among the most common STIs in the United States.

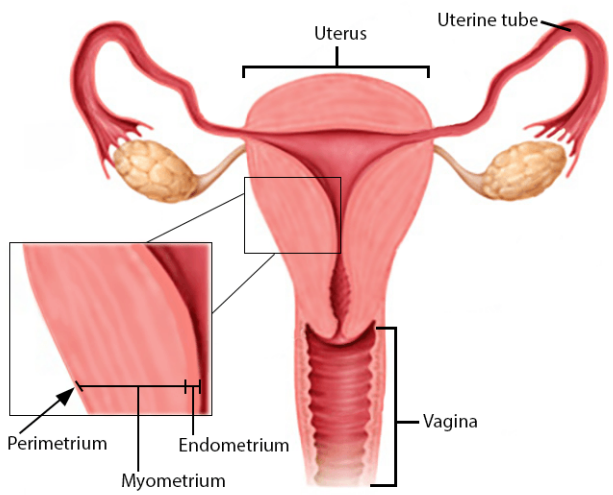
Treatment

PID is treated with antibiotics. Mild cases are usually managed with oral medications, while more severe infections may require intravenous antibiotics. Symptoms often begin to improve within a few days of starting treatment.

Sexual partners should also be treated to prevent reinfection. Even after the infection has resolved, scar tissue within the uterine tubes may remain and can block the passage of an oocyte, increasing the risk of infertility or ectopic pregnancy.

Uterus and Cervix

The uterus is a muscular organ that supports and nourishes a developing embryo. When a female is not pregnant, the uterus is about 5 cm wide and 7 cm long, roughly the size of a small pear.



The uterus has three main regions:

- **Fundus**: the rounded, upper portion of the uterus, located above the openings of the uterine tubes
- **Body (corpus)**: the large central portion of the uterus
- **Cervix**: the narrow, lower portion of the uterus that extends into the vagina

The cervix produces mucus that changes throughout the menstrual cycle. When estrogen levels are high, this mucus becomes thin and slippery, which helps sperm move more easily through the cervix and into the uterus.

Layers of the Uterine Wall

The wall of the uterus consists of three layers *(see figure on the right)*:

- **Perimetrium**: the thin, outer layer that covers and protects the uterus
- **Myometrium**: a thick layer of smooth muscle that makes up most of the uterine wall. It is responsible for uterine contractions. Strong contractions occur during labor to help deliver the baby, while weaker contractions occur during menstruation to help expel menstrual blood. Near the time of ovulation, gentle uterine contractions may also help move sperm through the reproductive tract.
- **Endometrium**: the innermost lining of the uterus. For more details see below:

The Endometrium

The innermost layer of the uterus is called the **endometrium**. It lines the uterine cavity and is the tissue that thickens each month in preparation for a possible pregnancy. The endometrium is made of connective tissue (called the **lamina propria**) covered by epithelial cells that face the uterine lumen.

Structurally, the endometrium has **two layers**:

- **Stratum basalis (basal layer)**
  This thin layer lies next to the myometrium (the muscular wall of the uterus). It does **not shed** during menstruation. Instead, it remains in place and serves as the source of cells that rebuild the endometrium after each menstrual cycle.
- **Stratum functionalis (functional layer)**
  This thicker, inner layer faces the uterine cavity. It contains uterine glands and blood vessels and is the portion of the endometrium that **responds to hormones**. This functional layer **grows and thickens in response to estrogen and**

progesterone. If pregnancy does not occur, this is the layer that is shed during **menstruation**.

Aging and the...

Female Reproductive System

Female fertility is highest in the twenties, declines gradually through the thirties, and decreases more rapidly after age 35. Fertility ends at menopause, which occurs when ovarian follicles are depleted and estrogen production falls. A woman is considered menopausal after 12 consecutive months without menstruation, with the average age occurring between 50 and 52 years.

As menopause approaches, declining inhibin levels lead to increased FSH secretion. Although more follicles are stimulated to grow, most undergo atresia, eventually resulting in a sharp drop in estrogen. This hormonal change is responsible for most menopausal symptoms.

