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.

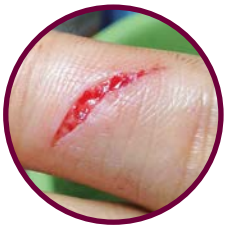
Let's get started!

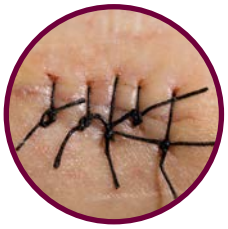
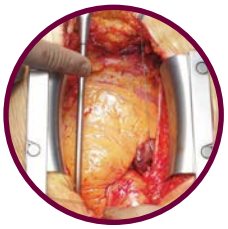
BLOOD

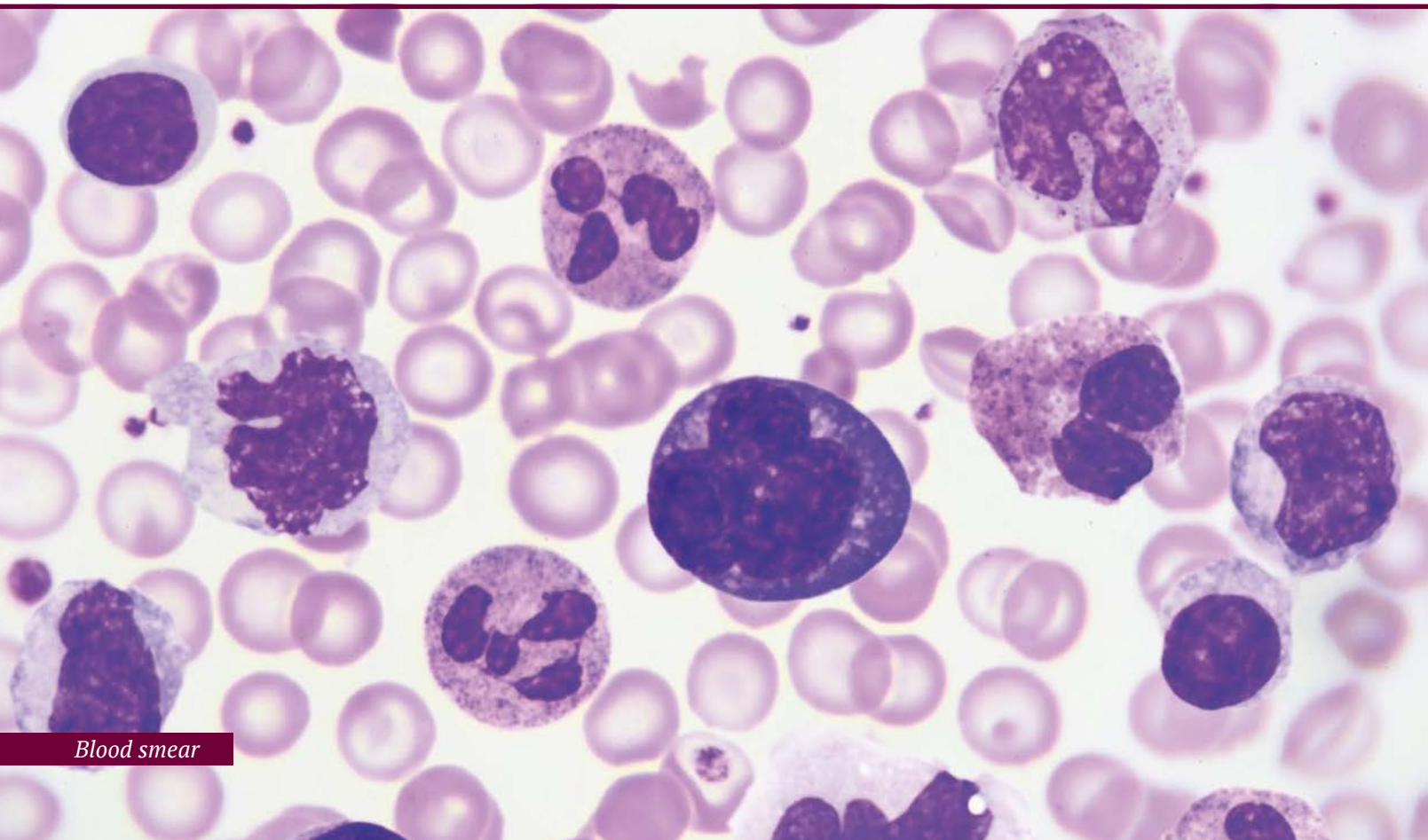
Introduction to Blood

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.

