wonders of the HUMAN BODY

Volume 2

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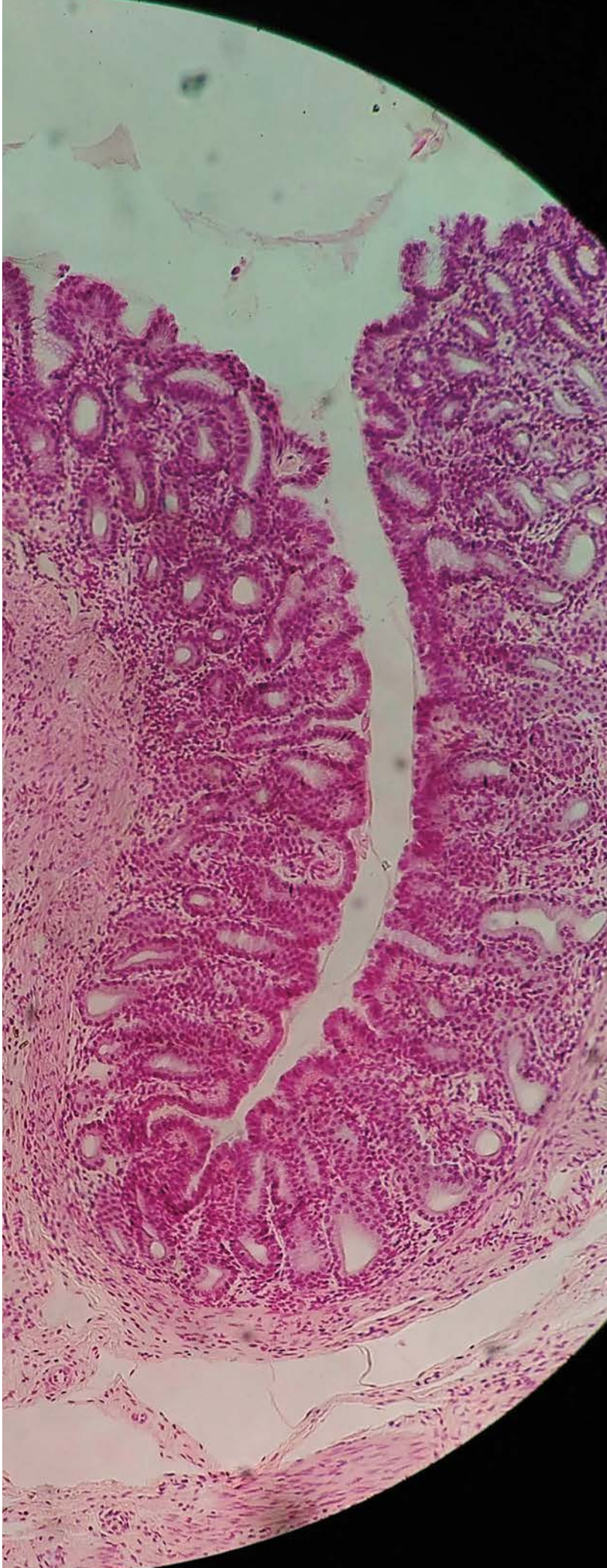
Dedication

For faraway family and friends —
Sissy and Mike McDuffee
Mark and Rhana Hackett
Missed every day, loved forever.



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UNIT 1

DIGESTIVE SYSTEM & METABOLISM

wonders of the HUMAN BODY

INTRODUCTION

Here is a simple fact. Our bodies need energy.

Without a constant supply of energy, we could not think because our brains would not function. We could not walk because our muscles would not contract. We could not . . . well, you get the idea.

Where does all this energy come from? It comes from the food we take in!

Our bodies also need raw materials to repair a bone when it is broken and even to build up stronger muscles when we exercise. These raw materials come from the food we eat.




So how does the cereal you had for breakfast become energy? Or the popcorn you had at the ballgame? How does the chicken you had for supper provide the amino acids the body needs to build proteins? These are some of the things we will examine in depth in this first unit of *Wonders of the Human Body Volume 2*.

Welcome to our exploration of the digestive system!

What is Digestion?

At first glance, this may seem like a simple question. After all, we use the terms "digest" and "digestion" almost every day. But what do these words really mean?

Digestion is the process by which the food we take in is converted to substances needed by our bodies. Those substances may then serve as fuel from which energy is obtained or raw materials, which are building blocks for more complex molecules or structures. After all, the foods we eat are made up of very complex substances, aren't they? An undigested carrot is of little use to the body. However, when the carrot is broken down into its much simpler components, it becomes very useful indeed. The same is true of the other things we eat. Yes, even Brussels sprouts can be broken down into things the body needs.

Think of it this way. The gasoline that we put into a car is used to power the car's engine. The gasoline is already in a form that the car can directly burn to produce energy. This fuel is burned in the engine to make the car go. The gasoline does not need to be broken down (in a sense, digested) to be useful. It is used "as is."

Food is different. It must be broken down into more useful forms before it can be used by our bodies, either as fuel or as raw material. It must be digested.

But things don't end there. The substances that result from the breakdown of food must then be absorbed into the bloodstream to be utilized by the body. You will soon understand how all this takes place!

We are a Special Creation

As with all our explorations into the complexity of the human body, when you see the incredible design of the digestive system, you ultimately have to ask yourself, "Can this all possibly be an accident? Something that happened by chance?" The answer is obviously a resounding, "No!"

We are not the product of evolution. We are not animals. We are a special creation.

Then God said, "Let Us make man in Our image,
according to Our likeness;
let them have dominion over the fish of the sea,
over the birds of the air, and over the cattle,
over all the earth and over every creeping thing
that creeps on the earth."
So God created man in His own image;
in the image of God He created him;
male and female He created them.

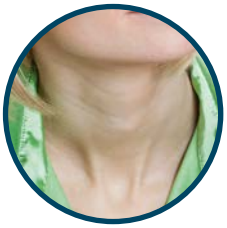
(Genesis 1:26–27)

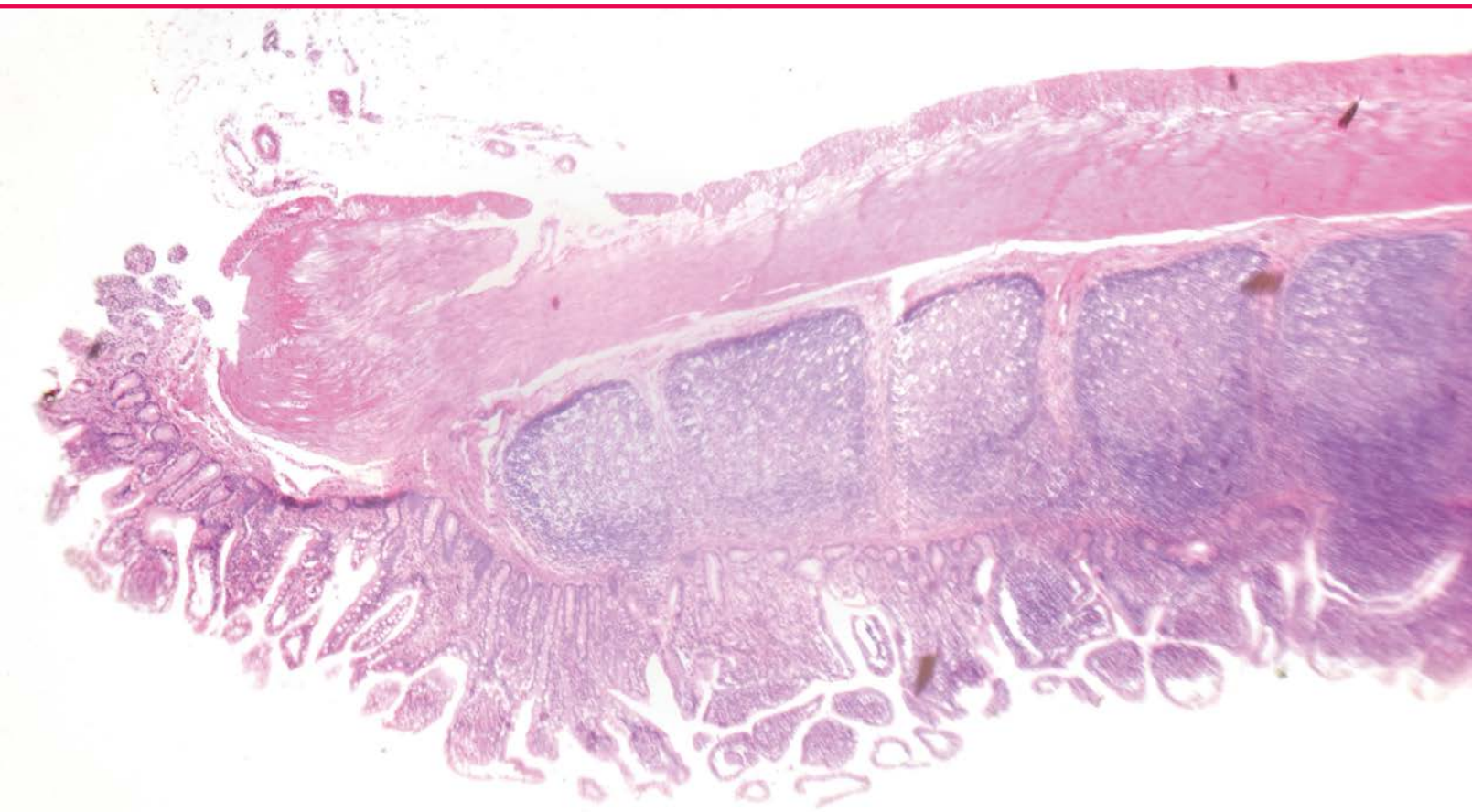
May we continually acknowledge God our Creator as we proceed though our study.

OVERVIEW OF THE DIGESTIVE SYSTEM

The digestive system is composed of two groups of organs — the gastrointestinal (GI) tract and the accessory digestive organs.

The gastrointestinal tract, also known as the alimentary canal, is a long tube that extends from the mouth to the anus. Contraction of the muscles in this tube propels food along its journey from beginning to end. The GI tract is comprised of the mouth, pharynx, esophagus, stomach, small intestine, and large intestine. It is about 20–24 feet long in the average person.



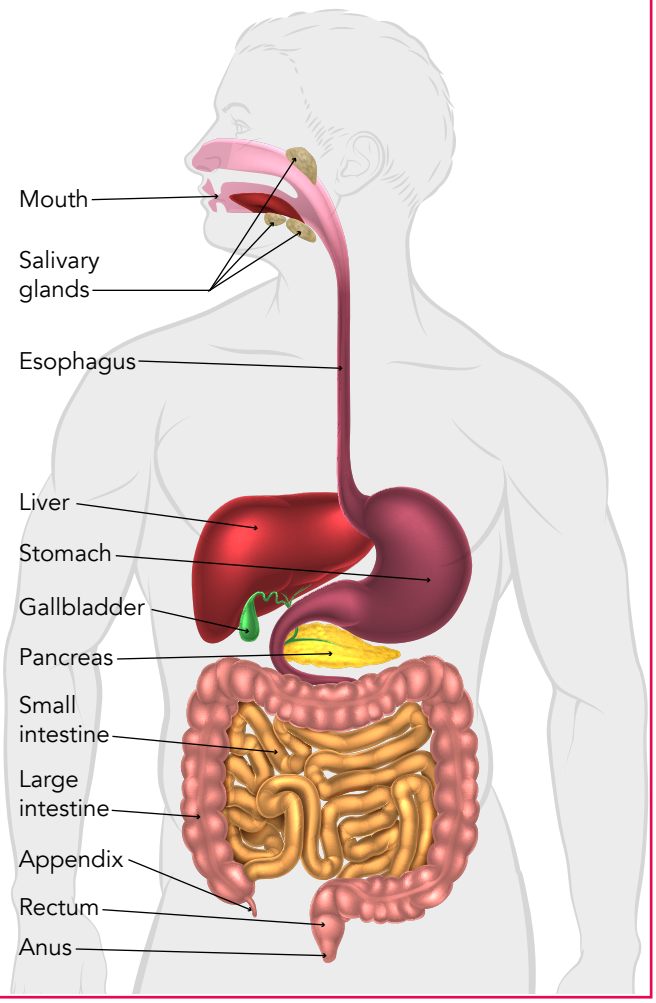
Microscopic section of the large intestine

The processes of digestion and absorption both take place in the GI tract. Interestingly, because the GI tract is open to the outside at both ends, food passing through it is technically not ever inside the body. Only the breakdown products from the digestion of food ever cross through the GI tract's walls to enter the body.

The accessory digestive organs are the teeth, tongue, salivary glands, liver, gallbladder, and pancreas. The teeth and tongue are involved with chewing and swallowing. These are the only accessory digestive organs that come into contact with the food. The remaining four accessory organs function by producing and/or delivering secretions that assist in the digestion and absorption of food.

TAKING A CLOSER LOOK

The Digestive System



Major Functions of the Digestive System

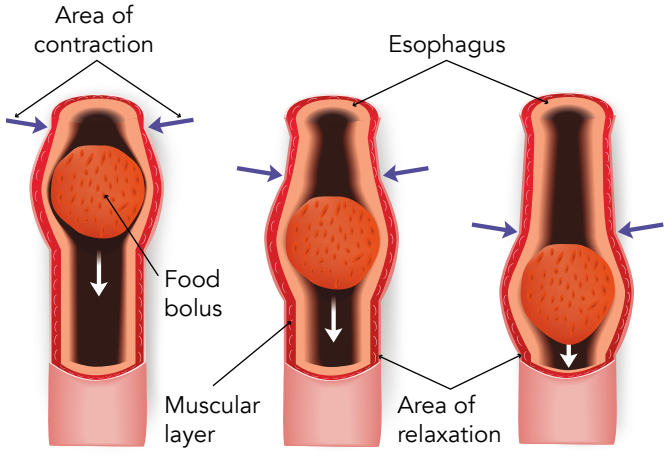
Even though the GI tract is, in one sense at least, simply a long tube, it performs remarkable functions. Our Creator designed the GI tract to carry out a complex set of activities. Let us examine the basic processes of the digestive system more closely.

The first function of the digestive system is called *ingestion*. No surprise here, right? This simply means taking food into the GI tract. Eating and drinking is ingestion.

The next function of the digestive system is *propulsion*. That is, the food is moved along the length of the GI tract. The muscular walls of the GI tract squeeze and relax in a process called *peristalsis*. As this muscle activity occurs, not only is food propelled along, but some mixing and grinding of the food also takes place.

TAKING A CLOSER LOOK

Peristalsis



Next, there is the process of *digestion*, and it has two components. First, there is *mechanical digestion,* which is the physical breaking down of food into smaller pieces. This includes the tearing and grinding of food by the teeth, and the churning of food in the stomach. Then, there is *chemical digestion*. Here, we find the various digestive enzymes breaking food down into its more basic components.

Next comes the process of *absorption*. Here, the breakdown products of chemical digestion move into the cells that line the lumen of the GI tract. From here, these substances then move into the bloodstream to be used throughout the body.

The final process is *elimination*. Here, indigestible material and other substances are removed as they reach the end of the GI tract. The material eliminated is called *feces* and leaves the body through the anus.

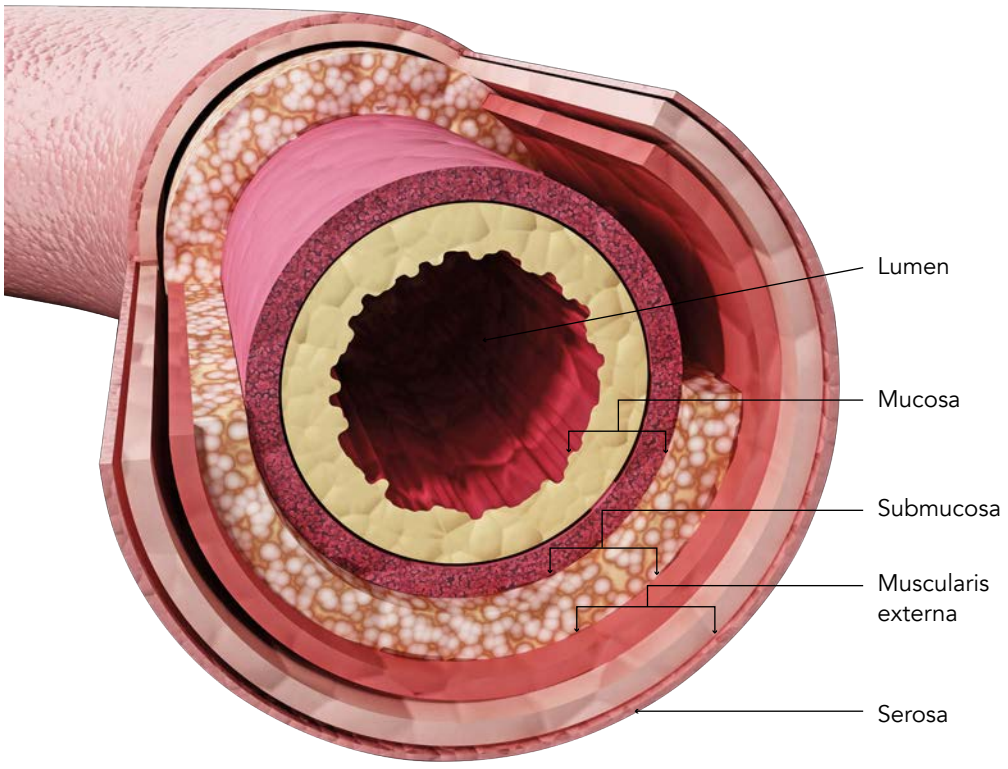
Layers of the GI Tract

The GI tract is essentially a long tube. The wall of the tube is made of several layers. In order for you to digest your food and absorb nutrients from it, the tissues in the GI tract wall must perform a variety of functions, such as squeezing the tube's contents, secreting chemicals that help digest food, and allowing the nutrients to travel through the wall. The wall of each section of the GI tract has its own anatomical features that enable it to do its jobs. While the oral cavity and pharynx have their own unique anatomy, the remaining sections of the GI tract, from esophagus to anus, have walls made of the same four basic layers. Let's see how they are arranged.

If you look at a cross section of the GI tract, you will see an opening in the middle, called the *lumen*. The food you chew up and swallow enters the lumen, where it is processed and moved along from section to section. The lumen is surrounded by four layers of tissue. Starting at the lumen and moving outward, these layers are the *mucosa*, the *submucosa*, the *muscularis externa*, and the *serosa*.

TAKING A CLOSER LOOK

Tissue Layers of the GI Tract



The Mucosa

The innermost tissue layer in the GI tract wall is called the mucosa. This layer lines the lumen of the GI tract and thus comes into contact with material passing though the digestive system. The mucosa is itself made up of three layers (wouldn't you just know it . . .).

The first is the *epithelium*. This is the layer in direct contact with the lumen. It is made up of different types of cells that perform needed functions. Some cells in the epithelium secrete mucus. This mucus not only helps food slide through the GI tract, but also helps protect digestive organs from being damaged by the chemicals secreted to digest food.

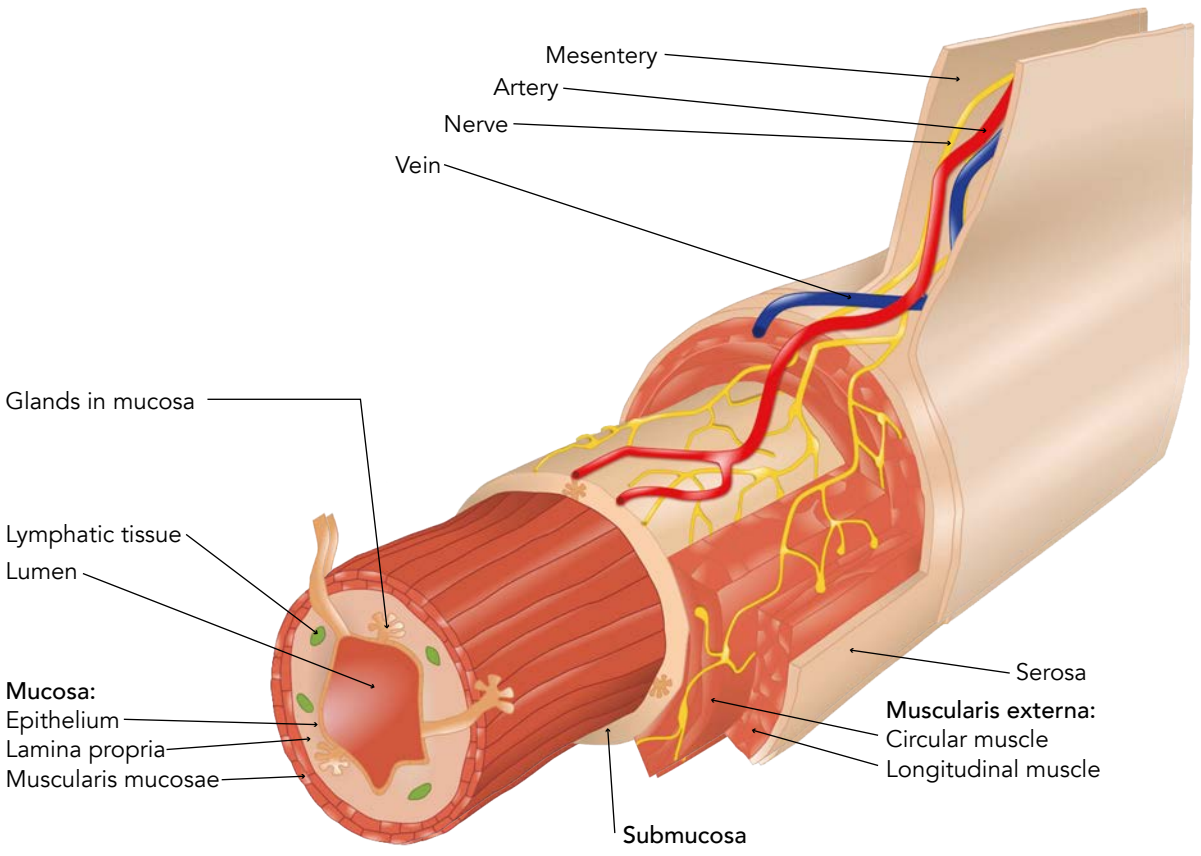
Scattered throughout the GI tract epithelium are several specialized cell types. Some secrete chemicals and enzymes that help digest food. Others aid in absorption of the breakdown products as food is digested. We will explore many of these in depth as our study progresses.