During perimenopause, menstrual cycles become irregular and progesterone levels decline, which can increase the risk of endometrial hyperplasia. Common symptoms include hot flashes, night sweats, sleep disturbances, mood changes, and vaginal dryness, though severity varies widely.

After menopause, low estrogen levels increase the risk of cardiovascular disease and osteoporosis. Hormone therapy may relieve symptoms in some women but is typically used at the lowest effective dose for the shortest possible time due to potential risks.

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13.14: Hormonal Regulation of the Female Reproductive Cycles

The ovarian and uterine cycles are hormonally coordinated, each with two main phases, to regulate ovulation, prepare the uterus for pregnancy, and reset the system when pregnancy does not occur.

Master this section and you'll be able to:

- Describe the ovarian and uterine cycles and explain how they work together to form the menstrual cycle.
- Identify the two phases of the ovarian cycle and the two phases of the uterine cycle, including the major events that occur in each phase.
- Distinguish between the outcomes of the luteal phase when pregnancy occurs versus when pregnancy does not occur.

Female Reproductive Cycles: Dual Cycles with Paired Phases

The **menstrual cycle** is the roughly monthly sequence of coordinated hormonal and tissue changes that prepares the body for pregnancy. It includes

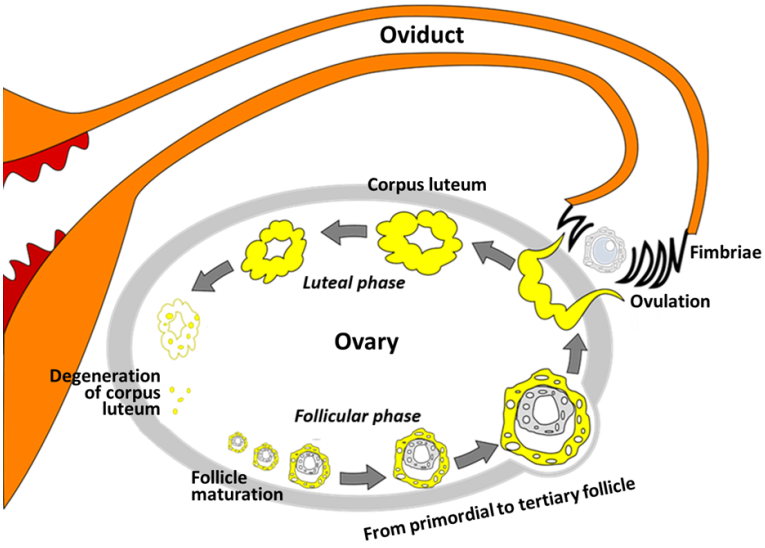
1. the **ovarian cycle,** in which an ovarian follicle matures, ovulation occurs, and the corpus luteum forms and then regresses if pregnancy does not occur, and

2. the **uterine cycle,** in which the endometrium thickens to support possible implantation and then sheds as menstruation if implantation does not happen.

The Two Cycles: Ovarian and Uterine Cycles

The ovarian and uterine cycles are **two coordinated, repeating cycles** that occur in the female reproductive system and together make up the menstrual cycle. The ovarian cycle takes place in the ovaries and focuses on the maturation and release of an oocyte, while the uterine cycle (also called menstrual cycle) occurs in the uterus and prepares the endometrium for a possible pregnancy. Although these cycles happen in different organs, they are **tightly linked by hormones** and occur on the **same timeline**. Changes in ovarian hormones drive predictable structural and functional changes in the uterus, ensuring that ovulation and uterine preparation are synchronized. Understanding how these two cycles work together is essential for understanding fertility, menstruation, and the hormonal regulation of the female reproductive system.