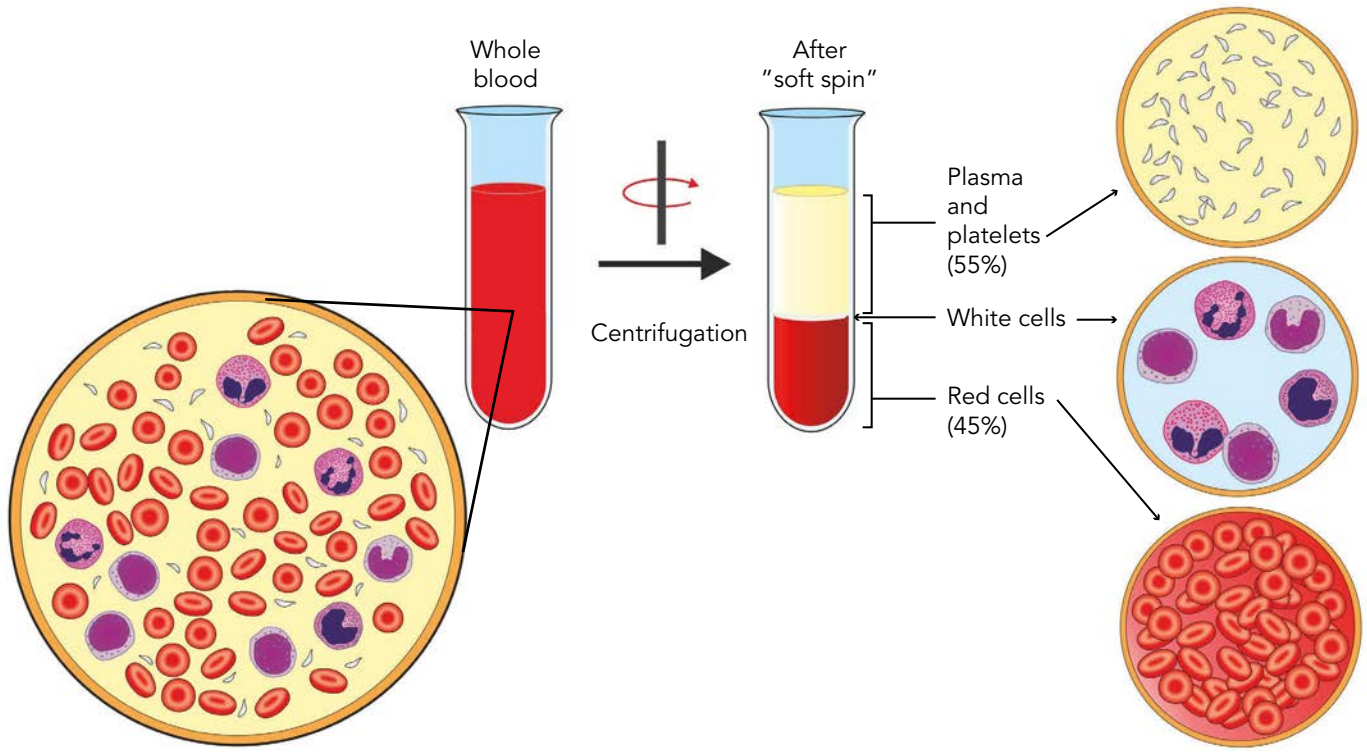
Blood's Components

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.

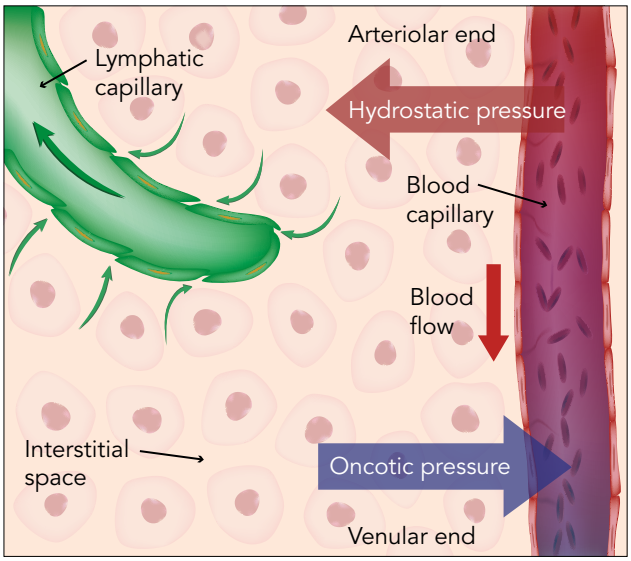
Plasma

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

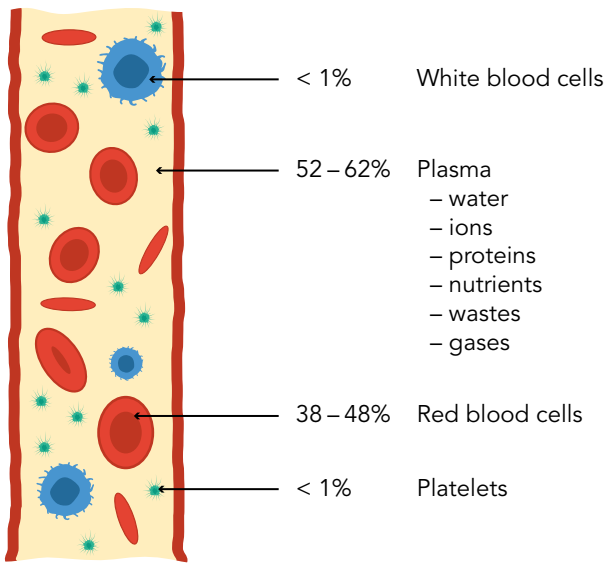
Oncotic Pressure



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.

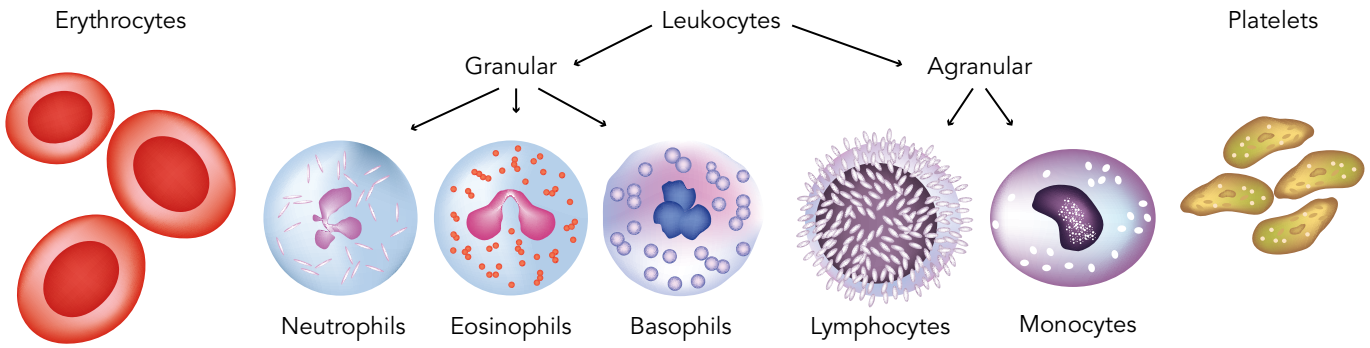
Of the formed elements, only leukocytes are complete cells. Leukocytes have nuclei and intracellular organelles. Erythrocytes lack these. Platelets are cell fragments.

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.