Cells in the epithelium are replaced rapidly. They usually last about 7 days. The old cells slough off into the lumen and are carried away and eliminated in the feces.

Moving outward from the lumen, we find the *lamina propria*. This layer of connective tissue contains lots of capillaries. Blood in the capillaries brings oxygen and nutrients to the epithelial cells. These blood vessels also carry away materials absorbed from the

TAKING A CLOSER LOOK

Layers of the GI Tract



lumen as food is digested. Also found in the lamina propria are special immune system cells. These cells prevent infectious agents (bacteria, etc.) from invading the body through the walls of the GI tract.

The third layer of the mucosa is the *muscularis mucosae*. This is a tiny layer of smooth muscle fibers. These fibers allow the epithelial lining of the mucosa to expand and contract as conditions warrant. This helps regulate the surface area available for secretion and absorption. This thin muscular layer is not the only muscle found in the GI tract wall. A more robust layer of muscle is found farther out in the wall.

The Submucosa

Below the mucosa is the *submucosa*, a word that literally means "below the mucosa," just like *submarine* means "below the sea." Indeed, the submucosa provides a foundation for the mucosa.

The dense connective tissue of the submucosa supports the overlying mucosa as it expands to accommodate food to be digested and shrinks back when digestion is completed.

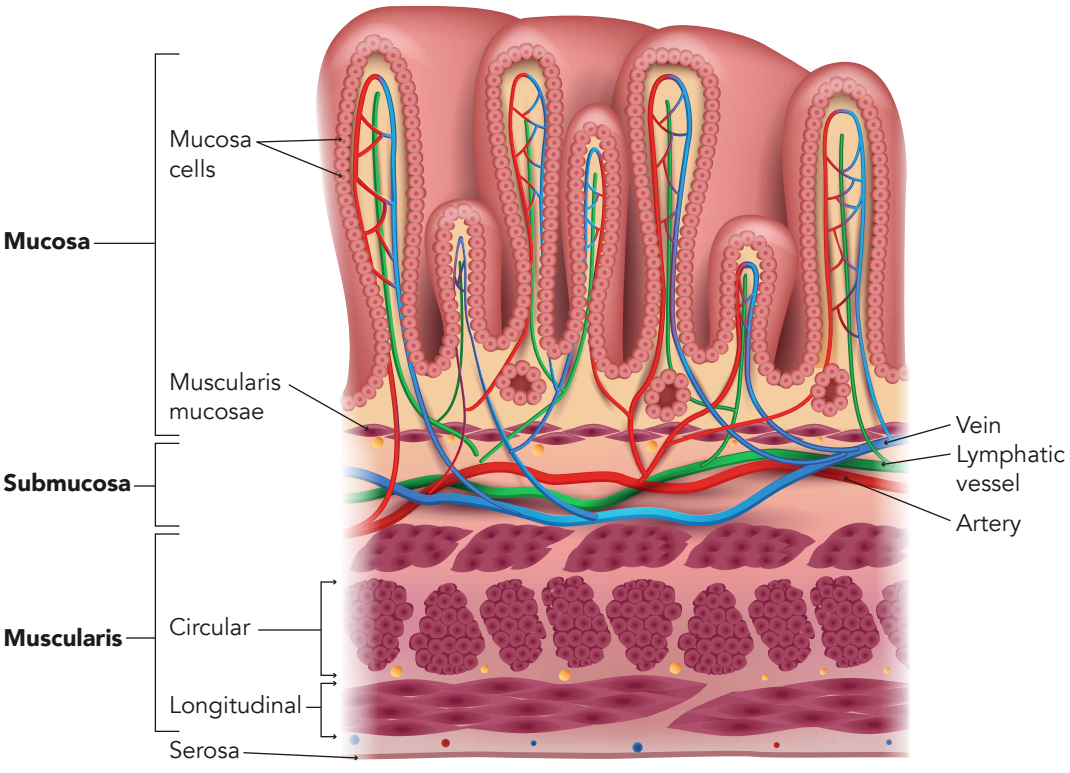
The blood and nerve supply of the GI tract run through this foundation. Nerve fibers regulate the GI tract's activities. The blood vessels carry away the breakdown products of food as it is absorbed. The blood vessels in the submucosa also bring oxygen and nutrients to the GI tract tissues, because the walls of the GI tract, though responsible for getting nutrients from the food we eat, are not directly supplied by those nutrients.

The Muscularis Externa

Moving farther away from the lumen, the next layer is the *muscularis externa*. This sturdy layer of muscle propels food through the GI tract.

TAKING A CLOSER LOOK

The Mucosa, Submucosa, and Muscularis



Two different types of muscle compose the muscularis externa. Which type dominates varies from section to section. In the mouth, pharynx, and upper esophagus, as well as in the final portion of the colon, the muscles in the muscularis externa are skeletal muscle. As you (hopefully!) recall, skeletal muscle is under voluntary conscious control.

This means you can control the act of swallowing and the mechanics of elimination. It does not take much imagination to appreciate the importance of having voluntary control of these activities.

Throughout the remainder of the GI tract, the muscularis externa consists of smooth muscle, which is not under voluntary control. This is just as it should be. After all, it would be very inconvenient if you had to consciously control each step of the digestive process, thinking, "That hamburger has spent enough time being processed in this part of my small intestine and is ready to slowly move along to the next." Fortunately, you don't. Your smooth muscle responds to the instructions provided by the mechanisms that automatically monitor and regulate all the activities of the marvelous factory-like assembly line that is your GI tract.

Once again, our Master Designer has put exactly the right kinds of muscles in all the right places! Skeletal muscle where you need conscious control, smooth muscle where you don't. Sounds like the right design to me.

The Serosa

Once you swallow your food, it enters the part of the GI tract that is located in the abdominopelvic cavity, starting with the stomach. From the stomach onward, the GI tract tube is covered by a layer of connective tissue called the *serosa*. The serosa is the outermost of the layers of the GI tract, and it helps provide support for the organs of the GI tract. The serosa forms not only the outer covering for the GI tract, but at the same time acts as the slick lining that covers the contents of the abdominopelvic cavity.

The words *serosa* and *serous membrane* are related to the Latin word *serum,* which is a thin, watery fluid. The serosa is made of connective tissue covered by a thin layer of epithelium called *mesothelium*. The epithelial tissue covering most internal organs and lining most body cavities is called mesothelium. Mesothelial cells secrete a lubricating fluid that helps organs covered by mesothelium slide past each other.

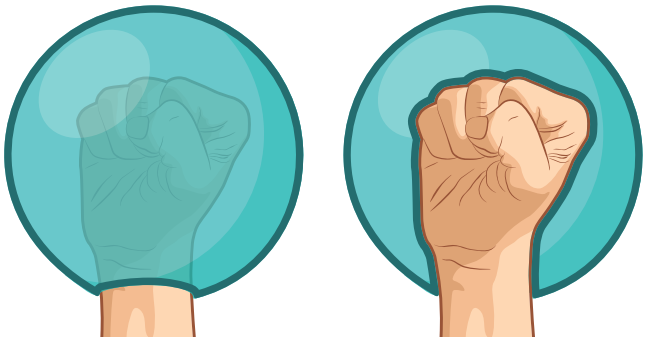
The outermost layer of the GI tract is slightly different for the esophagus. This organ resides in the thoracic cavity and lacks a full serosal covering. The esophagus, as we shall see later, is anchored in the chest cavity and doesn't need to slide past anything. The esophagus, therefore, instead of a serosa, has only a thin connective tissue layer helping hold it in place. This layer is called the *adventitia*.

The Peritoneum

The double-layered serous membrane that lines the abdominopelvic cavity is called the peritoneum. The peritoneum covers, at least partially, most of the organs in the abdomen. It also forms the innermost layer of the abdominal wall.

The peritoneal membrane, like other body cavity linings, consists of connective tissue covered by a thin layer of mesothelium. Does this sound familiar? Does this sound like the serosa we learned about earlier? You recall that the serosa — made of connective tissue covered by mesothelium — covers the outside of the GI tract. Well, the part of the peritoneum that covers the surface of the organs is called the *visceral peritoneum*. This is just another name for the serosa! They are one and the same. The other portion of the peritoneum that lines the abdominopelvic cavity just beneath the abdominal wall is called the *parietal peritoneum*.

The double-layered construction of the peritoneum is most easily understood by a simple analogy. If you take a partially inflated balloon and push your fist slowly into it, you get the idea of how the peritoneum works. Think of your fist as an organ. Your fist is covered tightly by a layer analogous to the *visceral peritoneum.* The other side of the balloon is analogous to the *parietal peritoneum,* the portion of the peritoneum that contacts the



abdominal wall. Your peritoneum-covered fist is now inside a peritoneum-lined abdominal cavity. That's pretty much how the peritoneum works. In fact, that's pretty much how the peritoneum forms in a developing baby, long before birth when its organs are taking shape.

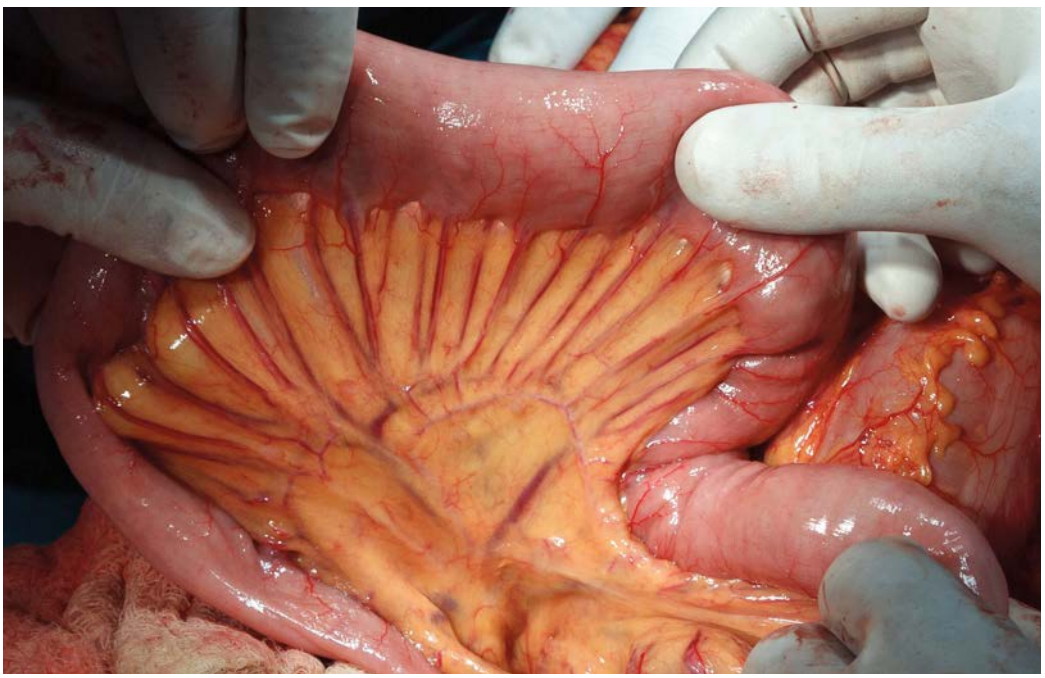
Remember, the reason that the peritoneum is called a serous membrane is that the cells of the mesothelium secrete a small amount of serum-like fluid to lubricate the peritoneal cavity. This lubrication allows the surfaces of organs to glide across one another easily, protecting the organs by preventing friction and snags.

Not all organs are completely surrounded by the peritoneum. Some organs are located in the very back of the abdominopelvic cavity. Only their front surfaces are covered by the peritoneum. These organs are said to be *retroperitoneal*. This word means "behind the peritoneum."

There are places where the peritoneal membrane's layers, after enveloping an organ, are actually fused together. This is another very important design. This fused membrane is called a *mesentery*. Mesenteries help secure organs to the body wall and hold them in the proper position so that they won't twist while also suspending them to allow them room to expand and to slide along other organs. These mesenteries are also a pathway by which nerves and blood vessels reach the organs suspended by them.

Regulation of the Digestive System

Your digestive system is sometimes very, very busy, and other times it is almost resting. How does it know when to get busy, or what it should do when presented with a chewed-up hamburger? You have probably been told that you should not swim right after you eat a big meal. That is because your digestive system will be very busy and, if you suddenly divert most of the blood and oxygen it needs to do its work to your arms and legs for a vigorous swim, you might get a painful cramp as your GI tract protests the interruption. So before moving into a detailed exploration of the digestive



Small intestine with mesentery

system, we need to understand the basics of how this system is controlled, or regulated.

Some of the activity of the digestive system is under local control. That is to say that some mechanisms that control digestion can be found in the digestive system itself. The lining of the GI tract contains lots of special receptors. Some are triggered by stretching of the surrounding structures, like when a rounded ball of chewed food — called a *bolus* — enters the lumen. Other receptors are triggered by the presence of certain hormones or certain types of food. Greasy food, for instance, requires certain chemicals to process it, chemicals not needed to process saltine crackers. Food leaving the stomach has been mixed with a strong acid, and changes in the acid levels in the contents of the lumen can also be detected by receptors in the GI tract walls.

When triggered, some receptors stimulate smooth muscle to contract. Others cause glands to increase or decrease release of digestive enzymes or other chemicals. Some receptors, when stimulated, trigger release of certain hormones into the blood. You see, lots of things happen in the walls of the organs in the digestive system.

Further, the GI tract has its own nervous system, called the *enteric nervous system*. These neurons found in the walls of the GI tract are essential to adequate regulation of the digestive system. It has been estimated that the enteric nervous system contains 100 million neurons (No, I don't know who counted them . . .)! Some have gone as far as to call this collection of neurons the "gut brain." These neurons help control not only the motility of the GI tract, but also the secretory activity of cells in the epithelium.

Lastly, there are control mechanisms involving the central nervous system. These bring a level of control from outside the digestive tract. It is control of this sort that may divert blood and oxygen from the digestive tract to your muscles when you swim, causing the digestive tract to cramp at the interruption until it has time to respond to the message.

These regulatory mechanisms will be described in more detail as we continue our study.

Peritonitis

Peritonitis is a condition resulting from an acute inflammation of the peritoneum. This is a serious medical condition and is most often (although not always) the result of bacterial contamination of the abdominal cavity. The contamination can be the result of leakage from a burst ulcer or from a ruptured diverticulum in the colon. One of the most common causes of peritonitis is bacterial leakage from a ruptured appendix.

Symptoms of peritonitis include abdominal pain and fever. Patients with peritonitis often exhibit significant pain during examination of the abdomen. Any movement of the abdominal wall is very painful to someone with an inflamed peritoneum.

Peritonitis can also result from penetrating injuries to the abdominal wall. Violent trauma to the abdomen, such as stabbing or gunshots, are always dangerous, but the risk of dying from them was even worse in the past. Even if trauma victims did not bleed to death right away, contamination of the peritoneal cavity by bacteria would soon cause peritonitis. Modern surgical procedures and the discovery of antibiotics have dramatically decreased the mortality rate from peritonitis, whether due to disease or trauma.

Treatment of peritonitis includes intravenous fluids and intensive antibiotic therapy, often with multiple antibiotics. Sometimes surgical intervention is required, even in those cases unrelated to trauma. Surgery may be needed to correct the cause of the problem (i.e., fix the leak) or to drain pus from a localized abscess. Peritonitis today is usually treatable. However, in severe cases, it can still be fatal.

UNIT 2

THE REPRODUCTIVE SYSTEM

wonders of the HUMAN BODY

THE REPRODUCTIVE SYSTEM

Introduction

Throughout the *Wonders of the Human Body* series we are examining the organ systems of the body, both how they have been designed by the Master Creator and how they function. No doubt, you have been awed by the complexity of the body and have been puzzled at how anyone could believe these systems could have come into existence by chance. In many ways, this volume of the *Wonders* books is no different. Here we will be exploring the reproductive system and how it works.

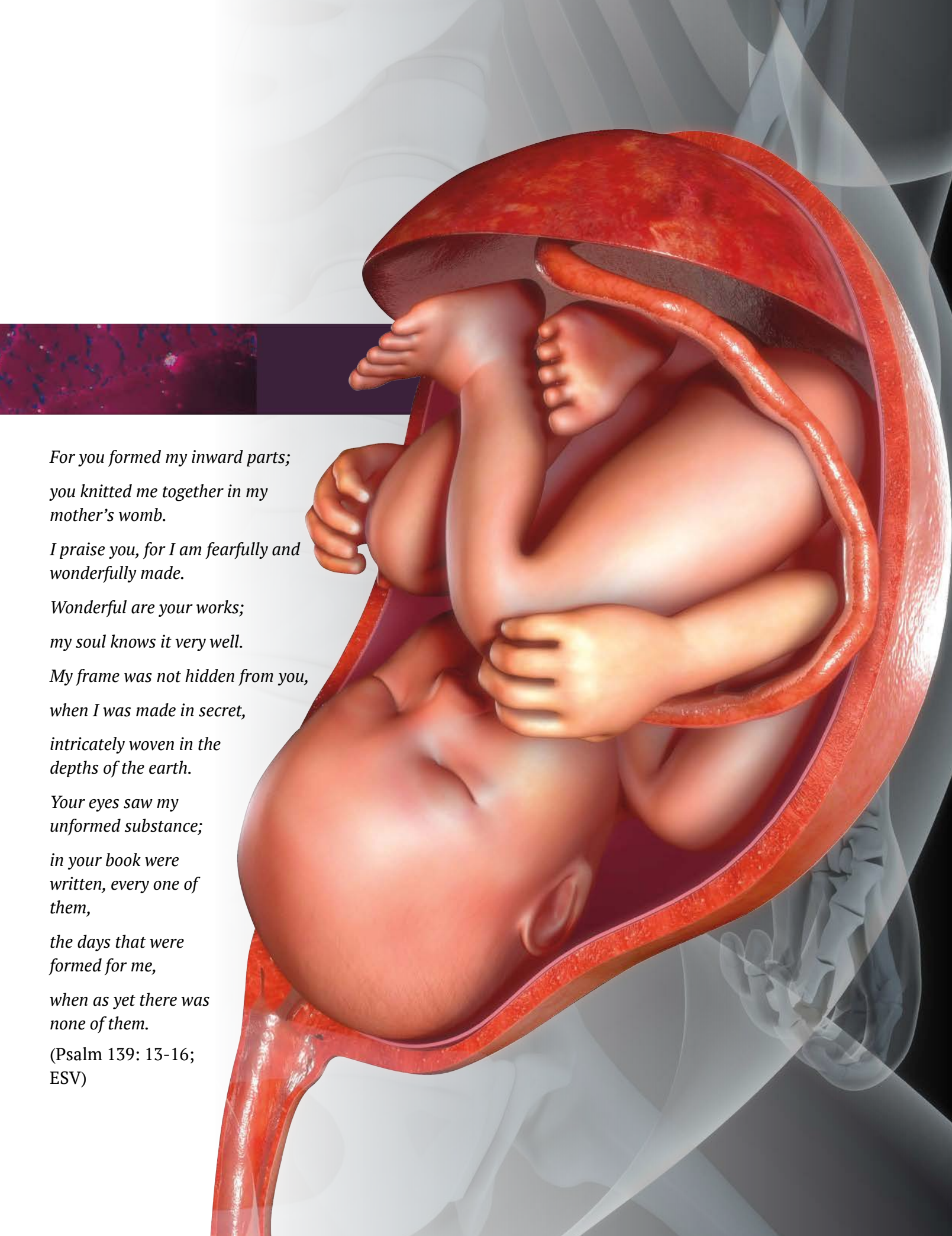
But there IS something different here. In this volume we will take a look back in time, back to about nine months before you were born. It's time to learn how you acquired the body you were born with. It's time to learn how you became you.

In the pages following, we will learn about the complex but orderly processes God designed to make the human body form correctly. Processes that are the same in everyone (assuming things work correctly, that is) but still allow each person to turn out to be a unique individual. This journey into your past will start with a cell, the basic building block of life. We will learn about the genetic code contained in your body's cells and how the collection of genes in your cells came to be. Then we will learn about the marvelous process God designed to form you from components of your mother's and your father's cells. Finally, we will delve into the secrets of the womb, where a baby forms in an unseen place for nine months to prepare him or her for life in this world.