The Ovarian Cycle

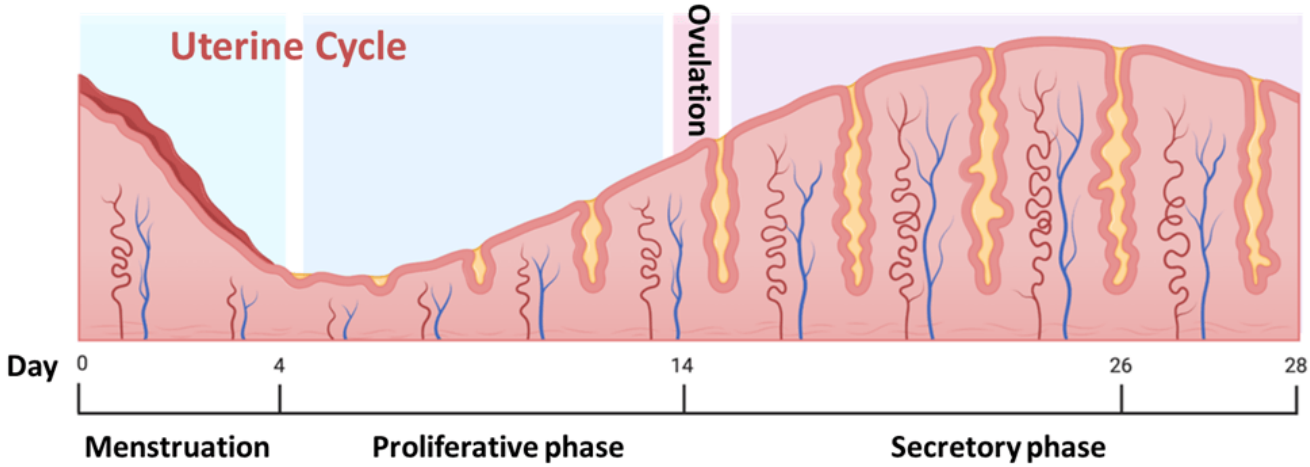


Primordial follicles are the "sleeping" follicles that make up a female's lifetime ovarian reserve. During the reproductive years, a small number of these primordial follicles are continuously activated (recruited) to begin developing into primary follicles. Most of the recruited follicles do not make it very far and instead die off through **atresia**. Only a small cohort continues developing into **secondary follicles** and then into **tertiary follicles**, and typically just one becomes the dominant **tertiary** (**Graafian**) **follicle** that will ovulate in a given cycle by releasing its egg in a process called **ovulation**. This pattern repeats month after month until the ovarian reserve is depleted, which ultimately leads to menopause.

After ovulation, the emptied follicle transforms into a temporary hormone-making structure called the **corpus luteum**, which releases hormones that support the uterus in case pregnancy occurs. If fertilization does not happen, the corpus luteum breaks down, hormone levels fall, and the next cycle begins.

The ovarian cycle has two main phases: **the follicular phase** and **the luteal phase.** The follicular phase begins on day 1 of the cycle (the first day of menstrual bleeding) and lasts until **ovulation**, when an oocyte is released. During this time, several follicles begin to grow, but usually only one becomes the dominant follicle. As it matures, it produces rising levels of estrogen, which supports follicle development and helps rebuild and thicken the uterine lining. After ovulation, the **luteal phase begins.** The emptied follicle transforms into the corpus luteum, a temporary hormone-secreting structure that releases mostly progesterone (and some estrogen) to stabilize and further prepare the uterine lining for possible implantation. If fertilization and implantation do not occur, the corpus luteum breaks down, hormone levels fall, and the next menstrual period begins.

The Uterine (Endometrial) Cycle



The uterine cycle, also called the endometrial cycle, describes the predictable monthly changes that occur in the **endometrium**, the innermost glandular lining of the uterus. These changes are driven by fluctuations in ovarian hormones and prepare the uterus for a possible pregnancy. The cycle is counted from the first day of menstrual bleeding, and a typical cycle lasts about **28 days**, although normal cycles vary in length.

During each cycle, the endometrium follows a repeating pattern of **shedding, regrowth, and specialization.**

After **menstruation**, rising estrogen levels stimulate the endometrium to rebuild and thicken, increasing glandular tissue and blood vessel supply. Following **ovulation**, progesterone further modifies the lining, making it highly secretory and capable of supporting an implanted embryo. If fertilization and implantation do not occur, ovarian hormone levels fall, the functional layer of the endometrium is shed, and a new cycle begins.