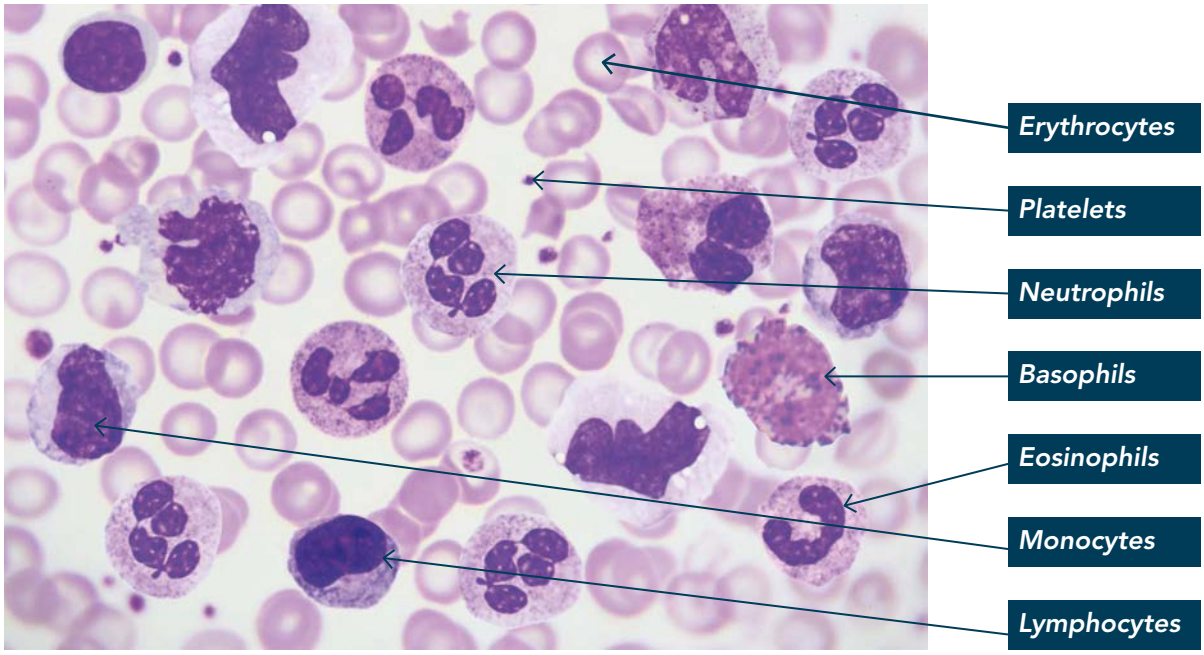
Let's first learn about red blood cells and then platelets and white blood cell types.

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.

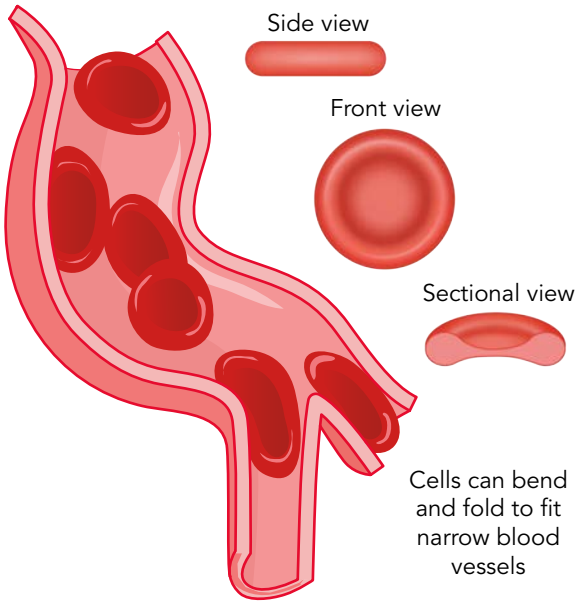
If blood becomes *too* hemoglobin rich — as seen in some people who immigrate to Tibet — the heart can be overworked due to elevated blood viscosity (thickness). However, the blood of Tibet's natives does not reach the excessive hemoglobin levels found in non-natives, naturally stopping the synthesizing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