In this volume, we will learn about many ways human rebellion against God and sin's curse have made things go wrong. Once we explore the complexity of God's plan for human reproduction, I think you will be amazed that things usually go right!

Psalm 139

You are the only you, and you were unique from the start. Here you will learn about the science behind this beautiful prayer poem about life before birth — poetry that God inspired in the Book of Psalms.



For you formed my inward parts;

you knitted me together in my mother's womb.

I praise you, for I am fearfully and wonderfully made.

Wonderful are your works;

my soul knows it very well.

My frame was not hidden from you,

when I was made in secret,

intricately woven in the depths of the earth.

Your eyes saw my unformed substance;

in your book were written, every one of them,

the days that were formed for me,

when as yet there was none of them.

(Psalm 139: 13-16; ESV)

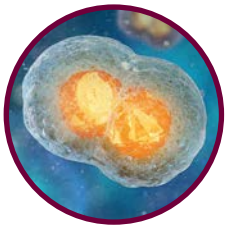
1

THE GENETIC BLUEPRINT FOR THE BODY

The Genome

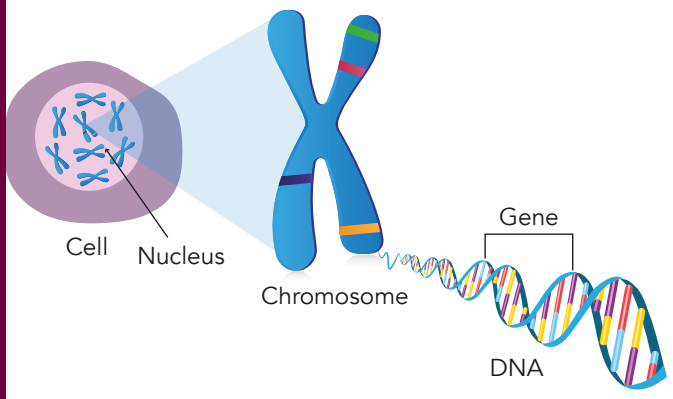
When God designed plants, animals, humans, and even single-celled forms of life like bacteria, He gave each kind of living thing its own genetic blueprint. That blueprint — also called a *genome* — is a complex storehouse of information. It is written in a special code, called the genetic code, on the DNA (deoxyribonucleic acid) molecules inside an organism's cells. The genetic blueprint inside an organism's cells determines how that organism develops and functions. The individual instructions encoded in the genome are called genes.






TAKING A CLOSER LOOK

The Genome



Genes are specific units of instructions that direct how a living organism is made and how its cells function. Each *gene* is coded into the organism's DNA molecules. An organism's DNA is divided up and packaged as *chromosomes*. One complete collection of chromosomes is like a set of encyclopedias for that organism. The full set is housed in a cell, even if a specific cell only needs to use a small fraction of the information in the set.

Each chromosome contains many, many genes. Each gene contains the instructions for making a particular protein important for that organism. The proteins in a cell, working together, do the work that cell must do. Of course, as you may have already learned in the other volume of the *Wonders of Human Body,* many different sorts of cells make up a multicellular organism, such as yourself. Yet whatever particular traits characterize an organism are largely the result of the proteins made by that organism's genes. That's why we can say that the genes are like a blueprint directing how an organism develops and how its cells function.

The DNA in a cell is copied and passed on whenever cells divide. Ultimately, the genetic blueprint — or *genome* — for a particular kind of organism is passed to offspring during reproduction.

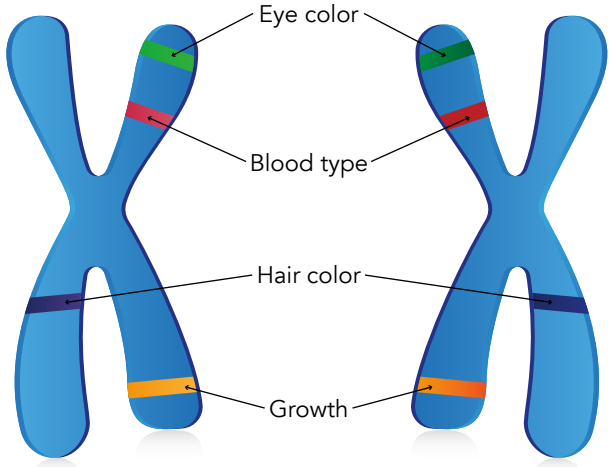
According to Their Kinds

The Bible tells us in Genesis chapter one that God created living things according to their kinds. We observe in biological science that each created kind has its own genome. This genome is the genetic blueprint that produces that kind of organism. Within a created kind's genome, there are many possible variations, such as those that determine our eye color and skin pigmentation. Many genes — the DNA instructions to make particular proteins and the traits associated with them — exist in varying forms, called *alleles*. The shuffling and mixing of these alleles during reproduction produces amazing variety, but never a new and different kind of organism. And never a more complex one.

This is precisely what is seen. No scientific observation has ever been made of one "kind" of creature turning into another "kind." Not once. Ever. Thus, every actual observation ever made shows that molecules-to-man, goo-to-you evolution — the process that some people believe made life evolve from chemicals, and people evolve from ape-like ancestors — has no basis in science and has never happened.

TAKING A CLOSER LOOK

Alleles



Thus, cats give birth to cats, dogs give birth to dogs, and humans give birth to humans. You may have noticed that kittens are not exact copies of either of their parents. And dogs are not exact copies of their parents. Human babies are not exact copies of either of their parents either. Cats' babies are cats, dogs' babies are dogs, and humans' babies are humans, but the offspring always differ from each of their parents. Why is that? The answer has to do with the way the genes from each parent are sorted and combined to make the genetic blueprint for a unique individual, different from either parent. As it happens, even identical twins, once thought to have completely identical genetic make-up, have some subtle differences, but we will go into that later. For now, let's learn more about the DNA in each of your cells. Then we will see how each parent's contribution produces a new, unique human being.

Genesis 1:20–25

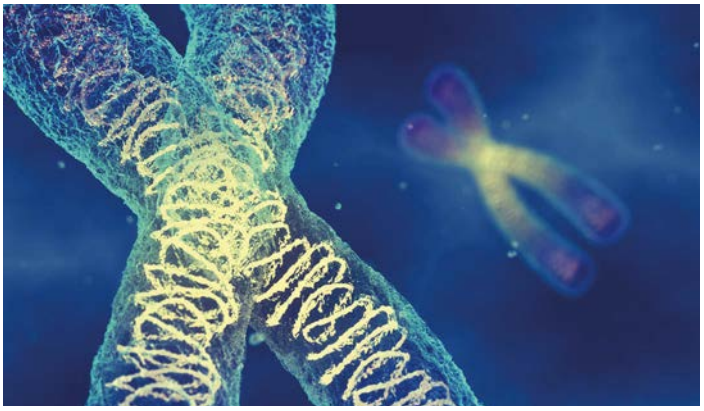
Then God said, "Let the waters abound with an abundance of living creatures, and let birds fly above the earth across the face of the firmament of the heavens." So God created great sea creatures and every living thing that moves, with which the waters abounded, according to their kind, and every winged bird according to its kind. And God saw that it was good. And God blessed them, saying, "Be fruitful and multiply, and fill the waters in the seas, and let birds multiply on the earth." So the evening and the morning were the fifth day.

Then God said, "Let the earth bring forth the living creature according to its kind: cattle and creeping thing and beast of the earth, each according to its kind"; and it was so. And God made the beast of the earth according to its kind, cattle according to its kind, and everything that creeps on the earth according to its kind. And God saw that it was good (Genesis 1:20–25).

God's incredible design allows living things, including humans, to vary a great deal within their created kinds. This variation depends on the particular combination of genetic material an organism possesses. However, there is nothing in the process of passing genetic information to subsequent generations that would allow one "kind" of creature to turn into a different "kind."

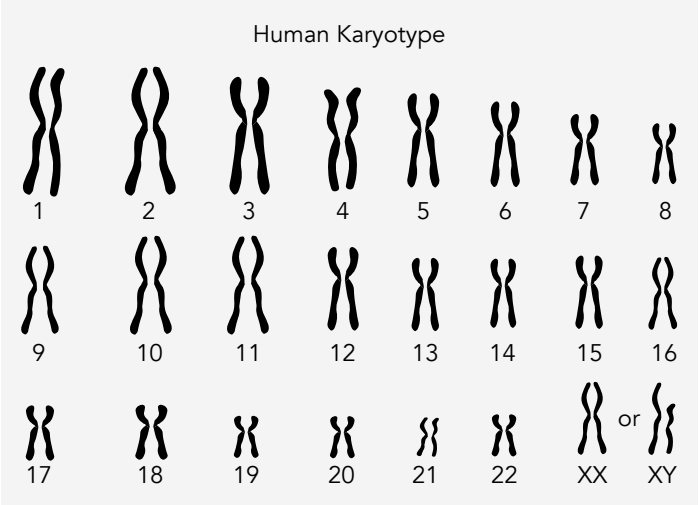
Basic Genetics — The Answer Is Forty-Six

The cells in your body contain your copy of the human genome. This genome, with all its variations that make you unique, is encoded on your DNA. Your DNA is coiled tightly and packaged as 46 chromosomes in the nucleus of each of your body's cells. You might be thinking, "But wait, my red blood cells don't contain any nuclei!" I'm proud of you for remembering that! Red blood cells in your



bloodstream do not contain nuclei, but they do contain nuclei when they are being formed in the bone marrow. Once the red blood cells are made, they eject their nuclei to save space.

Each nucleated human body cell contains 46 chromosomes. (A "body cell" is not the same as a "reproductive cell," as we shall soon see.) Chromosomes come in pairs, so you have 23 pairs of chromosomes. They are known by their number — 1 through 22 — which is so much easier to remember than some special Latin name. The 23rd pair is the chromosome pair that determines whether you are male or female, so the chromosomes in that pair are called the "sex chromosomes," even though they also contain genes that affect things other than your gender. A person with two X chromosomes is female, and a person with one X and one Y chromosome is male.



Dominant and Recessive Alleles

Each pair of chromosomes contains two copies — or *alleles* — of each of the genes on them. In many cases, the alleles vary a bit. They are still the same gene, but with slight variations. Those slight variations may cause the protein produced by the gene to vary slightly. Proteins are molecules made of long chains of many amino acids. Our DNA contains codes for the 20 different amino acids used to build our proteins. Just exactly which amino acids are hooked together to make a particular protein is determined by the gene directing its formation. Sometimes, changing just one amino acid in a protein destroys its ability to function. Changing another amino acid, located elsewhere in the protein, may impair its ability to function efficiently. And changing an amino acid in various other locations in the protein molecule may not hurt its function at all. Such changes are the genetic variations we keep mentioning.

In a gene pair — the two copies (alleles) of a gene located on a chromosome pair — one variant may have more effect than the other. We call the one that "rules" the *dominant* variation, or the *dominant allele.* The variant that is over-ridden by the dominant one is called *recessive,* because its effects "recede" into the background and are not noticed.

Let's consider, for example, the nature of your earwax. Earwax is produced by glands in the outer third of the external auditory canal. Those glands secrete several types of alcohol and lipid molecules, the chemical components of earwax. This oily substance lubricates the lining of your ear. It also helps clean away debris and dead skin cells. Your eardrum constantly makes new cells, and the worn-out dead ones would accumulate in your ear if not removed. These dead skin cells are moved along the ear canal as your jaw moves. They, along with any debris that may have gotten into your ear, stick to the earwax, which also moves gradually toward the outside.

Earwax can be wet, sticky, and brown. It can also be dry, flaky, and gray. Whether your earwax is wet or dry is not determined by your age or how often you shower. It is determined by a gene located on chromosome 16. Depending on which particular "letter" in the genetic "alphabet" is present — and we'll talk more about that alphabet soon — either the amino acid glycine or arginine is inserted at a certain crucial location in the protein encoded by that gene.

The allele that causes glycine to be present is the dominant variation. Therefore, people who have two copies of the glycine-variation — we can call them GG — have wet earwax. And people who have one copy of the glycine variation and one of the arginine variation — the Ga people — also have wet earwax. This is because the arginine allele is recessive and is "overpowered," if you will, by the dominant glycine allele. People who have two copies of the recessive arginine variation — the aa people — have dry earwax. The aa people have dry earwax because they have no dominant G allele.

EARWAX	AMINO ACID	GENE ALLELES
Wet 	Glycine	Glycine-Glycine (GG)
Wet 	Glycine	Glycine-Arginine (Ga)
Dry 	Arginine	Arginine-Arginine (aa)

Genetic Expression

We've said that a complete copy of the human genome is present in every nucleated body cell. But that is an enormous amount of information for one cell to handle! Therefore, in a particular cell, most of that information remains unused. The genes needed by that particular cell are the ones that are *expressed*. God designed a special group of molecules associated with the chromosomes to regulate which genes are expressed in each cell type.

Protein-Building Amino Acids

Some lists now say that 21 amino acids are used in human proteins. This is done by including selenocysteine, which has been found in fewer than 100 of our proteins. However, unlike other protein-building amino acids, selenocysteine is never stored in cells, for it is highly reactive. Its synthesis is directed by the cell's amino acid-building machinery in an unusual way on an as-needed basis. Further, selenocysteine is not represented directly in the genetic code.

For our purposes, we'll just stick with 20 amino acids. That seems sufficient for now.

More About Genetic Expression

In the case of earwax — you didn't think I was through talking about earwax, did you? — the wet/dry gene is expressed by the cells in the glands in your external auditory canal. Depending on whether you are a GG or Ga or aa person, your earwax will contain a slightly different assortment of molecular secretions. And it is those different molecules, and different amounts of those molecules, that make your earwax wet or dry.

It happens that the "wet/dry earwax gene" is expressed by cells in one other location in your body — the cells in the glands in your armpit! People who have wet earwax produce stronger smelling molecules in their armpit perspiration. They tend also to perspire more than dry earwax people. In the rest of your body's cells, the wet/dry earwax gene — which is called the ATP-binding cassette C11 gene, if you must know — is not expressed. It just remains silently in its place in chromosome 16, getting copied and passed on every time a cell divides.

Population Genetics

Scientists can track the historical path of population movements through earwax genetics. It turns out that people with dry earwax are far more prevalent in East Asian, Northeast Asian, and Native American populations than in the rest of the world. Remember, to have dry earwax, you must have two copies of the recessive allele. That means that you must have received the recessive version from both of your parents. You see, during the reproductive process, a special cell from your mother (an egg), containing only 23 chromosomes — not the usual 46 — combines with a cell from your father (a sperm) that also contains only 23 chromosomes. When those cells — called *gametes* — come together, a single 46-chromosome cell called a *zygote* is produced. *This is called fertilization.*

That zygote was the beginning of you. Every bit of genetic information required to produce the body you were born with and to enable you to grow and function was contained in the 46 chromosomes you received from your parents. We'll cover more about that later. For now, let's focus on earwax.

A person who has the aa gene pair on chromosome 16 is *homozygous* for the recessive "a" allele of that gene. He or she received an "a" from mom and an "a" from dad. Since having just one copy of the "G" allele makes you have wet earwax, you can deduce that if everyone in a particular people group has dry earwax, that people group must have gotten isolated from the wet earwax people at some time in their history. Any idea when that might have happened? Yep — after God's judgment on people at the tower of Babel.

Genesis chapters 10–11 describe the centuries soon after the worldwide Flood of Noah's day. God had told people in Genesis 9:7 to spread out and populate the earth. Instead, many people gathered themselves together on a plain in the land of Shinar. They were determined to remain together, building a powerful nation that they thought would be secure and great enough to enable them to do anything they pleased. They all spoke the same language. They started building a great tower to symbolize their united stand against their Creator's command. God foiled their plans by confusing their languages. Suddenly, various groups of people were unable to understand what other groups were saying. No longer able to easily work together, groups of people who spoke the same language would have banded together and left the region to make a home elsewhere in the great, now unfamiliar, world. In this way, people dispersed throughout the post-Flood world.

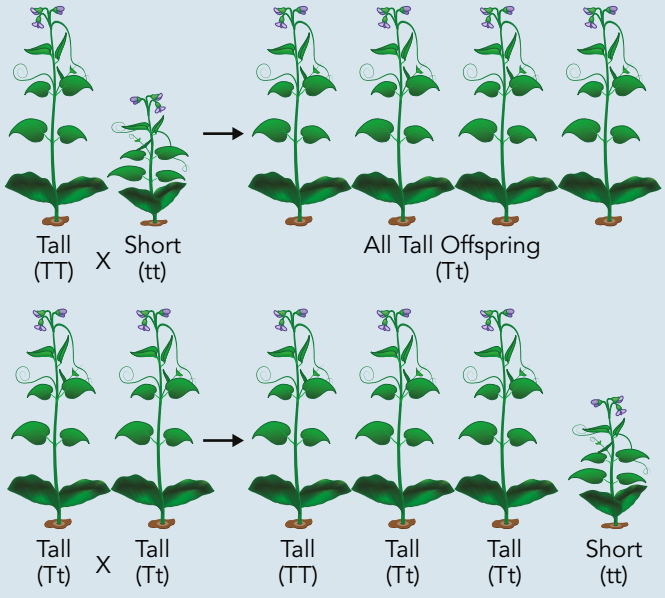
The original group of people at the Tower of Babel would have, in their combined gene pool, all the genetic variety in the human population descended from Noah's family — the people on the Ark. If they had remained forever together, most variations would have been passed around pretty evenly. However, once small groups moved out into the world, *only the variations present in the gene pools of those smaller groups would be available to the children born in those groups*. Thus, if a group of people that moved toward eastern Asia happened to have mostly folks with dry earwax, East Asian people descended from that group would have dry earwax, the "G" allele having been lost to their gene pool. Such genetic isolation is one way that variations characteristic of a particular population group develop.

Origins of Human Genetic Variety

So you must surely be asking, if we are all descended from just two people, Adam and Eve, how did people end up with different variations of the same gene? There are a couple of different ways. It happens that many of our characteristics are actually regulated by more than one pair of genes. We call those characteristics *polygenic*. ("Poly" means "many" — so "polygenic" means "many genes." Get it?)

Gregor Mendel

The existence of the simplest of inheritance patterns — the dominant-recessive pattern of inheritance of traits (phenotypes) controlled by a single gene — was discovered in the 1800s by a monk named Gregor Mendel. He grew pea plants. Those plants had a number of characteristics — such as their height, whether the flowers were purple or white, and whether or not the peas were wrinkled — that were controlled by single genes functioning with dominant-recessive inheritance patterns. Mendel cross-pollinated plants with certain characteristics to see what would happen. He kept careful records. By analyzing those observations, he figured out that the characteristics he was observing were passed on in a simple, logical fashion. Some were dominant, and some were recessive. It is good for the history of genetic science that Mendel just happened to experiment with characteristics that are passed on through simple *Mendelian genetic* patterns. If he had chosen traits that turned out to be polygenic, our appreciation of the power of genetics may have been delayed a good deal longer.



The particular collection of variations you happen to inherit for a polygenic trait determines the polygenic characteristics you have. Eye color is a great example. Scientists used to think that something as simple as blue versus brown eyes was inherited as simply as the nature of earwax. Eventually we learned that there are several genes located on more than one chromosome that work together to determine eye color. Therefore, for many characteristics, the variations present in Adam and Eve's original human genome was sufficient to mix and match as they were shuffled between people over the years to produce the enormous variety of people in the world.

Mutations — Another Source of Genetic Variation

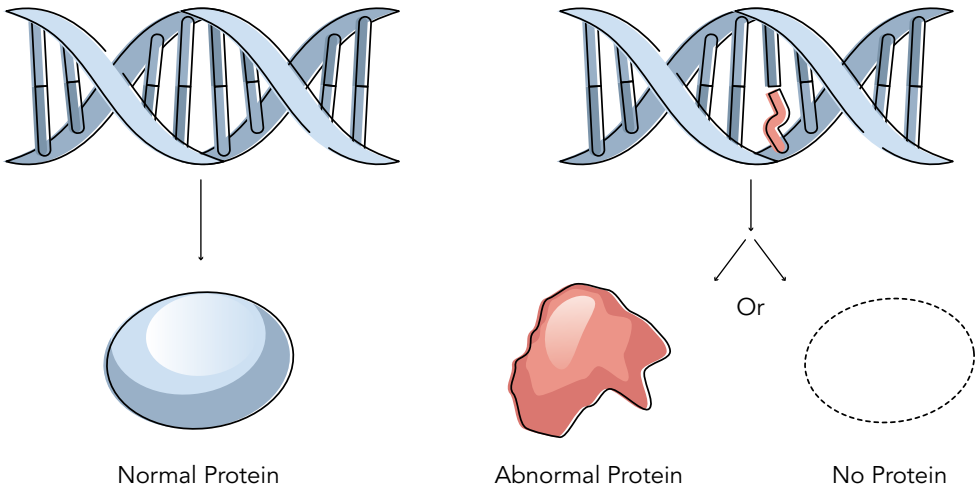
Other variations have come into our human gene pool through mutations. A *mutation* is a genetic mistake. We know that in the beginning God saw that all He had made was very good. After man sinned, God's judgment allowed things to go wrong, and sickness and death entered the world. Genetic mutations are some of the things that go wrong, and they are the cause of many problems.