Like the ovarian cycle, the uterine cycle has two main phases: the **proliferative phase** and the **secretory phase.** The proliferative phase begins on day 1 with menstrual bleeding, during which the superficial functional layer of the endometrium is shed. As estrogen levels rise during the follicular phase of the ovarian cycle, the endometrium regenerates and thickens in preparation for possible pregnancy. After ovulation, the secretory phase begins under the influence of progesterone released by the corpus luteum. During this phase, the endometrium becomes highly vascular and glandular and secretes nutrients that support potential implantation. If implantation does not occur, progesterone and estrogen levels decline, triggering breakdown of the endometrial lining and the onset of the next menstrual period.

Each Cycle Has Two Phases

As you have seen above, the ovarian and uterine cycles are closely linked and follow a predictable pattern each month. Also, in both cycles, events are organized into two main phases. Here is a little closer look at the 4 phases:

The Follicular Phase (Ovary) and the Proliferative Phase (Uterus)

The first half of a typical ovarian cycle is called the follicular phase, while the equivalent time frame in the uterus is called the proliferative phase.

In the ovary, several primordial follicles (each containing an oocyte surrounded by supporting follicle cells) begin to grow. **FSH** from the anterior pituitary stimulates follicle growth by causing granulosa cells to multiply. As the follicles enlarge, they produce increasing amounts of **estradiol** (a major estrogen). Typically, **one follicle becomes the dominant follicle** and continues to mature, while the others stop developing and undergo atresia (they break down).

The uterus — as estradiol levels rise — responds by **rebuilding and thickening the endometrium** (that is why this time period

in the uterus is called the proliferative phase). Estradiol also makes **cervical mucus thinner and more slippery**, which helps sperm survive and move through the cervix. Near the end of this phase, high estradiol triggers a surge of **LH** (luteinizing hormone). This **LH surge** is the signal that leads to **ovulation**, which typically occurs about **30 ± 2 hours after the LH surge begins**.

Ovulation

Ovulation is the part of the ovarian cycle when a **mature tertiary (Graafian) follicle breaks open** and releases an **ovum** (also called an **oocyte**, female **gamete**, or **egg.**

The Luteal Phase (Ovary) and the Secretory Phase (Uterus)

In the **ovaries**, the **luteal phase begins immediately after ovulation** as **FSH and LH** stimulate the remnants of the dominant follicle to transform into the **corpus luteum**. The corpus luteum grows for a short time and secretes **large amounts of progesterone** and smaller amounts of **estrogen**. Progesterone prepares the endometrium for implantation by thickening it and stimulating glandular secretions that support early embryonic development. Progesterone also causes a measurable rise in basal body temperature.

The luteal phase ends in one of two ways: **pregnancy or luteolysis.**

If pregnancy occurs, the implanted embryo produces human chorionic gonadotropin (hCG), a hormone similar to luteinizing hormone (LH). hCG maintains the corpus luteum, allowing continued secretion of progesterone. Progesterone preserves the endometrium and sustains the elevated basal body temperature characteristic of the luteal phase. After approximately eight to twelve weeks, the placenta takes over progesterone production. Because hCG is unique to pregnancy, most pregnancy tests detect this hormone.

If pregnancy does not occur, luteolysis takes place. The corpus luteum degenerates, causing progesterone and estrogen levels to fall. This decline in ovarian hormones triggers an increase in follicle-stimulating hormone (FSH), which initiates follicle recruitment for the next ovarian cycle.

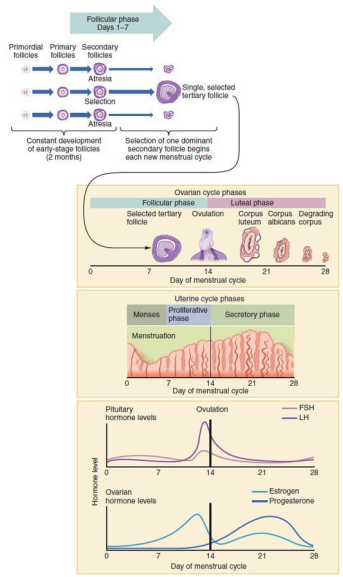


Figure 13.14.1: **Hormone Levels in Ovarian and Uterine Cycles.** The correlation of the hormone levels and their effects on the female reproductive system is shown in this timeline of the ovarian and menstrual cycles. (Image Source: OpenStax Anatomy & Physiology 2E, CC BY 4.0. Access for free at *OpenStax Anatomy and Physiology 2E* online)

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