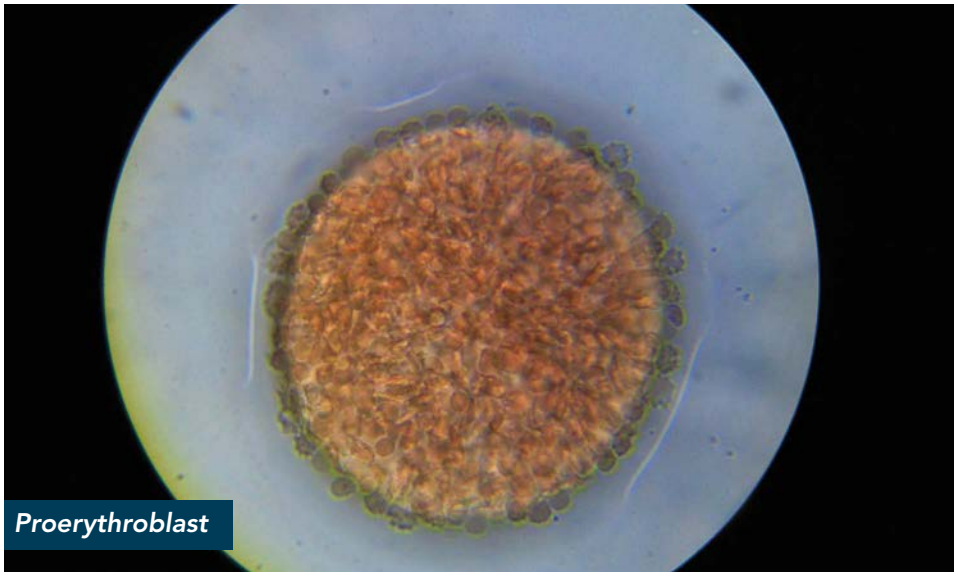
TAKING A CLOSER LOOK

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

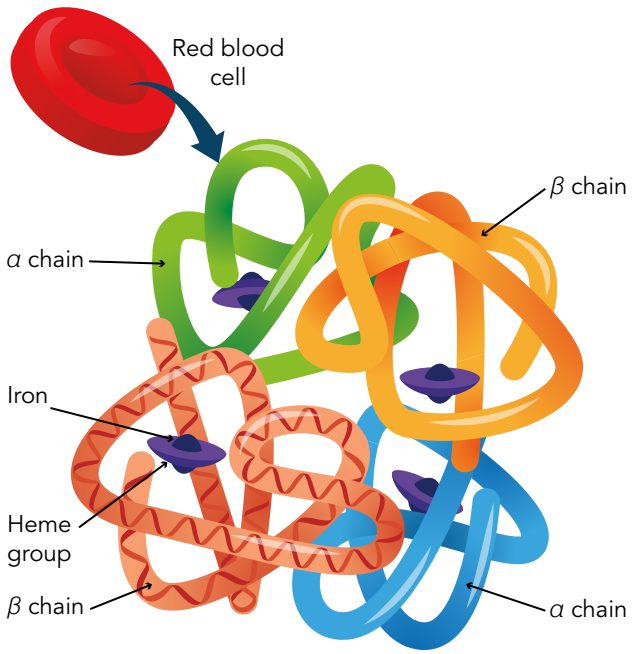
This daily resupply comes from bone marrow. Bone marrow is a spongy tissue inside many bones. A type of bone marrow cell called a *proerythroblast*, when stimulated to divide, produces cells that mature into new erythrocytes. These are released into the circulation. The process of producing new red blood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



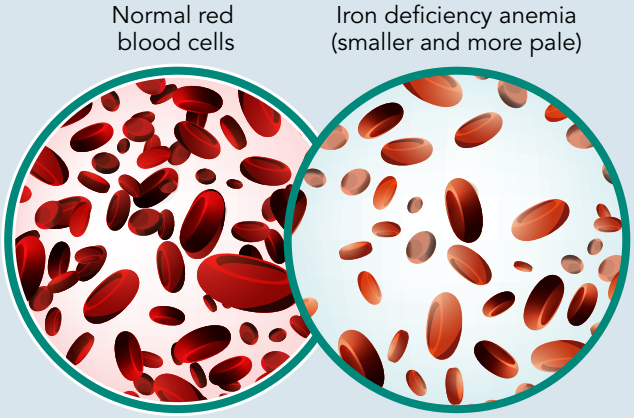
Highly trained athletes sometimes use this phenomena. They train at high elevations where air is thinner and atmospheric oxygen levels are lower. Training at high elevations can stimulate their bodies to make more erythropoietin, resulting in increased RBC production. They hope to then have greater than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

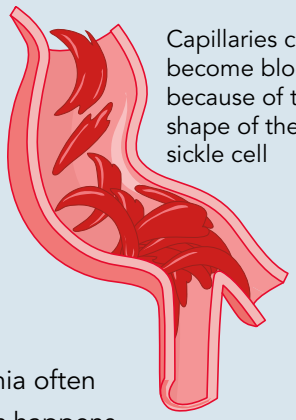
Hemoglobin consists of four polypeptide chains — two alpha chains (α) and two beta chains (β). Each chain contains a heme group. A mutation in a gene directing manufacture of a hemoglobin chain results in abnormal hemoglobin. Sickle cell anemia results from such a mutation. This mutation substitutes 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.

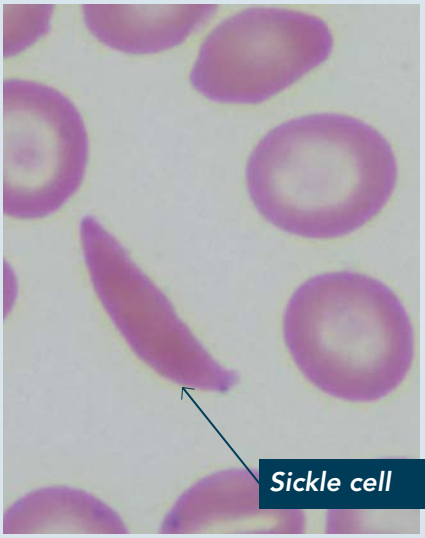


Capillaries can become blocked because of the shape of the sickle cell

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.

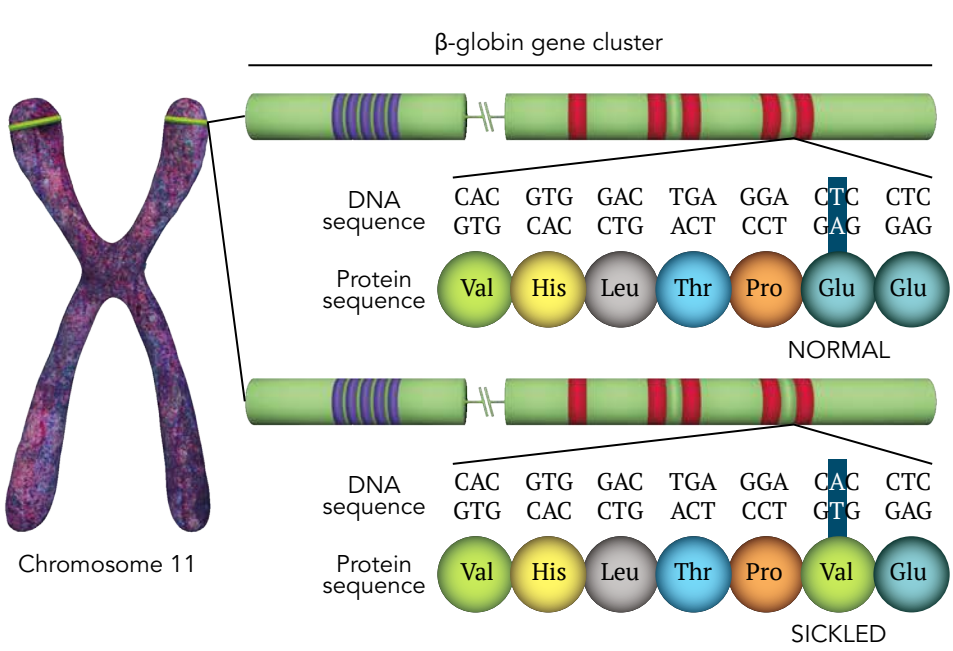
Sickle cell crisis is characterized by abdominal pain, pain in the arms and legs, and shortness of breath. Because sickled cells are fragile and rupture easily, patients with sickle cell disease also have chronic anemia, further reducing their blood's ability to transport oxygen. Many sickle cell patients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