Many types of mutations occur, and we will cover how they happen in more detail later. Most cells in your body divide frequently, making copies of themselves quite often. (Your nerve cells are one big exception.) When cells divide, their DNA must be duplicated. If something goes wrong when DNA is being copied — if some information is left out, damaged, scrambled, substituted, or even duplicated — that change is a mutation. The cell has proof-reading mechanisms in place — ways that the DNA-duplication process polices itself and self-corrects. However, a mutation that is not caught and corrected by these proof-reading safeguards may be passed on when that cell divides.

If a mutation occurs in one of your skin or bone or blood cells, that mutation cannot be passed on

TAKING A CLOSER LOOK

Normal Genes vs Mutated Genes



to your children. You may develop some problem yourself. You might even develop a cancer, if that mutation is a serious one associated with uncontrolled acceleration of cell division. But you cannot pass on that sort of mutation to anyone else.

If a mutation — a DNA copying error — occurs in reproductive cells, then the mutation may be passed on to offspring. Just as the normal genetic variants for eye color and skin tone are passed on to offspring, so a mutation for a trait like color-blindness or sickle cell hemoglobin may also be passed on. Mutations that occur in a *gamete* — one of those 23 chromosome-containing cells we mentioned earlier — can be passed on to your children. *Sperm* are the gametes produced in males. *Ova* — or eggs — are the gametes produced in females. If a sperm or an *ovum* (singular of ova) contains a mutation, and that gamete is joined to another gamete to produce a zygote, the zygote will contain that mutation.

Some mutations are deadly. When a person with a deadly mutation is conceived, he or she will at some point die as a result of the malfunction caused by the mutation. Some mutations are harmful but not deadly. An example is the sickle cell mutation. People who have the sickle cell mutation in one or both of their copies of their hemoglobin-producing genes are harmed by the presence of an abnormality in their hemoglobin.

Many mutations, however, even though they are genetic mistakes, cause no harm at all. A harmless mutation might result in a noticeable but harmless characteristic. The results of a harmless mutation might not even be noticeable. These insignificant mutations are useful to scientists trying to track population movements through history. People descended from the same isolated people group will often have many of the same mutations in their genes. These can be traced through DNA analysis even if the people have no noticeable manifestation of the mutations.

While on the subject of what sorts of things mutations can do, let's get straight about one thing mutations never do. Mutations can damage or destroy some of the genetic information in a set of chromosomes. However, mutations can never supply the necessary genetic information for one kind of organism to evolve into a new, more complex, different kind of organism. Thus, many variations in people have occurred since God created Adam and Eve about 6,000 years ago. But all people that have ever lived — from Cain to Noah to Neanderthals to your brother — have had a *completely human* genome containing the variations developed from the shuffling of genetic material passed down from Adam and Eve and from the mutations that have occurred over the past 6,000 years.

Genotype and Phenotype

By now you've seen that two people with different genetic variations are sometimes indistinguishable from the outside. We have good words to describe this. *Genotype* is the particular collection of genetic variations present in an organism's DNA. *Phenotype* is the resulting characteristic in the organism. With earwax for instance — you didn't *really* think I was finished with earwax, did you? — a person's genotype might be GG, Ga, or aa. People with the GG and the Ga genotypes have the *same* phenotype — wet earwax and smelly sweaty armpits. People with the aa genotype have the other phenotype — dry earwax and less smelly sweaty armpits. (Yes, I do have a way with words. . . .)

GENOTYPE	PHENOTYPE
Glycine-Glycine (GG)	Wet 
Glycine-Arginine (Ga)	Wet 
Arginine-Arginine (aa)	Dry 

The *genotype* is the *information in the genes*. The *phenotype* is *the way that information ultimately gets expressed.* In dominant-recessive inheritance patterns, any genotype containing the dominant gene manifests the "dominant" phenotype. And only genotypes containing two recessive alleles manifest the recessive phenotype.

There is a simple way to keep track of the genotypes of two parents — whether people or pea plants — and those of their offspring. This is called the Punnett square. For the gene under consideration, the genotype of each parent is written above and to the left of a square divided in fourths. Remember, we said that each parent gives just one of his or her two alleles for this gene to a particular one of their offspring. Write each parent's genotype with one allele above each little box. Then imagine combining each allele from one parent with an allele from the other parent. This is sort of like flipping a coin. Each flip of a coin has two possibilities. But two coins must be flipped at the same time to get the composition of each result. Each "flip of the genetic coins" — the coming together of a randomly selected allele from each parent to form the genotype of the offspring — therefore has *four* possibilities.

Let's take our earwax example. (You knew that was coming.) If both parents have the GG genotype, we write the GG above and to the left of the four-patch square. No matter what allele is selected from each parent, the outcome is always GG. All four "possibilities" are the same — the GG genotype and the wet wax phenotype. The same is true if both parents are aa. The only possibilities for their children are the aa genotype, and the dry wax phenotype.

		FATHER'S GENES (GG-WET) 	
		G	G
MOTHER'S GENES (GG-WET) 	G	GG (Wet)	GG (Wet)
	G	GG (Wet)	GG (Wet)

		FATHER'S GENES (aa-DRY) 	
		a	a
MOTHER'S GENES (aa-DRY) 	a	aa (Dry)	aa (Dry)
	a	aa (Dry)	aa (Dry)

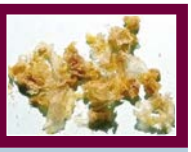
However, let's see what the possibilities are if each parent has wet earwax, smelly armpits, and the Ga genotype. We write the G and the a for each parent above the little squares. Then we match up the possibilities. Do you see that each child of two Ga parents has a 25% (one-in-four) chance of being GG, a 25% chance of being aa, and a 50% (one-in-two) chance of being Ga? Since only the child with aa will have dry earwax and minimal smell to his or her armpits, there is a three-in-four chance that any child the Ga parents have will have wet earwax and smelly armpits like the parents.

		FATHER'S GENES (Ga-WET) 	
		G	a
MOTHER'S GENES (Ga-WET) 	G	GG (Wet)	Ga (Wet)
	a	Ga (Wet)	aa (Dry)

It is important to understand that this does not mean that if the parents have four children, one will be aa, one GG, and two Ga. The odds "reset" for each child. If we were talking about the color of a garden full of flowering peas and hundreds of seeds — like those Gregor Mendel experimented on — then, statistically speaking, about a fourth of the seeds would have the recessive phenotype, and about three-fourths would exhibit the dominant phenotype. But in a family of just four children — instead of hundreds — it is important to remember that the possibilities apply to each individual child.

Of course, there are additional possible combinations. Consider a wet earwax GG person paired with a wet earwax Ga person. This couple's children would all have wet earwax, but each would have a 50% chance of having a GG genotype and a 50% chance of having a Ga genotype. On the other hand, a wet-dry couple with Ga and aa genotypes would produce children with a 50% chance of having dry earwax (and genotype aa, of course). And any wet earwax children they have will have the Ga genotype.

		FATHER'S GENES (GG-WET) 	
		G	G
MOTHER'S GENES (Ga-WET) 	G	GG (Wet)	GG (Wet)
	a	Ga (Wet)	Ga (Wet)

		FATHER'S GENES (aa-DRY) 	
		a	a
MOTHER'S GENES (Ga-WET) 	G	Ga (Wet)	Ga (Wet)
	a	aa (Dry)	aa (Dry)

Diseases Inherited through Dominant-Recessive Patterns

In the 6,000 years since Adam sinned, many mutations have occurred. Some of those mutations have resulted in diseases. Of course, the first time a mutation occurs, the person thus afflicted cannot be said to have inherited the resulting disease from anyone. But once a mutation gets passed on to children and children's children, its inheritance pattern is observable.

Disease-causing mutations may occur in a single gene, or disease may result from a collection of mutations that appear in many genes on different chromosomes. Disease-causing mutations also include mutations that produce extra copies or loss of a particular chromosome.

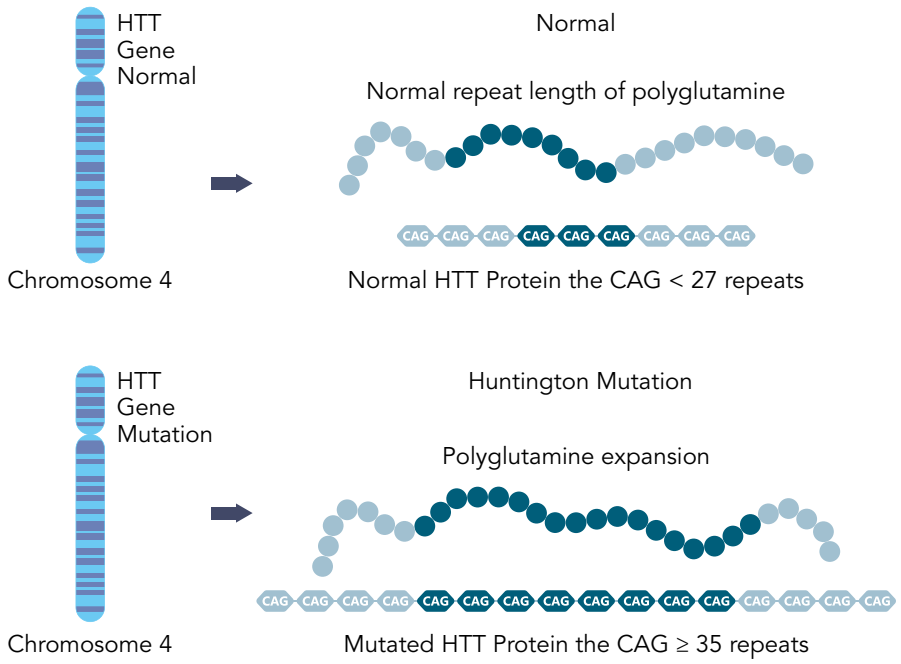
A few of the diseases caused by a mutation on a single gene are cystic fibrosis, polycystic kidney disease, Tay-Sachs disease, Huntington's disease, Marfan syndrome, and sickle cell disease. Like earwax — but with much greater consequences — most of those on this list are inherited with a dominant-recessive pattern. (Sickle cell disease is passed on with a different pattern, which we will discuss farther on.)

Huntington's disease is a classic example. Here the presence of a single allele with the disease variation means the person will ultimately have that disease. Huntington's disease is caused by a mutation in the HD gene located on chromosome 4. The mutant allele causes the protein thus formed to be defective.

The abnormal protein clumps in the brain and causes nearby nerve cells to die. Eventually, a person carrying the dominant mutant gene will develop severe neurological disease involving excessive involuntary movement and a deterioration of mental function. Because this does not usually occur until adulthood, people afflicted by the disease have usually had children of their own by the time the disease affects them. Each of their children has a 50% chance of inheriting the dominant mutant form of the HD gene and of therefore also developing the disease.

TAKING A CLOSER LOOK

Huntington's Disease



Let's look at a Punnett square to see how this works. We usually use an uppercase letter to denote dominant conditions, so H = the Huntington's dominant mutation. Hh would thus be the genotype of a parent carrying one copy of the dominant mutation, and hh would be a parent without the mutation. Here in this Punnett square you see there is a 50% chance that any child of this couple will inherit the H allele, and a 50% chance he/she will not.

		PARENT WITH HUNTINGTON'S DISEASE (Hh)	
		H	h
PARENT WITHOUT HUNTINGTON'S DISEASE (hh)	h	Hh (has disease)	hh (no disease)
	h	Hh (has disease)	hh (no disease)

Because the dominant mutant allele for this disease exists on chromosome 4, not one of the X or Y chromosomes, we say that Huntington's disease is *autosomal dominant*. The word *autosomal* means the genotype in question is on one of the 22 "autosomal" chromosomes, not an X or Y chromosome.

Tay-Sachs disease is another disease passed on through a mutation on a single autosomal gene, located on chromosome 15. A mutation in the Hex-A gene prevents the production of the enzyme Hex-A. Hex-A removes a particular lipid from the nervous system. Because this mutation is *recessive*, so long as a person has one normal allele, he or she makes enough of the enzyme to remove the lipid. However, without the Hex-A enzyme, that lipid builds up in the nervous system. That buildup soon begins causing deterioration in the brain. By the time a baby is just a few months old, many problems develop, including seizures, loss of the ability to move normally, and intellectual disability. Tay-Sachs disease usually kills in the first few years of life.

The mutation causing Tay-Sachs disease is *autosomal recessive*. A parent carrying one copy of the mutation has no symptoms. But if each parent happens to carry one copy of the mutant allele, it is possible for their child to receive the mutant allele from both of them. That child will have Tay-Sachs disease. It is also possible for their child to receive a normal allele from each of them. That child will not develop Tay-Sachs disease and cannot pass it on to his or her children. Finally, it is possible for their child to receive one normal and one mutant allele. That child will never develop Tay-Sachs disease, but his or her children may eventually receive the mutant allele from them.

What are the odds of two Tay-Sachs "carrying" parents giving birth to a child with the disease? About 25%. In other words, there is a one-in-four chance that any child they have will have the disease. There is also a one-in-four chance that any child they have will have neither the disease nor the abnormal gene. And there is a 50% — a one-in-two — chance that any child they have will be a carrier of the disease.

With an autosomal recessive condition, anyone carrying two copies of the recessive allele will have the condition. People who do not have the condition may be free of the allele — in which case they cannot pass it on to their children. Or they may have one copy of the recessive copy of the allele. Anyone with a copy of the recessive allele may pass it on to their children. However, only couples in which both parents carry the recessive allele can produce a child with the condition.

Autosomal Dominant Inheritance

Can you use a Punnett square to determine the likelihood of an autosomal dominant condition — like Huntington's disease — being passed on to a child if *both parents* carry the dominant gene? Use Hh as the genotype for each parent.

		PARENT WITH HUNTINGTON'S DISEASE (Hh)	
		H	h
PARENT WITH HUNTINGTON'S DISEASE (Hh)	H		
	h		

Here you see that if both parents carry an autosomal dominant allele (like H), then each of their children has a 75% chance of inheriting the dominant allele and therefore the condition it causes.

UNIT 3

SPECIAL SYSTEMS

BLOOD, LYMPHATIC, IMMUNE, URINARY, ENDOCRINE, AND INTEGUMENTARY SYSTEMS

wonders of the HUMAN BODY

SPECIAL SYSTEMS

Introduction

In this volume of *Wonders of the Human Body* we complete our exploration of the organ systems. Just as you have been amazed by the complexity of the heart, lungs, brain, and other organs, so here you will be awed by the creativity of the Master Designer. It is no accident that each organ system is perfectly designed to perform its task and work in harmony with the other systems.

The musculoskeletal system cannot function to its fullest without the nervous system. The lungs' ability to take in oxygen would be meaningless without a cardiovascular system to transport oxygen to the tissues. Without a digestive system providing raw materials for the body to rebuild tissues or convert to energy, our bodies would soon cease to work.

And make no mistake, the organ systems we are about to explore are just as vital as all the rest. Just because they are presented at the end of the *Wonders* series does not mean they are less important. The systems explored in this final unit tie all the rest together.

First of all, we will learn about blood and its components. Blood is on the job 24 hours a day throughout our lives. Moved by the cardiovascular system, blood ceaselessly transports oxygen and nutrients, carries cellular waste products away from tissues, and protects us from "invaders."

Next, we will focus on the urinary system, the system that makes urine. Also called the renal system, this system's main organs, the kidneys, rid the body of many water-soluble chemical wastes. In addition, kidneys play an important role in controlling blood pressure and helping maintain the correct fluid balance in the body. The kidneys even help produce a hormone that stimulates production of red blood cells. Again, the organ systems are tied together.

We will then proceed to the endocrine system. The endocrine system is a collection of glands and tissues responsible for secreting hormones. *Hormones* are molecules that act as messengers, helping control and coordinate a variety of cellular activities in the body. Without a functioning endocrine system, it would be impossible to achieve *homeostasis* in the body. Homeostasis is the body's tendency to maintain conditions within appropriate limits. For example, hormones help regulate blood glucose levels, *metabolic rate* (how fast the body uses energy), and the kidneys' output. The endocrine system coordinates other systems, keeping them in communication with each other, thus preventing them from working too fast or too slow or from making too much or too little of their products.

Finally, we will look at our *integumentary system* — the skin, hair, and nails. The skin helps keep out dangerous bacteria and maintain a stable body temperature. Without skin, our bodies would quickly lose large amounts of fluid by evaporation, and we would dehydrate. Plus, the sensory nerves in our skin are a primary means for us to interact with our environment as we touch things and sense the heat and cold around us.

And, as with all other organ systems, in a fallen, sin-cursed world, things can go wrong. We will deal with some of these things too.

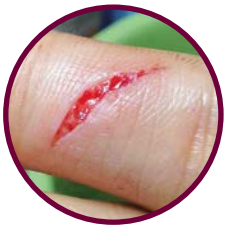
Let's get started!

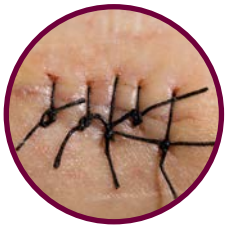
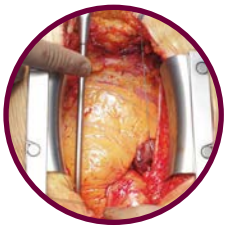
BLOOD

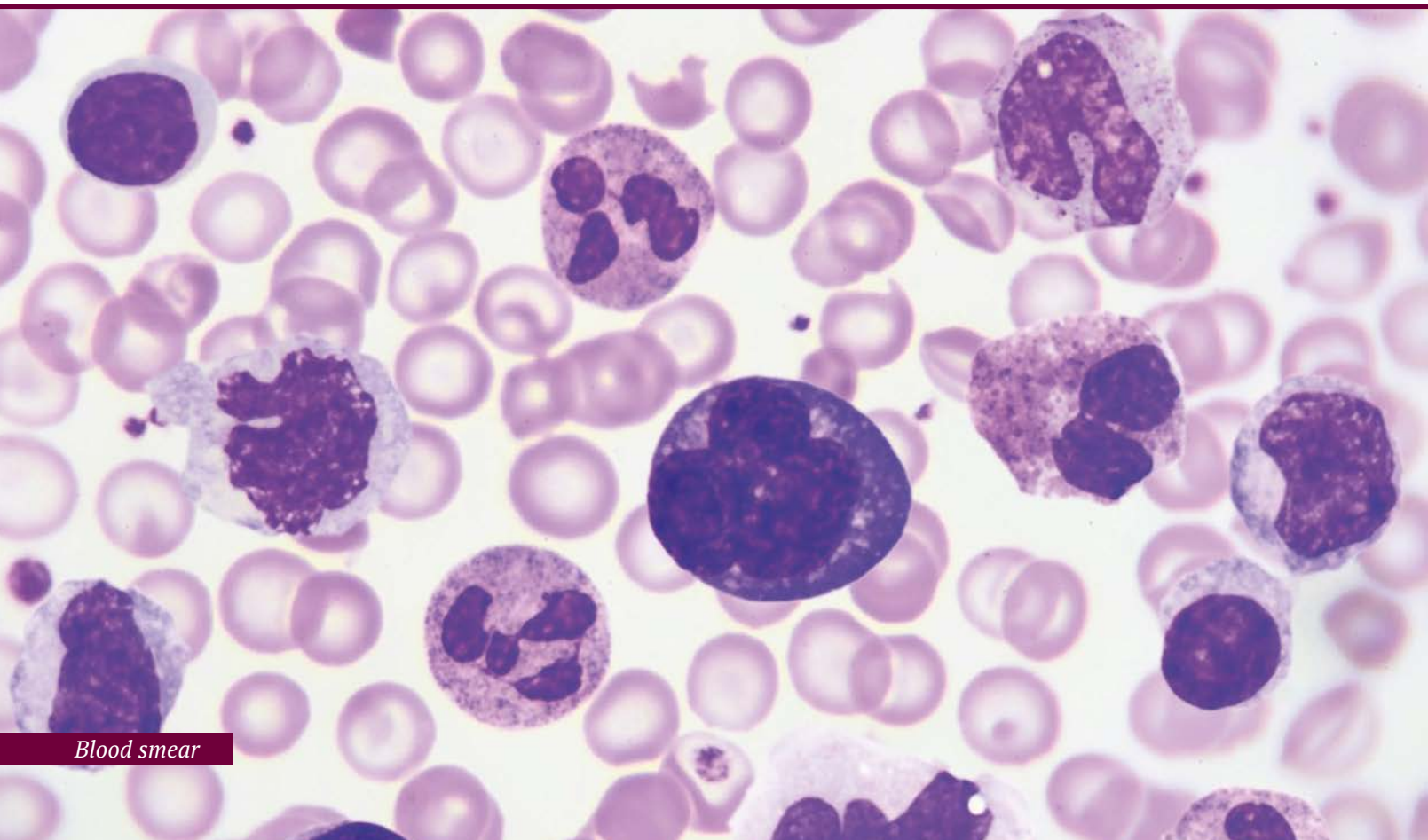
Introduction to Blood

The heart beats an average of 72 times per minute, for life. The purpose of each beat is to circulate blood.

Blood is liquid connective tissue. Does that seem strange? A liquid tissue that connects things together? Yet such a substance is needed to flow through ever-narrowing blood vessels until it reaches capillaries where the majority of its "work" is done. Blood then circulates back to the heart, and the process repeats, over and over.