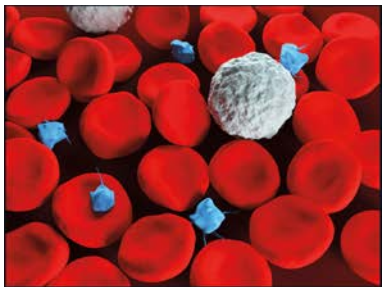
Sickle cell anemia damages capillaries and the organs that depend on them. Patients are therefore at high risk for stroke, infection, necrosis (tissue death) in major joints, hypertension, kidney failure, and right heart failure. Treatment includes pain management, antibiotics for infection control,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



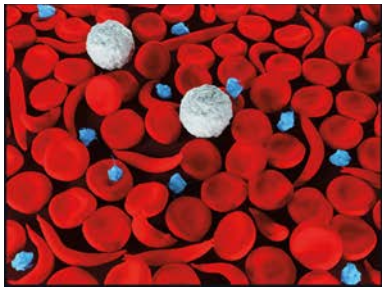
TAKING A CLOSER LOOK

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.

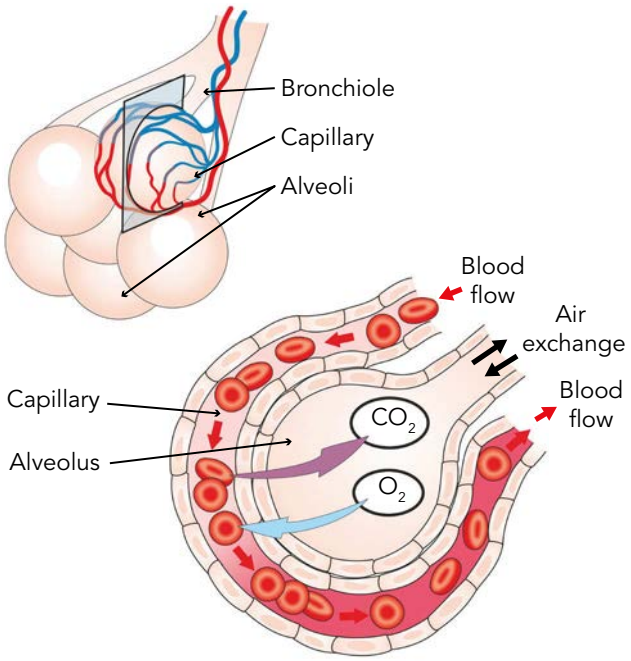
Iron gives hemoglobin its ability to carry oxygen. Each iron atom can bind one oxygen molecule. Therefore, each hemoglobin molecule can bind four oxygen molecules. With around 270 million hemoglobin molecules in each red blood cell, one red blood cell could carry about a billion oxygen molecules!

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

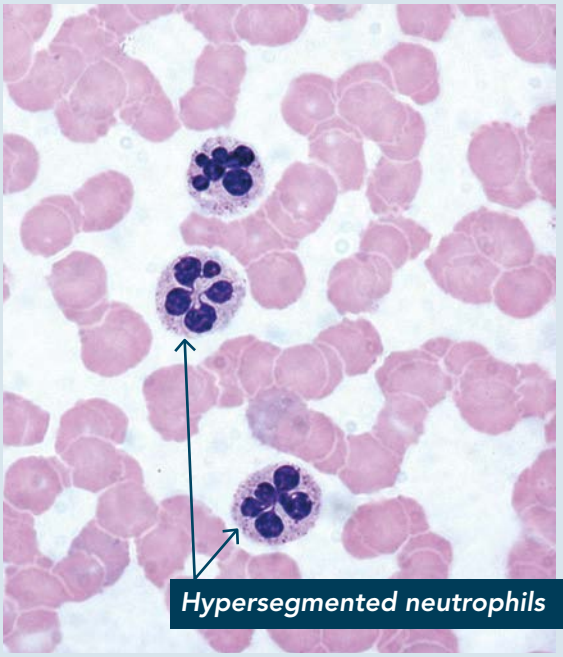


Megaloblastic Anemia

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.

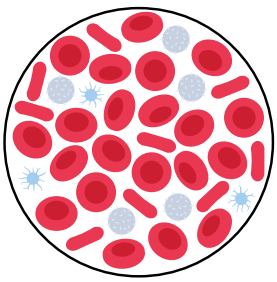
Polycythemia

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.

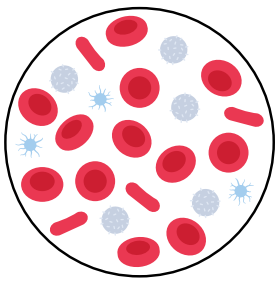
There are other conditions which cause *polycythemia* — an increase in the percentage of blood that is made up of RBCs. (*Poly* means "many," *cyt* means "cell," and *hemo* means "blood" — hence "too many cells in the blood.") These include mutations in erythropoietin receptors, cancers that make extra 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.

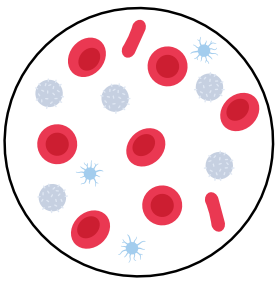
As we said when discussing the situation in Tibet, too much of a good thing can be a problem. Beyond a certain point, thicker blood doesn't flow as easily through capillaries, interfering with the blood's ability to oxygenate tissues. Thicker blood is also harder for the heart to pump, leading to heart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



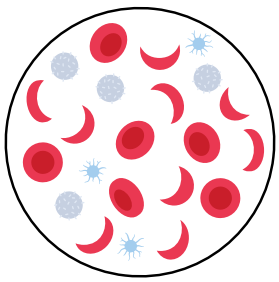
Polycythemia



Normal blood



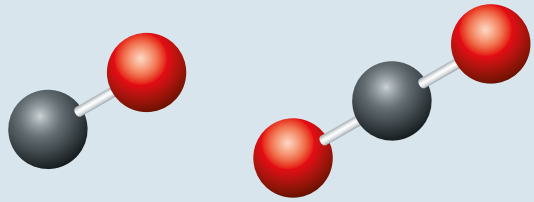
Anemia



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.

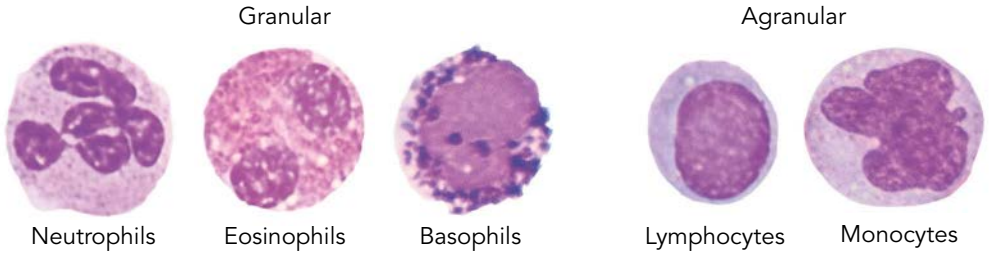
Their ultimate purpose is to protect the body from invaders. Whether these invaders are bacteria, viruses, or parasites, leukocytes are constantly on guard.

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



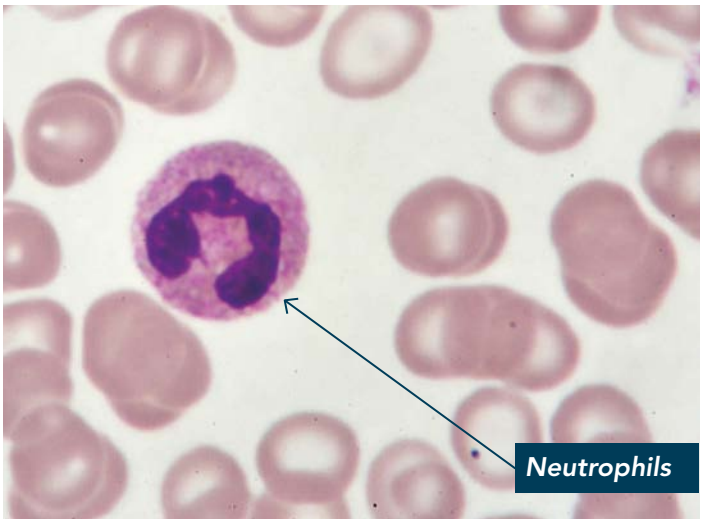
Neutrophils

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.

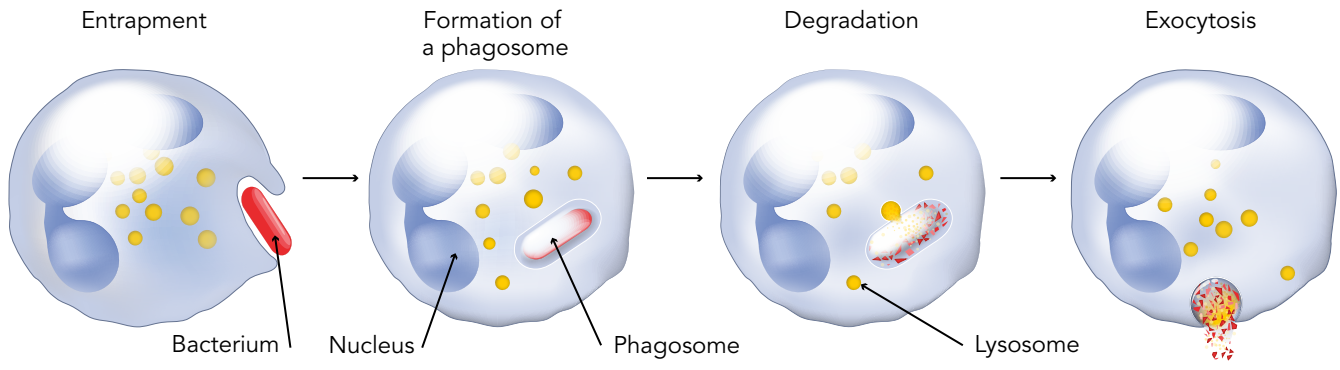
During an infection, the inflammatory response to tissue damage releases chemical factors that attract neutrophils. This chemical attraction phenomenon is called *chemotaxis*.



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



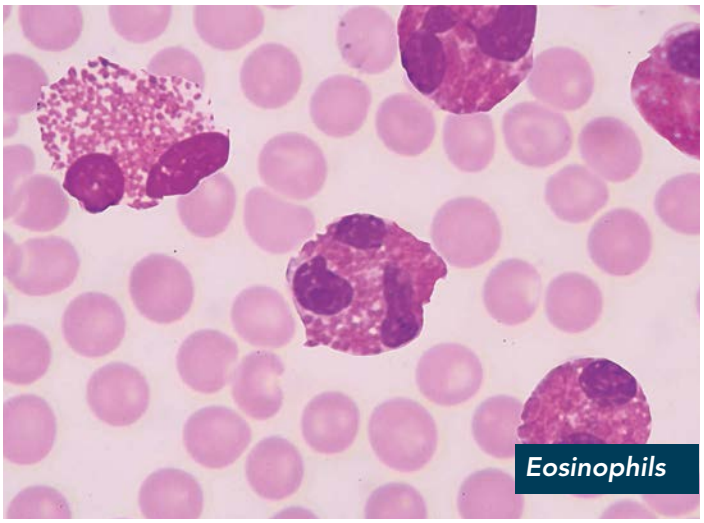
Eosinophils

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

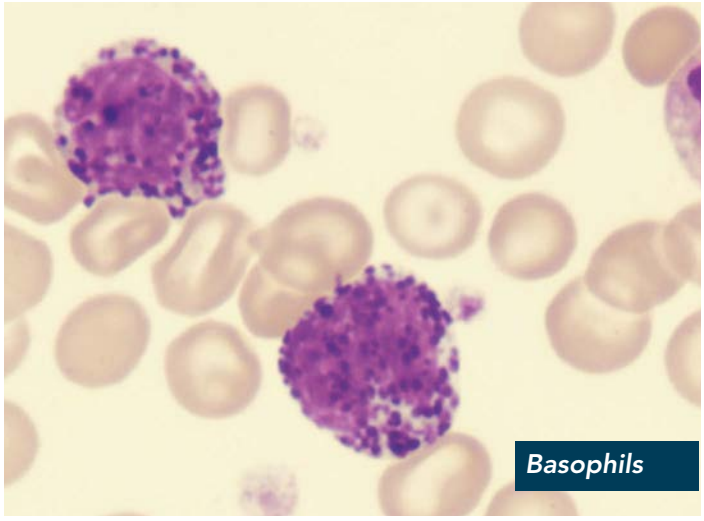
Basophils are the least common leukocytes, less than 1% of the WBC population.