Blood smear

The average adult male's blood volume is around 5 to 5 1/2 liters. This is just under 1 1/2 gallons, or about 11 pints. Blood comprises about 7% of a person's total body weight. In a 200-pound person, about 14 pounds would be blood.

Blood is a slightly thick red liquid. Blood that has taken up a lot of oxygen by passing through the lungs — becoming *oxygenated* — is bright red. Blood returning from the peripheral tissues after releasing much of its oxygen — *deoxygenated* blood — is not "blue" as commonly pictured. It is just a darker red.

Blood's Functions

At first glance, blood's purpose seems obvious. Like a freight train, blood transports things to their destinations, unloads them, picks up other stuff, and carries that stuff to a different place.

The main thing blood carries is oxygen, which it transports from the lungs to the body's tissues. There, oxygen is taken up by cells and used in metabolic processes that generate energy. Blood also transports carbon dioxide produced by cellular metabolism back to the lungs where is it eliminated with every breath.

Similarly, blood delivers vital nutrients to tissues. There, metabolic waste products are collected and transported to the liver and kidneys for processing and elimination.

Blood is also necessary for the proper function of the endocrine system. Without blood to transport hormones to target destinations, the endocrine system would not function at all.

But blood also performs many regulatory functions.

First of all, blood helps control overall body temperature. Metabolic activities generate heat. Circulating blood absorbs heat and takes it away. When blood circulates through skin, excess heat can effectively be radiated away.

Life Is in the Blood

"For the life of the flesh is in the blood, and I have given it to you upon the altar to make atonement for your souls; for it is the blood that makes atonement for the soul" (Leviticus 17:11).

When explaining the sacrificial system, God said that life is in blood because, without blood to carry oxygen throughout the body, life ends.

Next, blood helps maintain acid-base balance in body fluids. Special substances in the blood, called *buffers*, regulate the level of acidity. If acid levels in the body get very high or very low, cells do not function correctly. Blood helps keep these things in balance. Keep thinking about homeostasis!

Blood also works with the immune system to protect the body. Special cells, called leukocytes, and special proteins, called antibodies, circulate in blood. These protect the body from invading bacteria and viruses. We will learn much more about this later.

Last, but not least, blood contains components needed for blood to clot. This is essential for minimizing blood loss when a vessel is cut!

Thus, blood is not only essential for transportation but also for homeostatic regulation and immune protection.

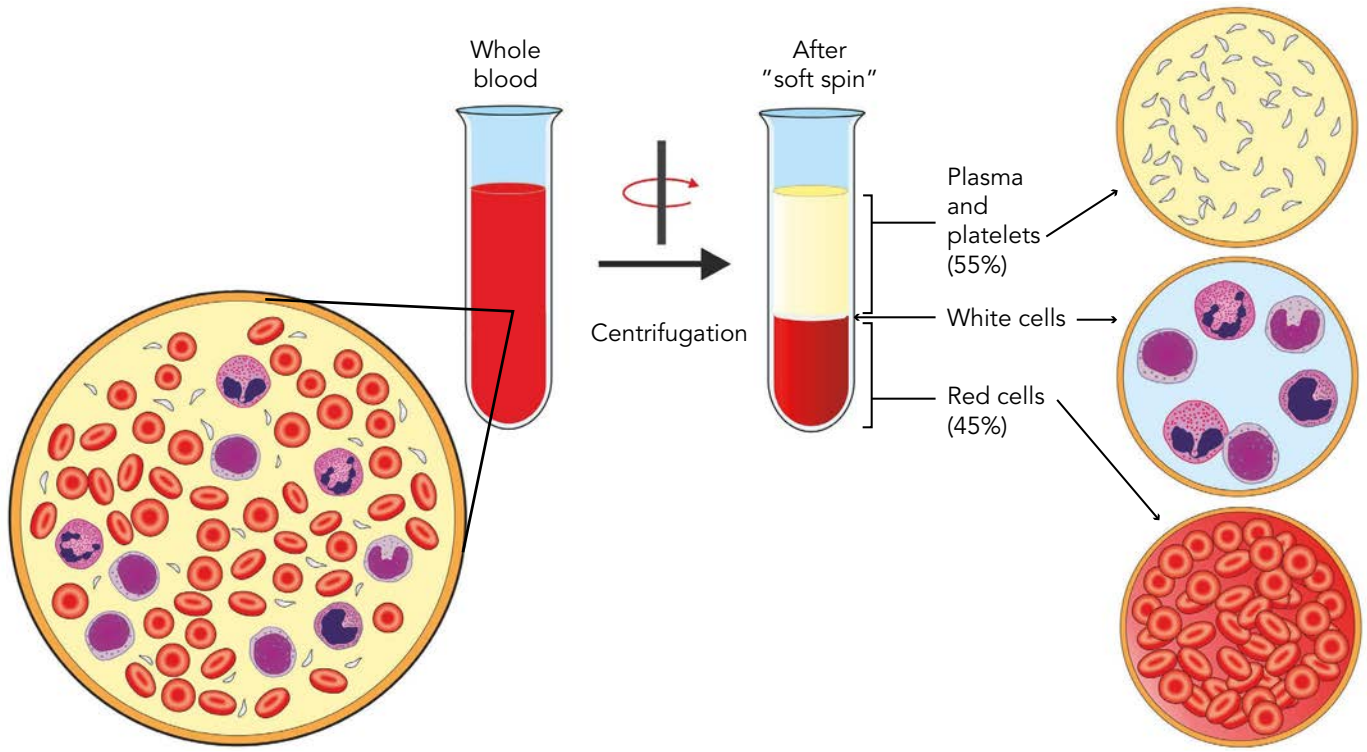
Blood's Components

Blood has a liquid portion — plasma — as well as cells and cell fragments. Later we will learn about red blood cells (erythrocytes), the many types of white blood cells (also called leukocytes), and the cell fragments called platelets.

If you put blood into a tube and spin it in a centrifuge, it separates into layers, as seen in the illustration. Denser components move to the bottom

TAKING A CLOSER LOOK

Blood's Components



of the tube, and less dense elements layer above as shown above.

After a "soft spin," there is a dark red layer at the bottom, representing about 45% of the blood volume. This layer consists of erythrocytes. The golden liquid forming the top layer is platelet-containing plasma. A "soft spin" can be used to separate whole blood into platelet-rich plasma and packed red blood cells for transfusion.

Plasma comprises about 55% of blood's volume. In between the red cell layer and the plasma is a thin light-colored layer consisting of white blood cells. A "hard spin," also pulls platelets down into this middle layer, called the *buffy coat*. The buffy coat represents less than 1% of blood's volume, but it's incredibly important.

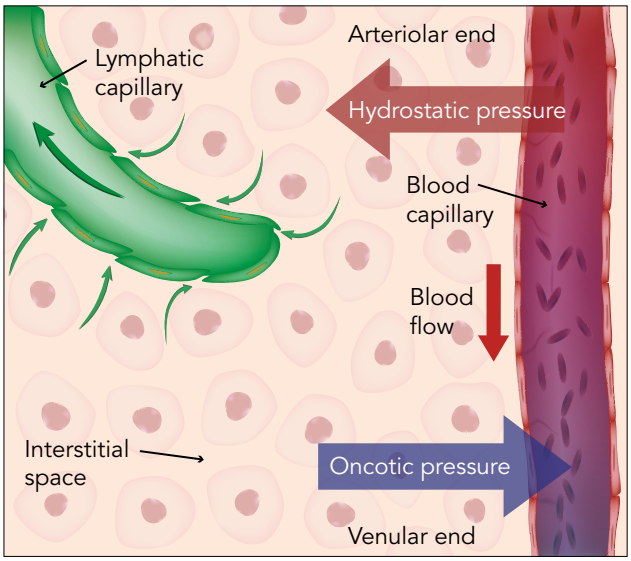
Plasma

Plasma is the liquid component of blood. This pale straw-colored liquid makes up about 55% of the blood's volume. Even though plasma is 90% water, proteins in it make it feel sticky. The main protein in plasma is *albumin*. Albumin acts as carrier for fatty acids, fat-soluble vitamins, hormones, *bilirubin* (a yellow pigment resulting from the breakdown of red blood cells), some ions, and many medications.

Albumin's presence in plasma maintains the balance between water moving out of blood into tissues and water moving back into blood from tissues. Hydrostatic pressure constantly pushes water out of capillaries. This force is opposed by *osmotic pressure* — the pressure generated by water's tendency to move in the direction required to dilute dissolved substances. The dissolved substances in this case are protein molecules, and the most abundant protein molecules floating in plasma are albumin.

TAKING A CLOSER LOOK

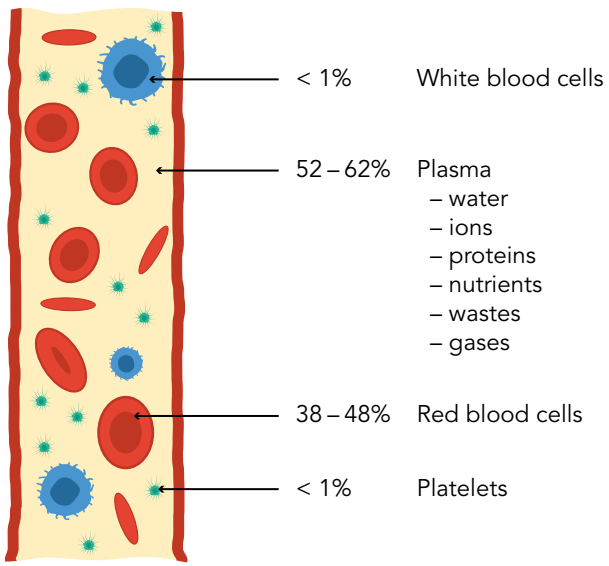
Oncotic Pressure



The capillary osmotic pressure generated by albumin is called *oncotic pressure*. Without this oncotic pressure, water leaving through capillary walls would not return. Because albumin molecules are in plasma, water is drawn back in, restoring balance between the concentration of water inside and outside capillaries.

TAKING A CLOSER LOOK

Blood's Components



Besides albumin, plasma also contains proteins called globulins. The most important of these are gamma globulins, also called *antibodies*. We will explore antibodies in some detail when we get to the immune system.

Other things found in plasma are hormones (chemical messengers that travel through the bloodstream), digestive products (such as amino acids, glucose, fatty acids, cholesterol, and vitamins), and electrolytes — ions like sodium (Na^+), potassium (K^+), calcium (Ca^{++}), chloride (Cl^-), and others. Metabolic wastes such as urea and creatinine are also dissolved in plasma. There are even dissolved gases such as carbon dioxide in plasma.

Types of Blood Cells

Blood's cellular components are called the *formed elements* of blood. They can be classified into three categories — erythrocytes, leukocytes, and platelets. Erythrocytes are red blood cells (RBCs). Leukocytes are white blood cells (WBCs). Platelets are needed for blood to clot.

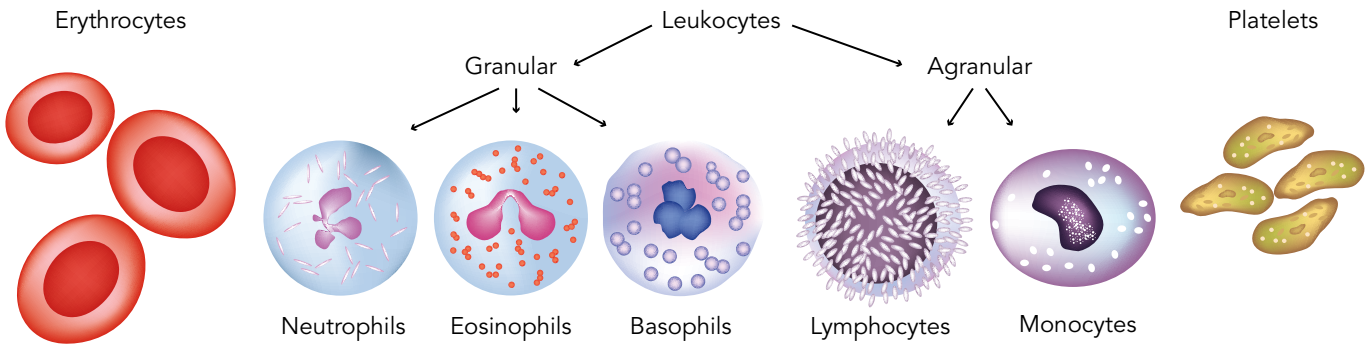
Of the formed elements, only leukocytes are complete cells. Leukocytes have nuclei and intracellular organelles. Erythrocytes lack these. Platelets are cell fragments.

Every erythrocyte does the same thing. And every platelet does the same thing. On the other hand, leukocytes perform many functions.

There are several kinds of leukocytes, classified into two major groups — granular leukocytes and agranular leukocytes. All leukocytes have granules, but this classification is based on whether or not the granules are large enough to be seen under the microscope. Granular leukocytes have larger granules that are visible, and the agranular leukocytes have smaller granules not easily seen.

TAKING A CLOSER LOOK

Formed Elements



There are three types of granular leukocytes — neutrophils, eosinophils, and basophils.

There are two types of agranular leukocytes — lymphocytes and monocytes.

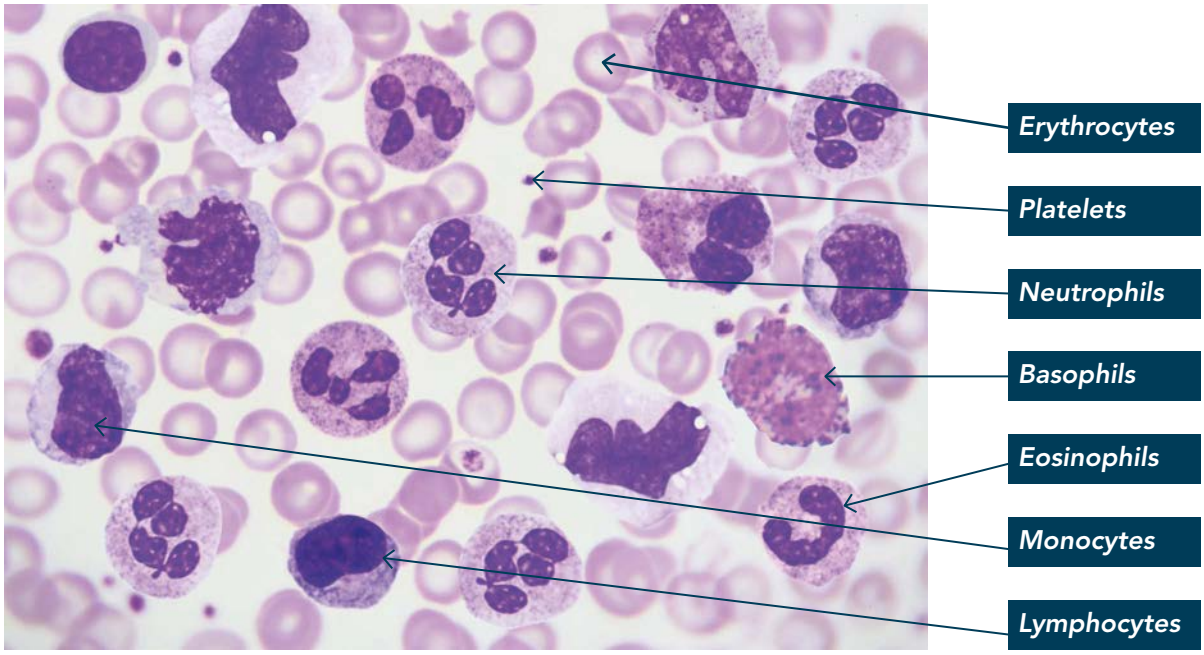
Let's first learn about red blood cells and then platelets and white blood cell types.

Erythrocytes

Erythrocytes are like tiny bags of fluid. Enclosed by a flexible plasma membrane, each is shaped like a *biconcave disc* — a flattened round shape with indented surfaces. Having no nuclei, red blood cells are packed with hemoglobin. *Hemoglobin* is the oxygen-carrying red pigment that gives erythrocytes their color.

Red blood cells have only one function — transporting oxygen. Our Master Designer perfectly designed them for this purpose.

It is no accident that each red blood cell looks like a doughnut without a hole. This special shape is important for two reasons. First of all, this shape gives a red blood cell lots of surface area. With an abundant surface area, gases diffuse efficiently into and out of red blood cells.



Second, this unique shape makes red blood cells flexible. Why is this important? As blood is pumped through ever-narrowing blood vessels, it reaches small caliber capillaries. Some capillaries are smaller than the diameter of red blood cells! Nevertheless, flexible red cells easily pass through. The red cells are well designed to do what they do!

Erythrocytes — Old and New

A red blood cell (RBC) has a lifespan of about 120 days. Traveling endlessly, flexing through capillaries, red cells' plasma membranes wear out. With no nuclei or organelles, they cannot repair or replace themselves. Old red blood cells are filtered out of

Hemoglobin and the Himalayas

At extreme elevations air is thinner. The body responds to low atmospheric oxygen there by synthesizing more oxygen-carrying hemoglobin and red blood cells. This increases blood's oxygen-carrying capacity. Within limits, this response is a good thing. But too much of this good thing is not good. In fact, it can be a problem for people who move to Tibet, more than 13,000 feet above sea level, in the Himalayan Mountains.

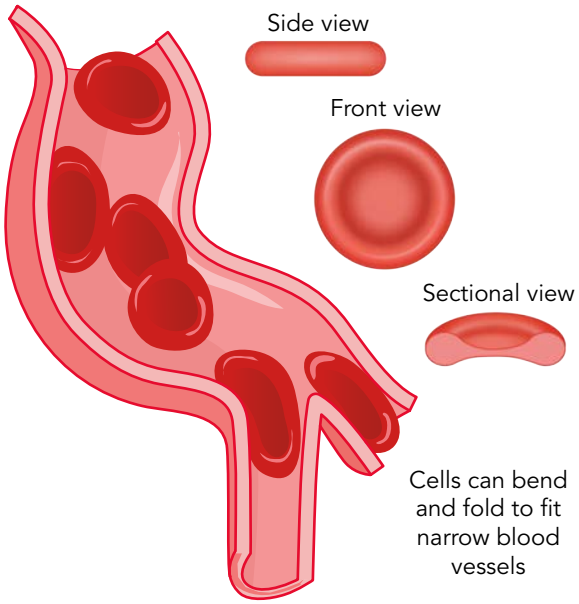
If blood becomes *too* hemoglobin rich — as seen in some people who immigrate to Tibet — the heart can be overworked due to elevated blood viscosity (thickness). However, the blood of Tibet's natives does not reach the excessive hemoglobin levels found in non-natives, naturally stopping the synthesizing process before dangerously high hemoglobin levels are reached.

This limit is due to a mutant form of a gene regulating increased hemoglobin synthesis. Tibetan natives probably inherited this mutation through intermarriage with a now-extinct group of people we call Denisovans. After Noah's descendants dispersed from the Tower of Babel, the genetic consequences of being separated into small groups produced people like Neanderthals and Denisovans. These people, all descended from Adam, were as human as you are. The fact that their genetic footprints can be tracked across the world's geography testifies not to human evolution but to the fact that all people are related.

Furthermore, this mutation demonstrates how natural selection can make a genetic variant into a helpful population characteristic. Mutations are genetic copying errors, and they do not produce brand new information needed to evolve a new kind of creature. Some mutations are harmless, some are harmful, and occasionally a mutation is helpful under particular circumstances. This harmless Tibetan mutation, by limiting a normal physiologic function, enables Tibetan natives to thrive in their unusual corner of the world.

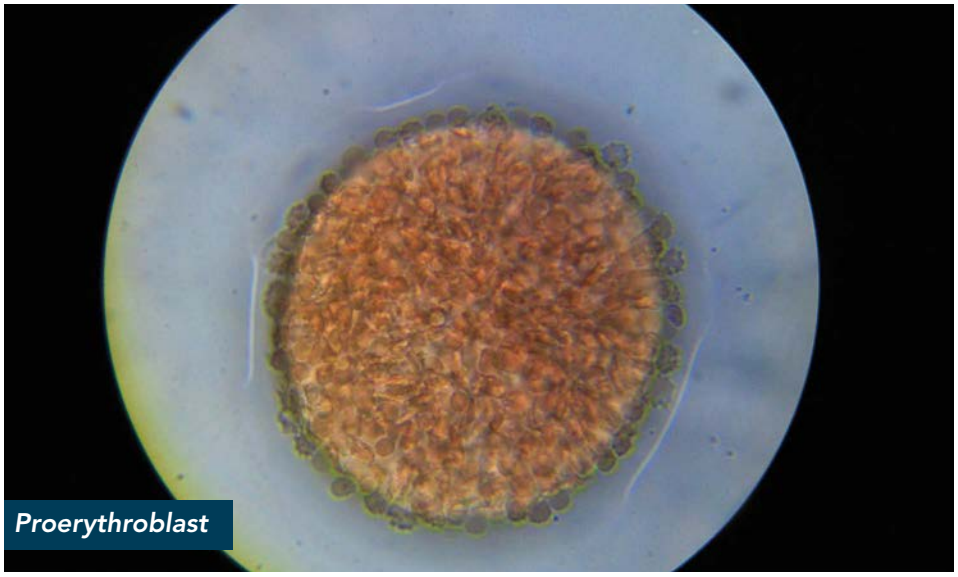
TAKING A CLOSER LOOK

Red Cell Flexing



circulation by the spleen. They are broken down, and many components are recycled.