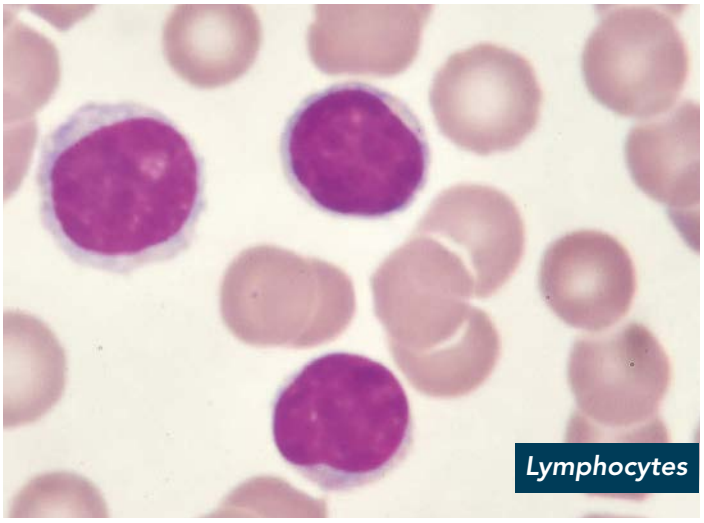
Basophils are the largest of the granular leukocytes. Like eosinophils, the basophil nucleus usually has two lobes. The cytoplasm contains large granules that stain purple, giving basophils their characteristic appearance.

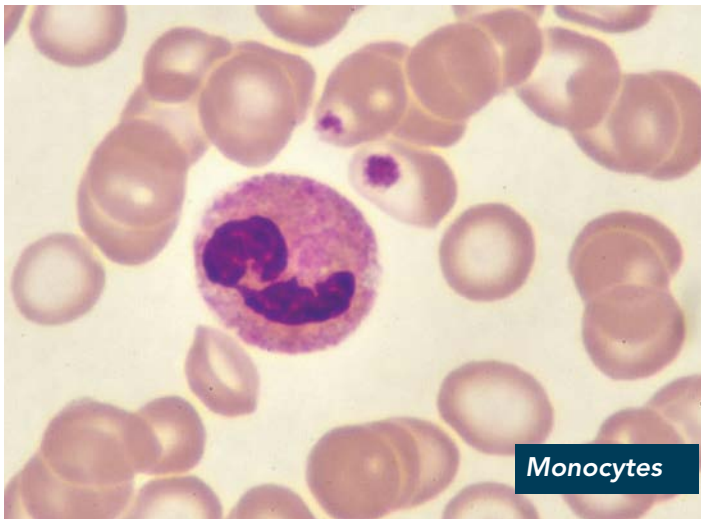
Basophils granules contain histamine, which promotes vasodilation. Histamine increases blood flow to tissues and attracts other leukocytes to the site of inflammation.

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

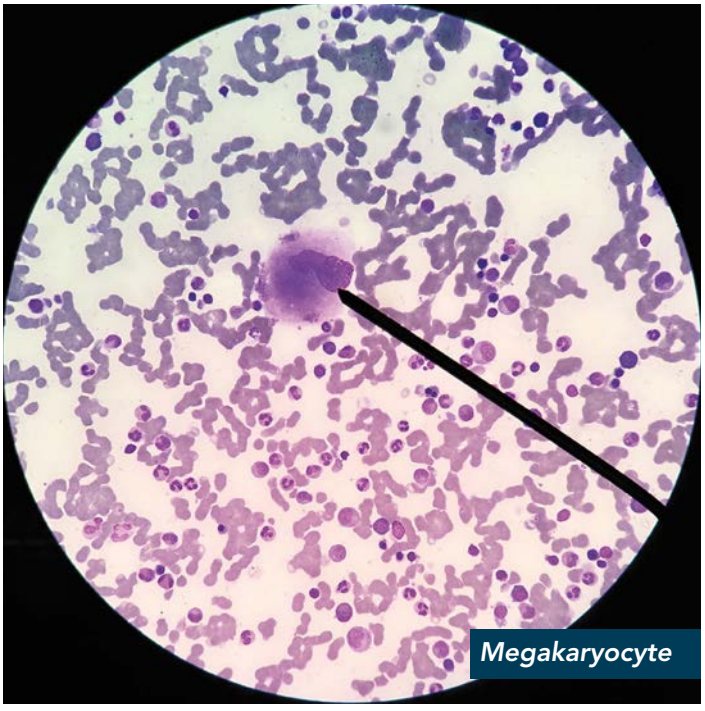

Lymphocytes

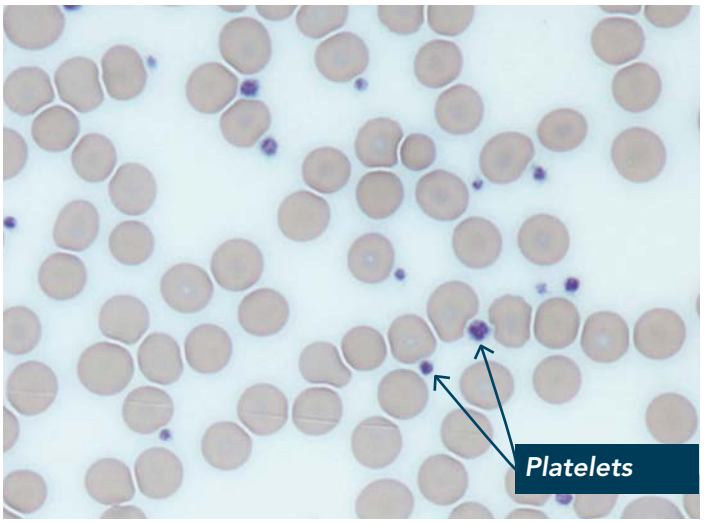

Monocytes

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.