With old red blood cells constantly being removed, there must be a constant source of replacements. New red blood cells are put into circulation at an estimated 2 million RBCs per second. Thus, in an average 24-hour day, your body makes around 170 billion RBCs!



Proerythroblast

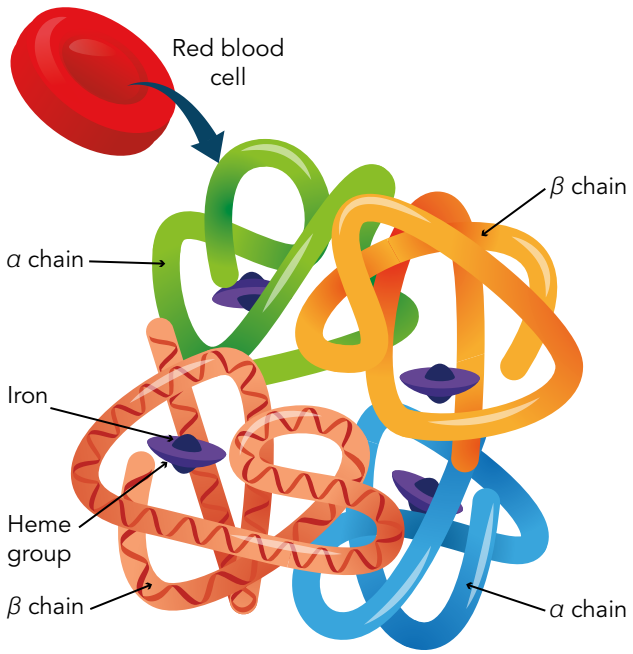
This daily resupply comes from bone marrow. Bone marrow is a spongy tissue inside many bones. A type of bone marrow cell called a *proerythroblast*, when stimulated to divide, produces cells that mature into new erythrocytes. These are released into the circulation. The process of producing new red blood cells is called *erythropoiesis*.

The driving force behind erythropoiesis is the hormone *erythropoietin*. Erythropoietin is produced by the kidneys. "Kidneys?" you may wonder. "Don't kidneys filter the blood and make urine?" Yes they do! Because all blood passes through the kidneys frequently, kidneys are a great location to monitor blood's oxygen-carrying capacity, which depends on adequate RBCs. Erythropoietin from the kidneys signals bone marrow to make more RBCs. Kidneys constantly produce erythropoietin, increasing as needed. This baseline secretion ensures a steady supply of RBCs to replace those filtered out by the spleen.

When blood loss happens, like from a bleeding ulcer or accident, the number of RBCs in circulation drops. The kidneys increase production of erythropoietin. Interestingly, this increase is *not* because the number of RBCs in circulation drops. It is because kidney cells detect less oxygen is being delivered to the tissues. The sudden drop in the RBC population reduces blood's oxygen-carrying capacity. As a result, production of RBCs and hemoglobin to fill them speeds up.

TAKING A CLOSER LOOK

Hemoglobin



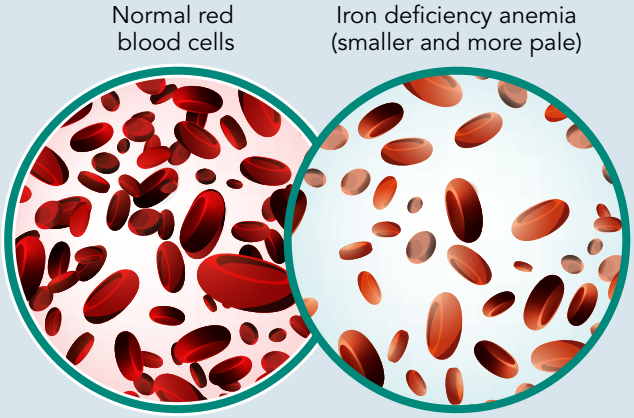
Highly trained athletes sometimes use this phenomena. They train at high elevations where air is thinner and atmospheric oxygen levels are lower. Training at high elevations can stimulate their bodies to make more erythropoietin, resulting in increased RBC production. They hope to then have greater than normal oxygen-carrying capacity and greater endurance when they compete where oxygen levels are closer to normal.

Hemoglobin

Hemoglobin is the oxygen-carrying protein filling red blood cells.

Each hemoglobin molecule has four polypeptide chains — two alpha chains (α) and two beta chains (β). Each chain contains a *heme group*. Heme groups are what give red blood cells their color. Each heme group has an iron atom at its center.

Iron-Deficiency Anemia



Anemia is an illness in which the amount of hemoglobin or the number of red cells in blood is too low. The most common type is iron deficiency anemia. Estimates suggest a billion people suffer from iron deficiency anemia.

Without adequate iron, sufficient amounts of hemoglobin cannot be produced. Without enough hemoglobin, adequate numbers of red blood cells cannot be made.

Symptoms of iron deficiency anemia are weakness, lack of endurance, and shortness of breath. Some patients just feel "run down."

Blood analysis shows a low hemoglobin level and/or a low number of red blood cells as well as low levels of iron in the blood. Microscopic examination of a blood smear reveals red blood cells that are small and pale.

This anemia can be caused by loss of iron, perhaps from a chronically bleeding ulcer, inflammatory bowel disease, or cancer. Alternatively, a diet low in iron might be the cause, or even inability to properly absorb iron from an otherwise adequate diet.

Iron deficiency anemia is treated by first dealing with any illness causing iron loss or addressing problems which result in the poor absorption of iron. Low iron stores can then be corrected with iron supplements.

Sickle Cell Disease

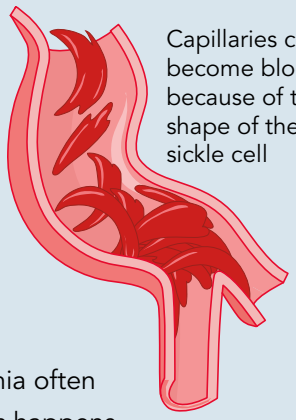
Hemoglobin consists of four polypeptide chains — two alpha chains (α) and two beta chains (β). Each chain contains a heme group. A mutation in a gene directing manufacture of a hemoglobin chain results in abnormal hemoglobin. Sickle cell anemia results from such a mutation. This mutation substitutes the sixth amino acid in the 146 amino acid beta chain. The resulting hemoglobin is called hemoglobin S.

Under low oxygen conditions, hemoglobin S beta chains link together. This causes red blood cells to change from their normal donut shape to that of a sharp sickle, or crescent. Additionally, hemoglobin S causes activation of sticky proteins on the cell surface, causing cells to stick together. This clumping and change of shape damages capillaries and causes red blood cells to rupture as they pass through, or prevents them from passing through at all. Sickled red blood cells stick together and to white blood cells and platelets, stopping blood flow and depriving tissues of the oxygen they need. This causes severe pain and organ damage.

A person's DNA has two copies of the gene that direct building hemoglobin's beta chains, one from each parent. People who have the sickle-causing mutation in only one copy and a normal gene in the other copy have *sickle cell trait*. Half of their hemoglobin is normal, and the other half has the S-type beta chain. People with *sickle cell trait* get along pretty well because they have enough good hemoglobin to compensate for the defective kind.

Sickle cell anemia is far more serious. People with sickle cell anemia have the sickle-causing mutation in both copies of their gene. They have inherited the sickle gene from each parent.

There are other mutations causing abnormal hemoglobin. If one copy of this gene has the sickle-causing mutation, and the other copy possesses another mutation, then none of the hemoglobin that person makes is normal. Such disorders are all forms of *sickle cell disease*. Sickle cell anemia and sickle/beta 0-thallasemia are the most severe.

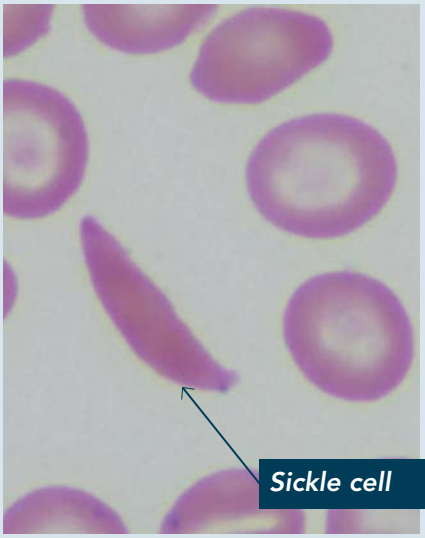


Capillaries can become blocked because of the shape of the sickle cell

People with sickle cell anemia often suffer a sickle cell crisis. This happens when capillaries are blocked by inflammation and clumped cellular elements. Because sickling occurs at lower oxygen levels, crisis often happens with exertion or in any situation where the metabolic rate — and therefore the oxygen needs of tissues — increases.

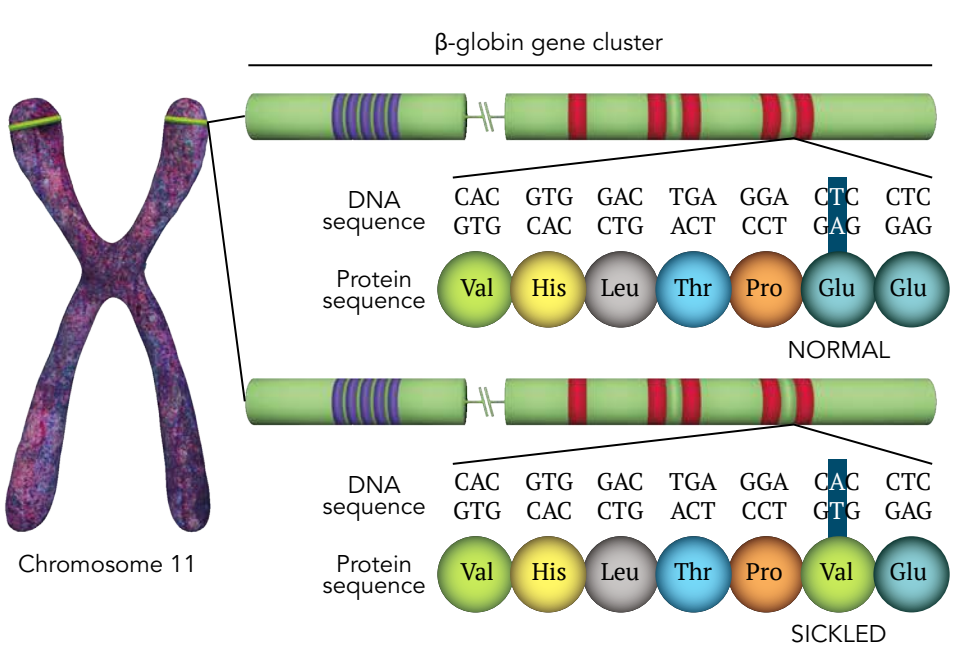
Sickle cell crisis is characterized by abdominal pain, pain in the arms and legs, and shortness of breath. Because sickled cells are fragile and rupture easily, patients with sickle cell disease also have chronic anemia, further reducing their blood's ability to transport oxygen. Many sickle cell patients require frequent transfusions both to correct anemia and to reduce the percentage of blood cells that can sickle.

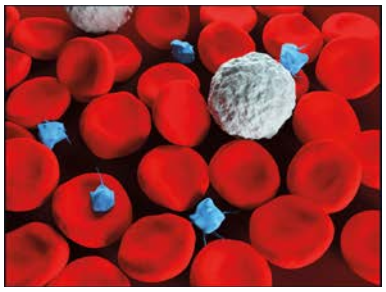
Sickle cell anemia damages capillaries and the organs that depend on them. Patients are therefore at high risk for stroke, infection, necrosis (tissue death) in major joints, hypertension, kidney failure, and right heart failure. Treatment includes pain management, antibiotics for infection control, and transfusions. Bone marrow transplantation has been effective in some.



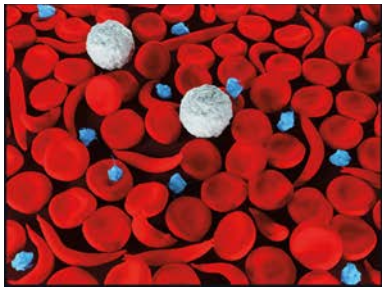
TAKING A CLOSER LOOK

Sickle Cell





Normal red blood cells



Sickled red blood cells

Sickle Cell Trait and Malaria

Sickle cell disease is the most common inherited blood disease. About 100,000 people in the United States suffer from it, and it afflicts millions worldwide. The sickle cell gene is most prevalent among people in sub-Saharan Africa as well as India, Sicily, Greece, southern Turkey, and India — places where malaria is also common. As it turns out, people with sickle cell trait are somewhat resistant to malaria. Therefore, sickle cell trait has ironically given them a survival advantage, making the gene's prevalence among those populations much higher than in the rest of the world.

You may have heard this called proof of evolution. It is not. Nothing about malaria or sickle cell demonstrates that humans are evolving into anything new! In fact, the way in which sickle cell trait defends the body against malaria demonstrates natural selection. With natural selection, a characteristic (even an otherwise undesirable one) makes it easier for many to survive and have children, leading to an increased prevalence of the gene associated with that characteristic.

Remember we said that red blood cells are biconcave discs? They have that shape because of a scaffold-like cytoskeleton inside each cell. Hemoglobin S interferes with formation of the normal cytoskeleton. That's why patients with sickle cell anemia have abnormally shaped cells.

When malaria parasites infect red blood cells and multiply in them, they hijack the molecules forming the cytoskeleton, instead building structures that help them multiply and also prevent the spleen from destroying infected cells. Hemoglobin S gets in the way of this process, making it difficult for malaria parasites to multiply and easier for the spleen to destroy infected cells. No surprise then that as many as 30% of the people in places where malaria is endemic carry the sickle cell gene.

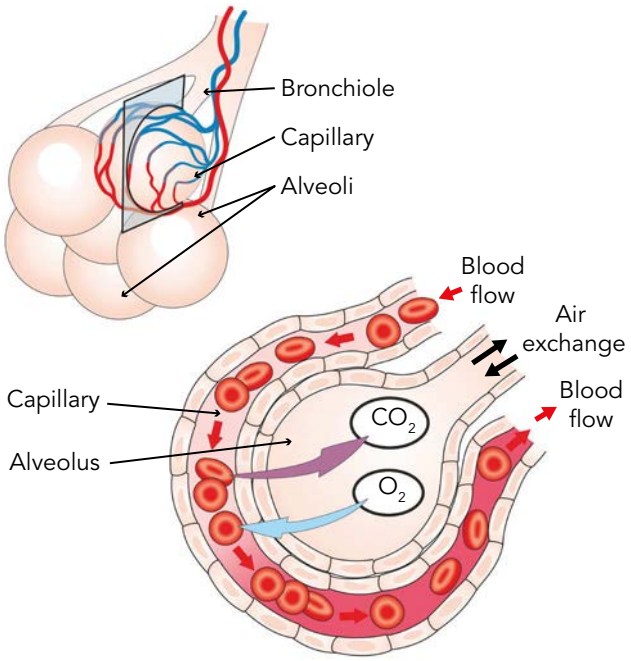
Iron gives hemoglobin its ability to carry oxygen. Each iron atom can bind one oxygen molecule. Therefore, each hemoglobin molecule can bind four oxygen molecules. With around 270 million hemoglobin molecules in each red blood cell, one red blood cell could carry about a billion oxygen molecules!

As blood is pumped through the lungs, blood in the capillaries surrounding alveolar air sacs is exposed to oxygen. Oxygen from the air filling alveoli diffuses easily into red blood cells in the capillaries. Hemoglobin packed inside these red blood cells loads up with oxygen. When bound to oxygen, hemoglobin is called *oxyhemoglobin*. Oxyhemoglobin is bright red. That's why oxygenated blood is bright red.

On the other hand, in tissues, oxygen must be released to supply the cells there. If hemoglobin grabs oxygen easily, what could persuade it to release

TAKING A CLOSER LOOK

Alveolar-Capillary Gas Exchange

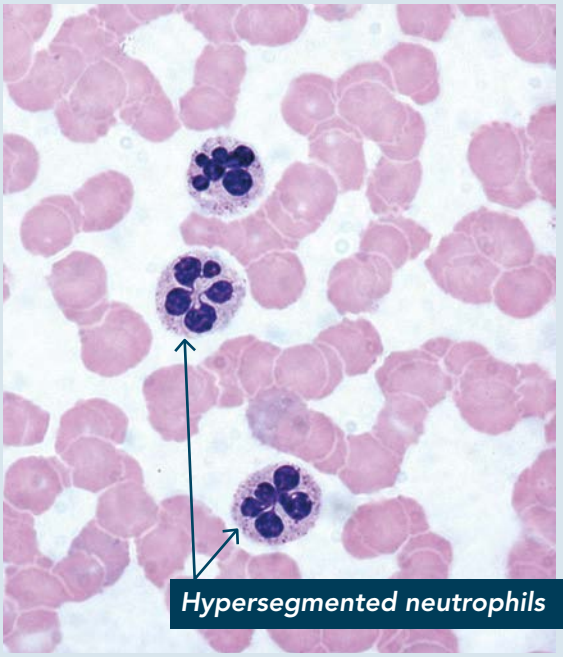


Megaloblastic Anemia

Megaloblastic anemia is another disorder in which there are too few red blood cells. The red blood cells being produced, however, are larger than normal. These larger-than-normal red cells are called *macrocytes*. Another characteristic of megaloblastic anemia are neutrophils that are "hypersegmented." Hypersegmented neutrophils—a kind of white blood cell—have more lobes (or segments) in their nuclei than normal.

The most common cause of megaloblastic anemia is a deficiency of either folate or Vitamin B12. These deficiencies can be caused by poor diet but are often the result of poor absorption. In the stomach, "intrinsic factor" is required to absorb vitamin B12. If caused by lack of "intrinsic factor," this anemia is also called *pernicious anemia*. Pernicious anemia is an autoimmune disease in which the body makes antibodies that attack and destroy intrinsic factor.

Symptoms of megaloblastic anemia are weakness, shortness of breath, and lack of endurance. As this disease progresses, more unusual symptoms can be seen such as a sore tongue and tingling of the extremities. Pernicious anemia could be fatal before the mid-20th century development of injectable vitamin B12.



Hypersegmented neutrophils

Oxyhemoglobin

Deoxyhemoglobin

its precious cargo? As it turns out, the environment in the tissues is somewhat different than that near the alveoli. Cellular metabolic activities produce heat and metabolic wastes, raising the temperature and acidity in the area. Hemoglobin is designed to release its oxygen in the presence of higher temperatures and higher acid levels, the very conditions found in peripheral tissues. Our Master Designer thought of everything.

Hemoglobin that has released some of its oxygen is called *deoxyhemoglobin*. It has a dull red color.

Hemoglobin never releases all of its oxygen. It usually remains about 75% saturated even after passing through peripheral tissues. This leaves plenty of bound oxygen in reserve. At rest, the body only uses about 25% of the oxygen in blood. At times of increased exertion, hemoglobin can release a higher percentage of oxygen.

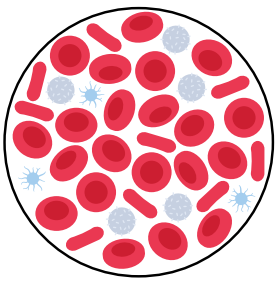
Polycythemia

What if there are too many red blood cells? We've already touched on one special situation associated with increased RBC production: changes that happen at high altitudes.

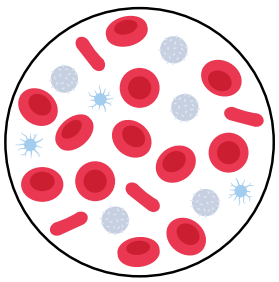
There are other conditions which cause *polycythemia* — an increase in the percentage of blood that is made up of RBCs. (*Poly* means "many," *cyt* means "cell," and *hemo* means "blood" — hence "too many cells in the blood.") These include mutations in erythropoietin receptors, cancers that make extra erythropoietin, and a disease in which cells in the bone marrow begin uncontrolled overproduction. Any of these situations leads to overproduction of RBCs.

Situations in which the body's tissues are crying out for more oxygen also lead to increased RBC production. The low oxygen tension at high altitude is one of these. Lung diseases and other conditions that interfere with oxygenation of the blood also trigger increased RBC production. Smoking interferes with the ability to properly oxygenate blood and is also a cause of polycythemia. As bone marrow makes more RBCs, the percent of blood volume composed of RBCs increases.

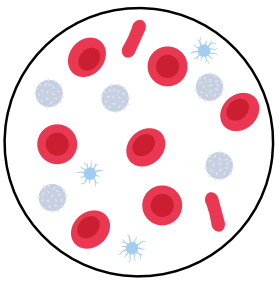
As we said when discussing the situation in Tibet, too much of a good thing can be a problem. Beyond a certain point, thicker blood doesn't flow as easily through capillaries, interfering with the blood's ability to oxygenate tissues. Thicker blood is also harder for the heart to pump, leading to heart disease. Treatment of polycythemia depends on its cause and severity.



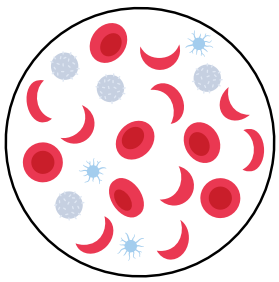
Polycythemia



Normal blood



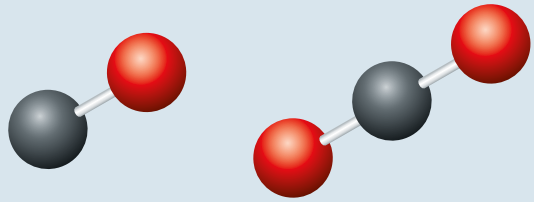
Anemia



Sickle cell anemia

Carbon Monoxide Poisoning

You already know that the air you breath contains about 21% oxygen, a lot of nitrogen, and a very small percentage of carbon dioxide. Carbon dioxide is also a normal waste product of cellular metabolism. When blood returns to the lungs, excessive amounts of carbon dioxide are released. But there is another carbon-containing molecule that your blood is unable to release, and it is dangerous. That molecule is carbon monoxide.



CO
Carbon monoxide

CO_2
Carbon dioxide

Each molecule of carbon dioxide (CO_2) contains one carbon atom and two oxygen atoms, whereas each molecule of carbon monoxide (CO) contains just one oxygen atom. Both CO_2 and CO are odorless, colorless, tasteless gases, but these molecules behave very differently. Carbon monoxide is highly toxic.

Carbon monoxide can be produced by any process in which incomplete combustion (burning) takes place. When coupled with inadequate ventilation, incomplete combustion can cause carbon monoxide poisoning and death. The most common causes of carbon monoxide poisoning are malfunctions in home heating systems, heaters used with inadequate ventilation, and motor vehicles in which exhaust leaks into the passenger compartment. Driving with the rear hatch open and letting a car run in a closed garage are dangerous because of the risk of carbon monoxide poisoning.

Smoking also causes chronic carbon monoxide exposure. This risk greatly increases during pregnancy, because carbon monoxide crosses the placenta and is very dangerous to the unborn baby.

Carbon monoxide is so dangerous because it binds to hemoglobin in place of oxygen. Carbon monoxide binds to hemoglobin 240 times more strongly than oxygen. Once bound, the hemoglobin molecule is unable to easily release it. Carbon monoxide can quickly incapacitate a lot of hemoglobin. Without adequate oxygen, organs like the heart and brain soon suffer damage. So when the battery alarm on your home's carbon monoxide detectors go off, put in fresh batteries! Those detectors, which are especially important to place near your home's bedrooms, are there to protect you from an invisible and very dangerous enemy.

Leukocytes

Leukocytes are not like erythrocytes. Leukocytes (white blood cells, or WBCs for short) have nuclei and the usual assortment of intracellular organelles. And while erythrocytes stay in blood vessels, leukocytes have the ability to leave the circulation. Moving like amoebae, they can exit through capillary walls to perform their duties.

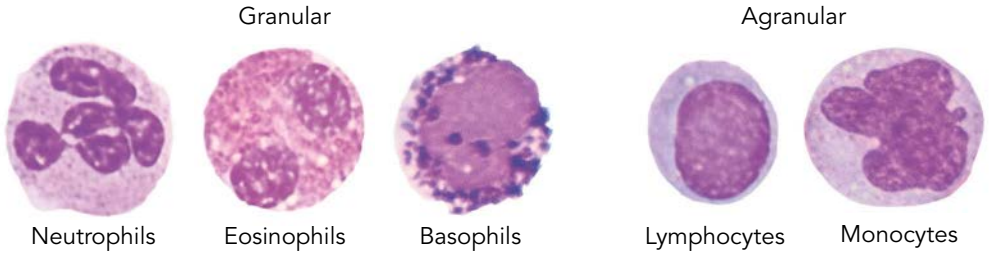
Their ultimate purpose is to protect the body from invaders. Whether these invaders are bacteria, viruses, or parasites, leukocytes are constantly on guard.

Remember there are three kinds of granular leukocytes: neutrophils, eosinophils, and basophils. And there are two kinds of agranular leukocytes: lymphocytes and monocytes.

Don't let the fancy names worry you. You will have this down before you know it.

TAKING A CLOSER LOOK

Leukocytes



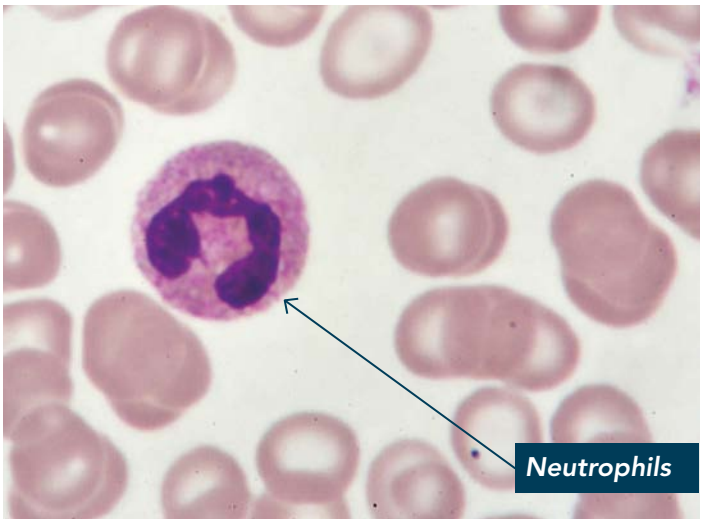
Neutrophils

Neutrophils are the most common type of leukocyte. They make up about 65% of circulating white blood cells.

When viewed under a light microscope with conventional stains, neutrophil cytoplasm is pink. The neutrophil nucleus typically has 3–5 lobes. Neutrophils are about twice the size of erythrocytes. Their lifespan ranges from 6 hours to 5 days.

The primary function of neutrophils is to combat bacterial infections. When confronted with an infection, their population increases dramatically.

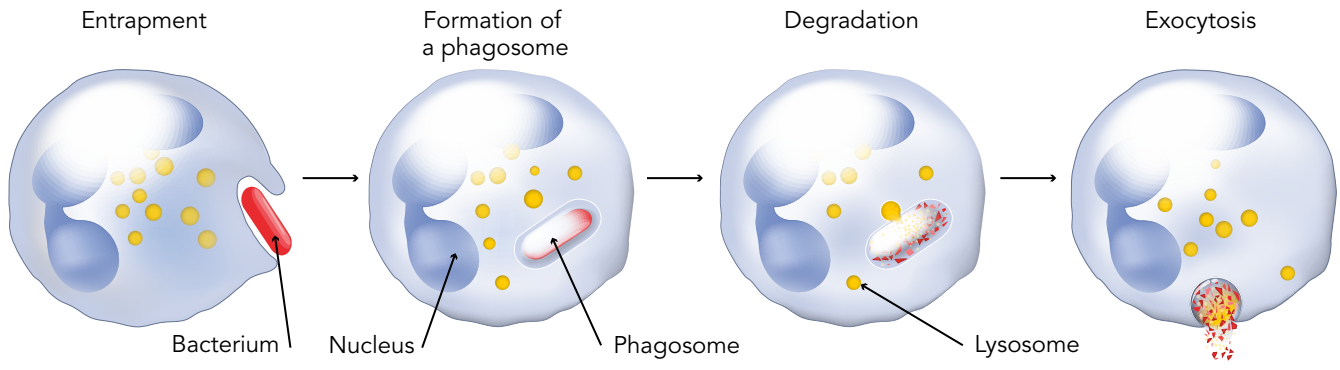
During an infection, the inflammatory response to tissue damage releases chemical factors that attract neutrophils. This chemical attraction phenomenon is called *chemotaxis*.



When circulating neutrophils reach the site of infection, they migrate through capillary walls into surrounding tissues where they ingest bacteria. This process of engulfing microorganisms or debris is called *phagocytosis*. Neutrophils then produce chemicals to destroy them.

TAKING A CLOSER LOOK

Phagocytosis



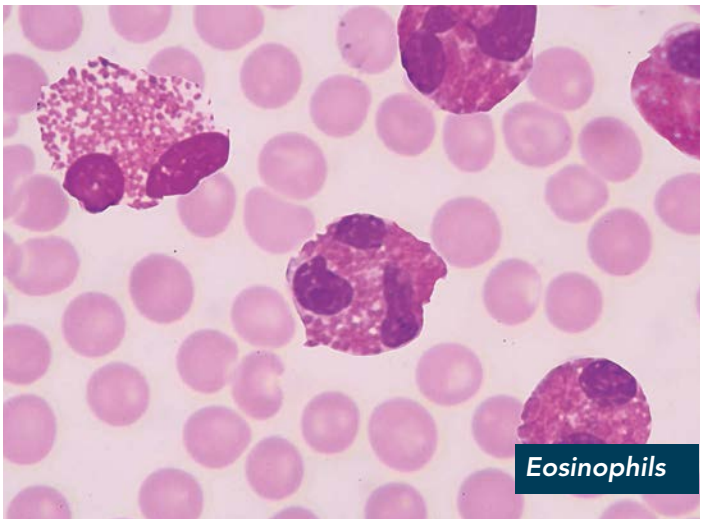
Eosinophils

Eosinophils make up only about 3% of WBCs. Not much larger than neutrophils, they are about three times the size of RBCs. The eosinophil nucleus usually has two lobes. In its cytoplasm are large granules that stain reddish orange.

Unlike neutrophils, eosinophils only play a minor role in combatting bacterial infections, although there is evidence they aid with defense against viruses. Eosinophils play a major role in defense against parasitic infections.

Also, eosinophils are involved in the inflammatory processes associated with asthma and some allergic reactions. They engulf invading substances that are tagged with antibodies. (More on this later.) And they release chemicals associated with allergic responses. If a person's blood analysis shows an elevated percentage of eosinophils, he or she may be experiencing an allergic reaction.

The lifespan of an eosinophil is about 5 days.


Eosinophils

Basophils

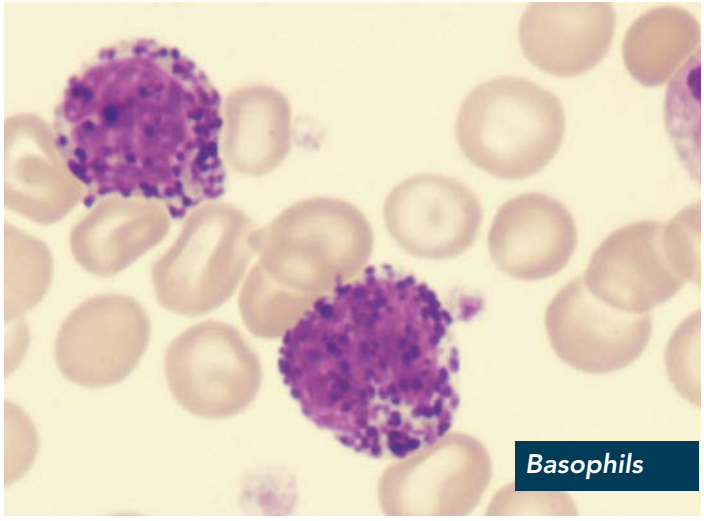
Basophils are the least common leukocytes, less than 1% of the WBC population.

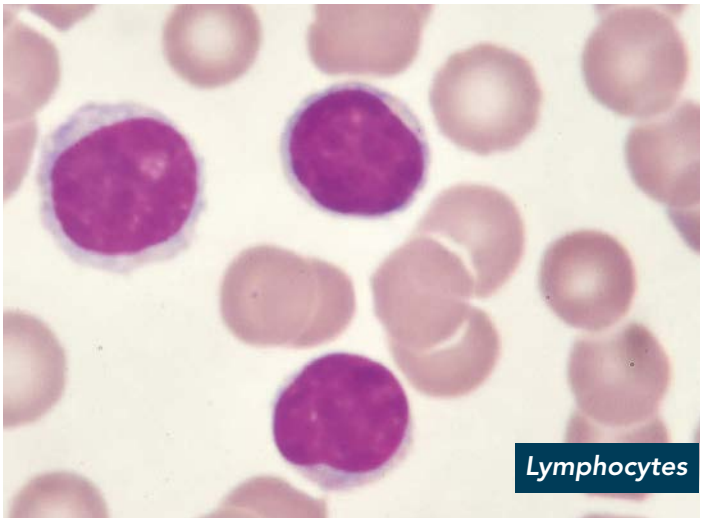
Basophils are the largest of the granular leukocytes. Like eosinophils, the basophil nucleus usually has two lobes. The cytoplasm contains large granules that stain purple, giving basophils their characteristic appearance.

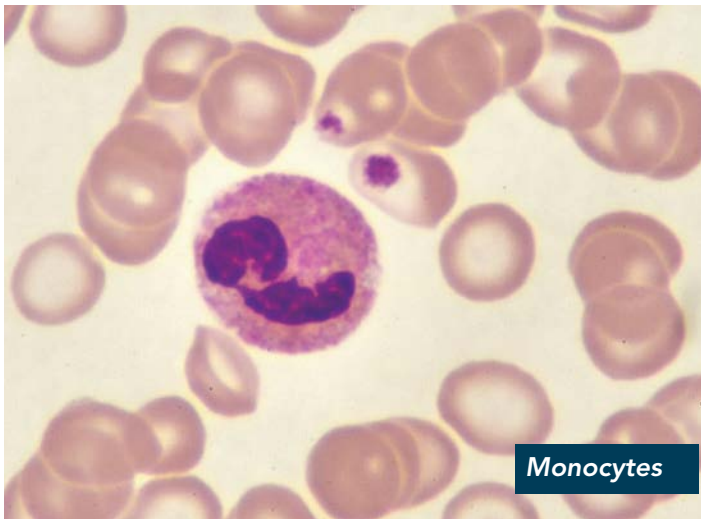
Basophils granules contain histamine, which promotes vasodilation. Histamine increases blood flow to tissues and attracts other leukocytes to the site of inflammation.

Lymphocytes

Lymphocytes make up about 25% of WBCs. The lymphocyte's round nucleus occupies most of the cell. The life span of a lymphocyte ranges from weeks to years.


Basophils

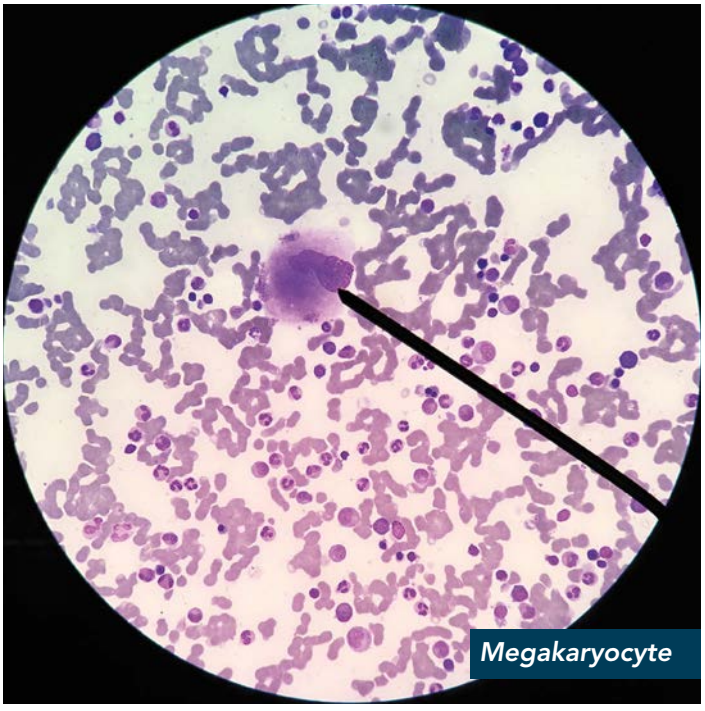

Lymphocytes

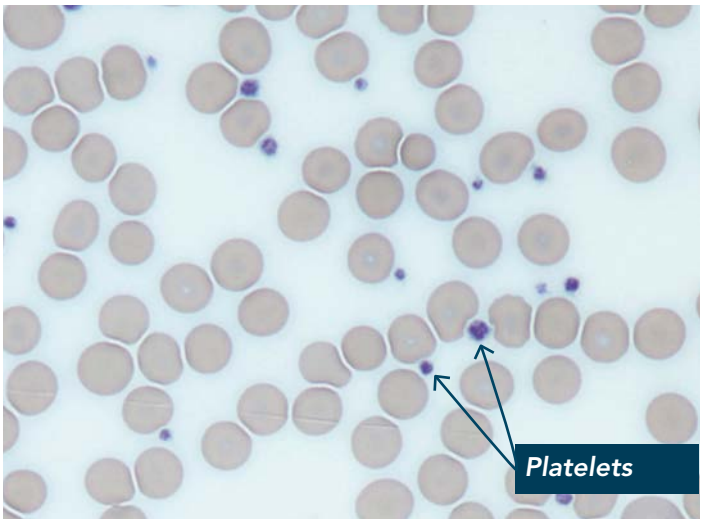

Monocytes

There are two types of lymphocytes. T lymphocytes attack bacteria, viruses, and cancer cells. B lymphocytes produce antibodies. Think of them as molecules that recognize and tag invaders. We will learn more about antibodies in the section covering the immune system.

Monocytes

Monocytes account for about 6% of WBCs. They are the largest leukocytes. The monocyte has a large, kidney-shaped nucleus and cytoplasm that stains pale blue.


Megakaryocyte


Platelets

Monocytes often leave the bloodstream and migrate into tissues. There they change into *macrophages*. Macrophages are active against bacteria and viruses. They also clear cellular debris after an infection.

Monocytes also help activate T lymphocytes.

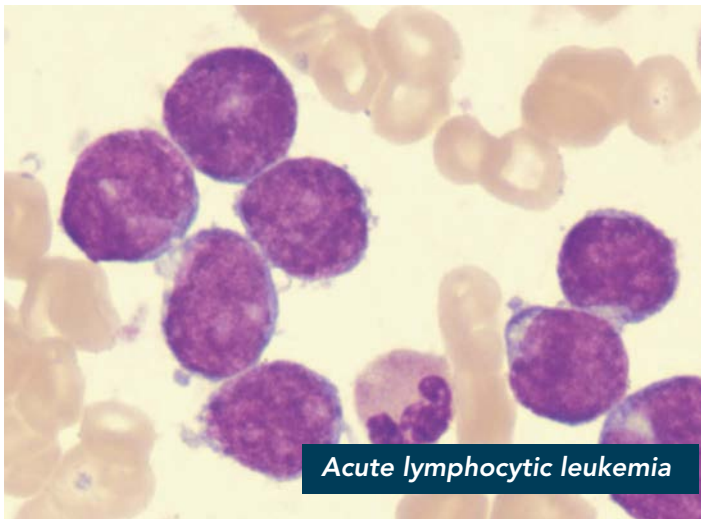
Platelets

Platelets are fragments of large cells called *megakaryocytes*. Megakaryocytes are found in the bone marrow. As they mature, each megakaryocyte fragments into 1,000 to 3,000 platelets. Those platelets enter the circulation where they have a life span of 8–9 days. Old platelets are removed from circulation by the spleen and liver.

Platelets are very important in blood clotting. When a blood vessel is damaged, platelets aggregate there. They form a plug that slows blood loss and activate the blood's clotting processes.

Leukemia

Leukemias are cancers resulting from overproduction of abnormal immature leukocytes in bone marrow. These abnormal cells are called *blasts*. As blasts increase in number, they can crowd out normal cells in bone marrow. This causes a decrease in the number of normal white blood cells, red blood cells,



Acute lymphocytic leukemia

and platelets. Loss of normal bone marrow function leads to severe problems.

Leukemias are classified by their rate of onset and cell type. Acute leukemias have a rapid onset, while chronic leukemias develop more slowly. These disorders are distinguished by their precursor cell type. Lymphocytic leukemias result from abnormal growth of lymphocyte precursors. Myelogenous leukemias involve cancerous change in cells that are precursors of the other blood cell types. Thus, the four major types of leukemia are acute lymphoblastic leukemia, chronic lymphocytic leukemia, acute myelogenous leukemia, and chronic myelogenous leukemia.

Common symptoms of leukemia include easy bleeding, bruising, fever, weight loss, fatigue, and frequent infections. In acute leukemia, symptoms appear rapidly and are usually severe. In chronic leukemia, symptoms at the onset may be minimal. However, as disease progresses, sufferers of chronic leukemia can also become quite ill.

Treatment of leukemia usually involves *chemotherapy*. Powerful drugs that target rapidly dividing cells are given in hopes of destroying cancerous cells. This type of treatment also kills normal cells, but normal cells will hopefully reestablish themselves after cancerous cells have been eradicated. Treatment may involve a bone marrow transplant. In a bone marrow transplant, all bone marrow is destroyed in order to kill all cancerous cells. Then, bone marrow from a healthy donor is used to replace the marrow.

Aplastic Anemia

Aplastic anemia is a disorder in which the body does not produce enough red blood cells, white blood cells, or platelets.

Symptoms of aplastic anemia are weakness, fatigue, recurring infections, easy bruising, and little red or purple spots on the skin. These spots, called *petechiae*, are caused by bleeding into the skin due to lack of platelets.

Causes of aplastic anemia include exposure to chemical toxins, radiation exposure, and certain infections. Some medications increase the risk of developing aplastic anemia. An example is chloramphenicol, a cheap antibiotic available in some countries without a prescription. Some cases of aplastic anemia result from an autoimmune disorder in which the body attacks its own bone marrow cells. In many patients, however, the cause remains unknown.

Aplastic anemia is sometimes treated with powerful drugs to suppress the immune system or a bone marrow transplant. Patients developing aplastic anemia at a younger age have a higher chance of survival than those who are older.

Blood Type

If you looked under the microscope at the red blood cells of healthy people, you would see no differences. They look the same. Yet they may differ invisibly in their blood type. If you have ever watched medical or detective programs, you have heard of blood type. Blood type is based on differences in the surfaces of red blood cells.

On the surface of every red blood cell are antigens. *Antigens* are substances that can trigger an immune response in the body. They are molecular labels that identify a cell to other cells. The presence or absence of certain antigens on the surfaces of red blood cells determines blood type.

Here's how it works.

The surfaces of some people's erythrocytes have an antigen classified as "Type A." These people have Type A blood. Other people have erythrocytes possessing an antigen called "Type B." They have Type B blood. Pretty easy, right? There are also people that have erythrocytes expressing both Type A *and* Type B antigens. What would their blood type be? Yep, you guessed it. Those people are Type AB!

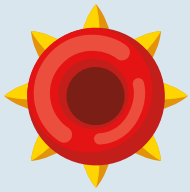
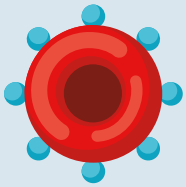
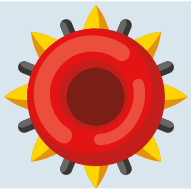
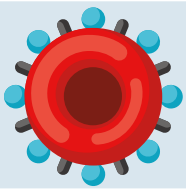
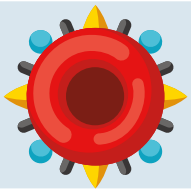
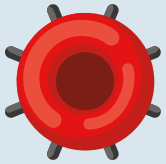
Some people don't have either Type A or Type B antigens on their erythrocytes. These people have blood Type O. (That's the letter O, not zero.)

These surface antigens help the body recognize "self" and "foreign." The immune system of people with Type A blood recognizes the Type A antigens on the erythrocytes as normal. They recognize their own erythrocytes as "self." The immune system is always asking, "Is this me or not me?"

In the case of blood types, the immune system knows what belongs and what doesn't. For example, a Type A person has Type A erythrocyte antigens. Type A cells belong. Type A people are born with antibodies on the lookout for Type B antigens. If Type B antigens show up, reactions take place to remove them.

Type A people have antibodies against Type B (anti-B antibodies). Type B people have antibodies against Type A (anti-A antibodies). Because Type AB people are supposed to have both antigens, they don't have either antibody!

BLOOD TYPES AND CROSS-REACTIONS

GROUP	A	B	AB	O
Red blood cell type (Rh negative)				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens on red blood cell	 A antigens	 B antigens	 A and B antigens	None
Blood types compatible in an emergency	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O^- is the universal donor)
 Rh antigen (Rh positive)				

What about Type O folks? Their antibodies are on the lookout for A antigens and B antigens, because both are foreign to them. Therefore, Type O people have *both* anti-A and anti-B antibodies.

But what about positive and negative types? I'm sure you've heard of types like "O positive" or "AB negative." There is one more important antigen on the surface of red cells. It's called the *Rh factor*. Rh factor is named for rhesus monkeys in which it was first discovered. People with Rh antigen are called "positive," and people without it are considered "negative." Interestingly, people who are Rh negative do *not* have

anti-RH antibodies from birth. Unlike the anti-A, and anti-B antibodies, anti-Rh antibodies only develop in those instances where Rh negative people are *exposed* to Rh positive blood.

Blood Transfusions

Blood transfusions are sometimes needed to save lives in this fallen world. People bleeding from severe accidents or major surgery may need blood or blood products. Those suffering from leukemias, sickle cell anemia, or other diseases may also need transfusions.

Blood type is important. Would you want to give Type B blood to a Type A patient? Of course not! Anti-B antibodies in the Type A patient would destroy the transfused Type B cells, causing a *transfusion reaction*.

Let's take a closer look. (We are going to leave out Rh factor for now, to keep things simple.)

Can you give Type A blood to someone who is Type A? Of course you can. The same goes for Types B, AB, and O. Transfusing someone with the "same type" of blood should cause no problems. (Okay, I'm oversimplifying a little. Transfused blood can contain other antigens or antibodies that cause reactions, but let's focus on blood types for now.)

Can you give Type B blood to a Type AB patient? Yes, you can. You can give Type AB, Type A, Type B, or Type O to a Type AB person. Remember, Type AB people don't have *any* anti-A or anti-B antibodies, so they don't reject any blood types. Type AB is called the *universal recipient*.

Now what about those pesky Type O folks. Can they receive Type A or Type B blood? No, they cannot, because they have anti-A and anti-B antibodies. They will reject any blood cells with A or B antigens. Type O people can only receive Type O blood. However, Type O can be *given* to anyone because it has no antigens on the red cells. Type O is considered the *universal donor*.

About 45% of people are Type O, 40% are Type A, about 10% are Type B, and 5% are Type AB.

Transfusion Reactions

When transfusing blood, things sometimes do go wrong. Occasionally a transfusion reaction can occur. This is most often due to incorrectly matched blood. Here the patient's antibodies attack the donated blood. This can happen within a few hours of the transfusion or on rare occasions up to a couple of weeks later.

Transfusion reactions are characterized by fever, chills, chest and back pain, and shortness of breath. Transfusion reactions are treated symptomatically. (This means that there is no way to undo them.) Pain control, oxygen as needed, and intravenous fluids to support blood pressure are often employed. Severe complications are fairly rare.

Less common causes of transfusion reactions include reactions to chemicals released by the white blood cells in the donor blood or an allergic reaction to substances contained in the donor blood.

But wait! What about antibodies in the transfused blood? Wouldn't it still a problem to give Type A blood to a Type AB person? After all, Type A blood contains anti-B antibodies present from birth. Aren't you causing the Type AB person's blood to be attacked by giving them antibodies against their own cells?

Well, if you transfused whole blood, that might indeed be a problem. Those antibodies would be floating in the plasma portion of the blood. However, in most cases, *packed red blood cells* are transfused. Packed cells are prepared by spinning donated blood in a centrifuge. The red cells are gathered, and most of the blood plasma is removed and utilized for other purposes. Therefore, the majority of the antibodies in donor blood are removed with the plasma before transfusion of packed red blood cells. Plasma is not wasted but is also a valuable blood product. Furthermore, in actual practice, types are usually matched for transfusion.

So How is Blood Type Inherited?

There is a single gene for blood type, and everyone has two alleles of this gene. We inherit one from our father and one from our mother. As we have seen, this blood type gene has three possible variations — A, B, and O. These variations code for the different antigens expressed on the surface of the red blood cells.

A and B are co-dominant alleles. Both are expressed if both are present. Someone with genotype AA has blood type A. Someone with genotype BB has blood Type B. And someone with genotype AB — possessing one A allele and one B allele — has blood Type AB. Co-dominant genes are expressed equally.

The only way someone can have blood Type O is if both alleles are O. Someone with genotype OA would be Type A since the A allele would be expressed. Someone who is OB would be Type B. Type O is only possible if you are genetically OO.

So, you might wonder, how can a couple have a baby with blood Type O if neither parent is Type O? Remember, A and B are both dominant. Therefore, each parent needs only one A or B allele to be phenotypically blood Type A or Type B. If each parent passes on an O allele to their baby, the baby will be Type O. If one parent is blood Type AB, however, then that parent has no O allele to pass on, and the baby cannot be blood Type O.

Let's say we have parents with genotypes AO and BO. Therefore, their blood types are A and B, respectively. Look at the chart to see the possibilities for each child. Each of their children has a 25% chance of being AB, a 25% chance of being AO, a 25% chance of being BO, and a 25% chance of being OO.

		FATHER'S GENOTYPE	
		A	O
MOTHER'S GENOTYPE	B	AB	OB
	O	AO	OO

What if one parent has genotype AO (with blood Type A), and the other has genotype OO? Again, look at the chart to see the combinations that are possible. Each of their children has a 50% chance of being blood Type A (genotype AO) and a 50% chance of being blood Type O (genotype OO).

		FATHER'S GENOTYPE	
		A	O
MOTHER'S GENOTYPE	O	AO	OO
	O	AO	OO

		FATHER'S BLOOD TYPE			
		A	B	AB	O
MOTHER'S BLOOD TYPE	A	A or O	A, B, AB, or O	A, B, or AB	A or O
	B	A, B, AB, or O	B or O	A, B, or AB	B or O
	AB	A, B, or AB	A, B, or AB	A, B, or AB	A or B
	O	A or O	B or O	A or B	O

Hemostasis

The smooth lining of blood vessels is ideal for blood flow. (This lining is called *endothelium*.) Normally, blood cells do not stick to vessel walls.

However, when a blood vessel is damaged, blood leaks out of the vessel and into the tissues or the outside world. Unchecked loss of blood would be a big problem, right?

Thankfully, God designed a mechanism to stop blood loss in the event of injury. This is called *hemostasis*, the process of stopping bleeding. There are three major steps in hemostasis — spasm, platelet aggregation, and coagulation.

The first step in hemostasis is spasm of the injured blood vessel. Chemical tissue factors are released from the damaged vessel. They trigger contraction of smooth muscle in the vessel wall. This slows blood

Blood Typing — Who Done It?

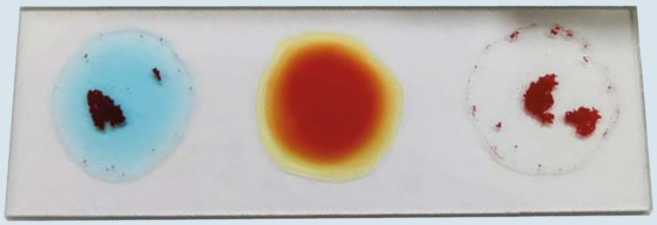
Let's use this blood typing thing to solve a crime.

You are the detective. You are called to a crime scene where you find a lockbox that has been opened with a crowbar. The contents of the lockbox are gone. There are no fingerprints, so the thief likely wore gloves. But you do notice one thing. There are drops of blood on the lockbox and crowbar. Perhaps the thief was injured committing the crime.

During your investigation, you narrow the list of suspects to three: Jessie, Jasmine, and Georgie — all well-known cat burglars. If we figure out whose blood was at the crime scene, we can identify the guilty party.

Jessie has blood Type A negative. Jasmine has blood Type AB negative. Georgie has blood Type A positive.

You take the crime scene blood to the lab. A small sample is placed on a glass slide. A few drops on anti-A serum is mixed with the blood. If there is any Type A antigen in the blood sample, there should be a visible reaction, called *agglutination*. As it turns out, there is a reaction. That means Type A antigen is present.



Anti-A serum *Anti-B serum* *Anti-Rh serum*

Unfortunately, this doesn't help much since all three suspects have Type A antigens.

Next, the crime scene blood is tested with anti-B serum. There is no reaction. Thus, Jasmine is ruled out as the perpetrator since she has Type AB blood. If the crime scene blood contains Type B antigen, it can't belong to her.

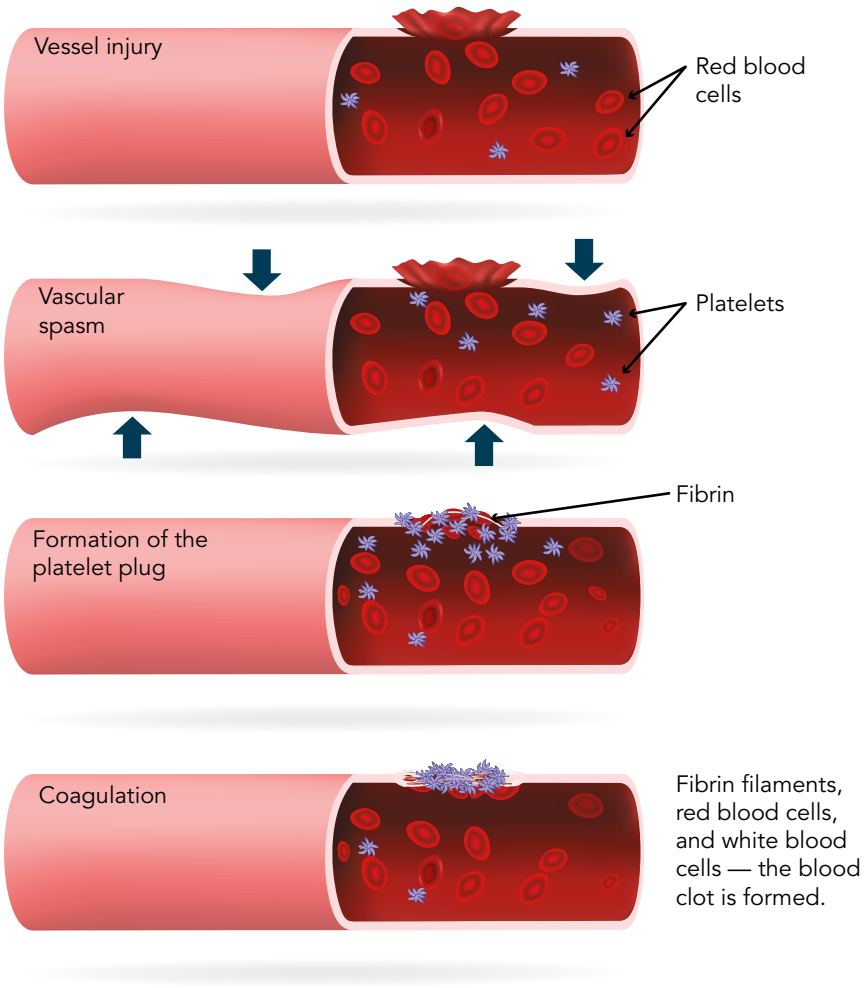
Now the blood is tested for Rh factor. The sample is mixed with anti-Rh serum. There is a reaction, so the blood is Rh positive.

The crime scene blood has Type A antigen and Rh antigen, but no Type B. The blood is therefore Type A positive.

This makes Georgie the likely culprit. Naughty, naughty Georgie. . . .

TAKING A CLOSER LOOK

Hemostasis



loss. Slowing blood loss allows time for the next steps to happen.

The next step is formation of a platelet plug. Normally, platelets do not stick to endothelium. However, when there is injury or damage to this lining, the underlying collagen is exposed. (*Collagen* is a structural protein found in connective tissue and skin.) Platelets aggressively cling to exposed collagen. As platelets stick to collagen, they become "activated." Activated platelets enlarge and extend small projections from their surfaces. These projections allow them to touch more platelets in blood flowing through the constricted vessel. They also release chemical messengers to attract even more platelets. This process is called *platelet aggregation*. Platelet aggregation produces a platelet "plug" that further slows blood loss.

The third step in hemostasis is blood clotting. Blood clotting is also called *coagulation*. Thus, the three steps of hemostasis are 1) spasm, 2) platelet aggregation, and 3) coagulation.

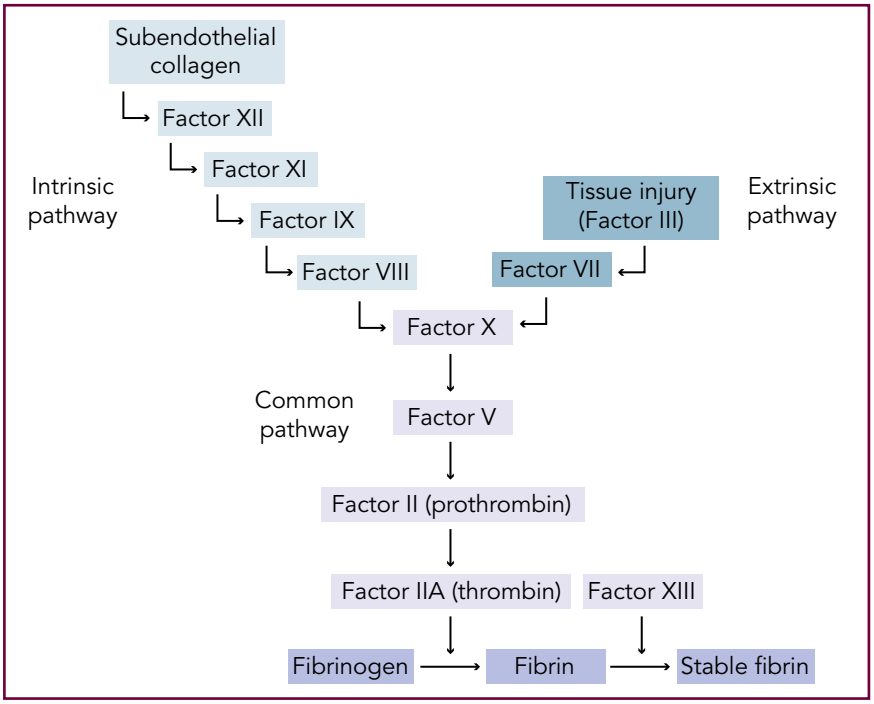
You see, even though platelet aggregation has formed a platelet plug, the plug is not enough to completely stop blood from leaking out of the blood vessel. A tighter seal must form. A real blood clot must be made. This is accomplished with the aid of plasma proteins known as *clotting factors*.

Check out the diagram of clotting pathways. Activation of a series of clotting factors is necessary for blood to clot. No doubt you will find this chart a little intimidating. (Your author felt the same way in medical school!) We are just going for the big picture here. Once the clotting cascade is triggered, the first clotting factor is activated. Then this activated factor activates the next clotting factor in the sequence. And so on, just like a series of dominos falling down.

Coagulation

There are three main phases to coagulation — cascade initiation, thrombin production, and fibrin production.

In the first phase, the clotting cascade is initiated. There are two pathways to accomplish this — "extrinsic" and "intrinsic."



Clotting cascade

The first pathway is the *extrinsic pathway*. This means that the pathway is started by something *extrinsic*, or *outside of*, the blood vessel. The extrinsic pathway is triggered by a protein called tissue factor. *Tissue factor* is released by damaged cells outside the blood vessel. Look back at that chart. Notice the extrinsic pathway involves fewer reactions than the intrinsic pathway.

The other pathway is called the *intrinsic pathway*. It is called *intrinsic* because the factors that trigger the clotting cascade are *inside* blood vessels. These factors come from damaged endothelial cells lining the vessel. The intrinsic pathway is slightly slower than the extrinsic, but the clotting cascade is initiated just the same.

Blood Clotting-Fingerprints of the Master Designer

Notice that each step in this blood clotting process requires the previous step to work properly. If one of the factors were not present, the whole cascade would fail. Furthermore, each of these factors serves just one purpose, its purpose in the clotting cascade. Clotting factors are like fingerprints of our wise Master Designer.

Random evolutionary processes — even if they could produce a bunch of complex molecules like these clotting factors — could not then produce the clotting cascade. Why do I say that? Because evolutionary principles would require that each factor have a purpose to keep getting made. Yet *all* the factors would have to be present for *any* of this process to work. Evolutionary processes could not evolve a clotting cascade one step at a time. God, on the other hand, is a Master Designer, and He designed the whole system to work from the beginning.

Both intrinsic and extrinsic pathways result in formation of *prothrombin activator*. This concludes the first phase of coagulation.

The second phase occurs as prothrombin activator converts a plasma protein called *prothrombin* into an enzyme called *thrombin*.

In the third and final phase of coagulation, thrombin converts *fibrinogen* into *fibrin*. Fibrinogen, like

Fibrin mesh

prothrombin, is just floating around in plasma waiting to be needed. Fibrin strands form a mesh that helps keep platelets firmly bound together. In the presence of fibrin, plasma becomes gel-like. The gel aids in trapping other cellular components. This strengthens the clot.

Hemophilia

Hemophilia is a bleeding disorder resulting from an inherited deficiency of certain coagulation factors. There are two primary forms of hemophilia. Hemophilia A is due to insufficient amounts of clotting factor VIII. Hemophilia B results from insufficient factor IX.

Both Hemophilia A and Hemophilia B occur mainly in males, resulting from inheriting an X chromosome with a nonfunctional gene. This is an X-linked recessive trait. Females that have one normal X chromosome will not have hemophilia, but they can pass on the abnormal gene to their children. Hemophilia became famous due to its prevalence in intermarried European royal families.

Symptoms of hemophilia are associated with easy bleeding. Often people with hemophilia bleed into their joints. That can occur with only minimal exertion and is quite painful. Bleeding in the brain can also occur.

Management of hemophilia consists of transfusions of fresh plasma containing the missing clotting factors. Also, it is possible to directly replace the deficient factors. However, after a period of time, a patient sometimes develops antibodies to the replacement clotting factors administered to them. In those cases, the antibody response may be overcome by giving much higher doses of replacement factors or using non-human replacement products that the body doesn't recognize as foreign.

Fibrinolysis

After clot formation, damage is repaired. Then the clot is no longer needed. The body has a mechanism called *fibrinolysis* for removing the now useless clot.

When a clot is initially formed, a plasma protein called *plasminogen* is incorporated into it. As healing proceeds, plasminogen is activated, forming an enzyme called plasmin. Plasmin then breaks down — or "lyses" — fibrin strands forming the clot.