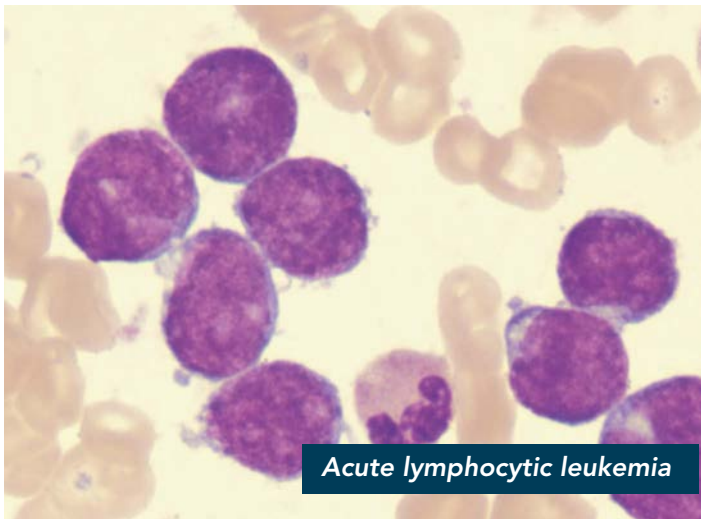
Platelets

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!

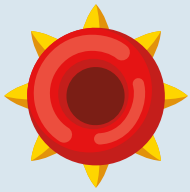
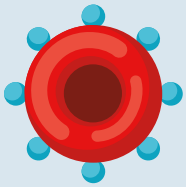
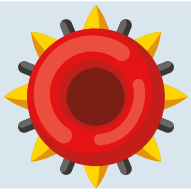
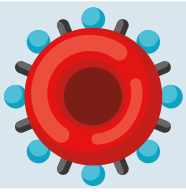
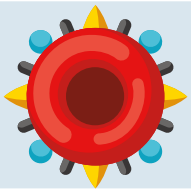
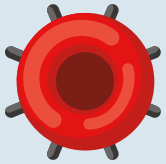
Some people don't have either Type A or Type B antigens on their erythrocytes. These people have blood Type O. (That's the letter O, not zero.)

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?

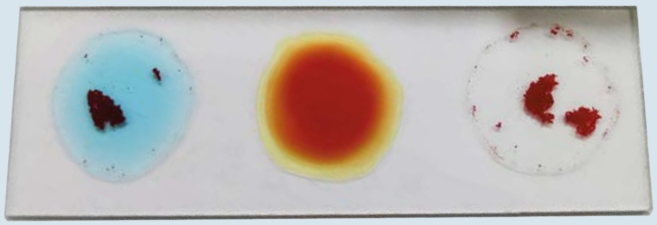
Let's use this blood typing thing to solve a crime.

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.

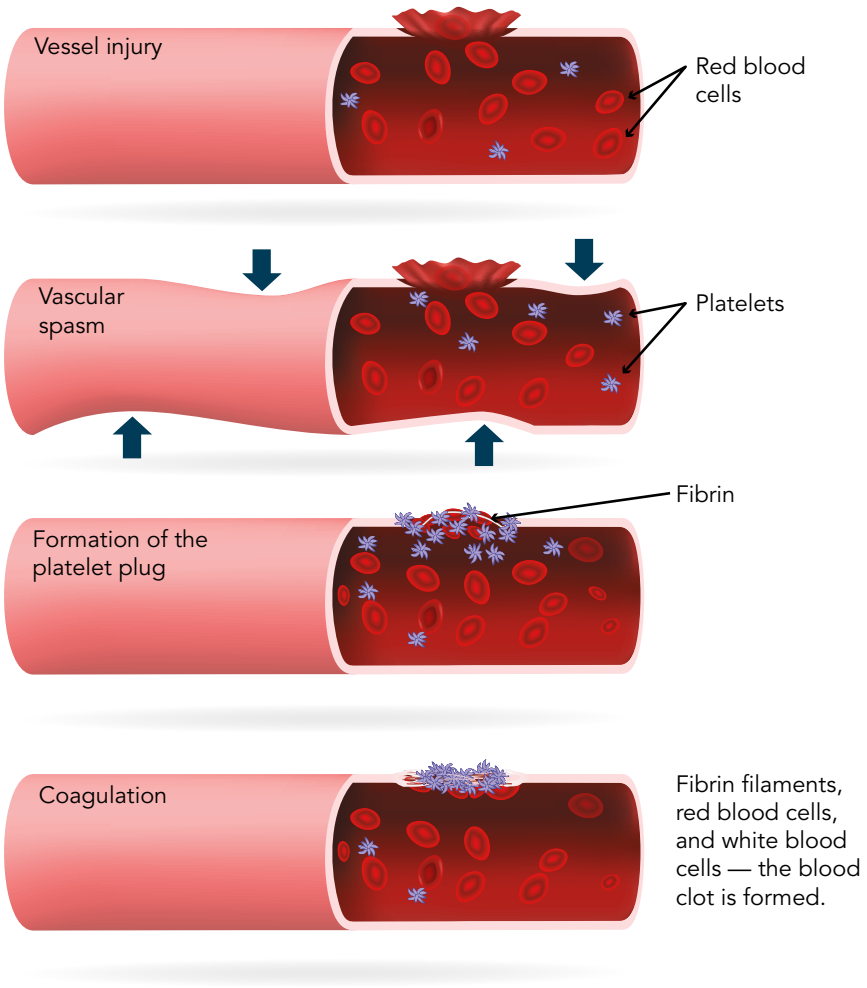
Now the blood is tested for Rh factor. The sample is mixed with anti-Rh serum. There is a reaction, so the blood is Rh positive.

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.

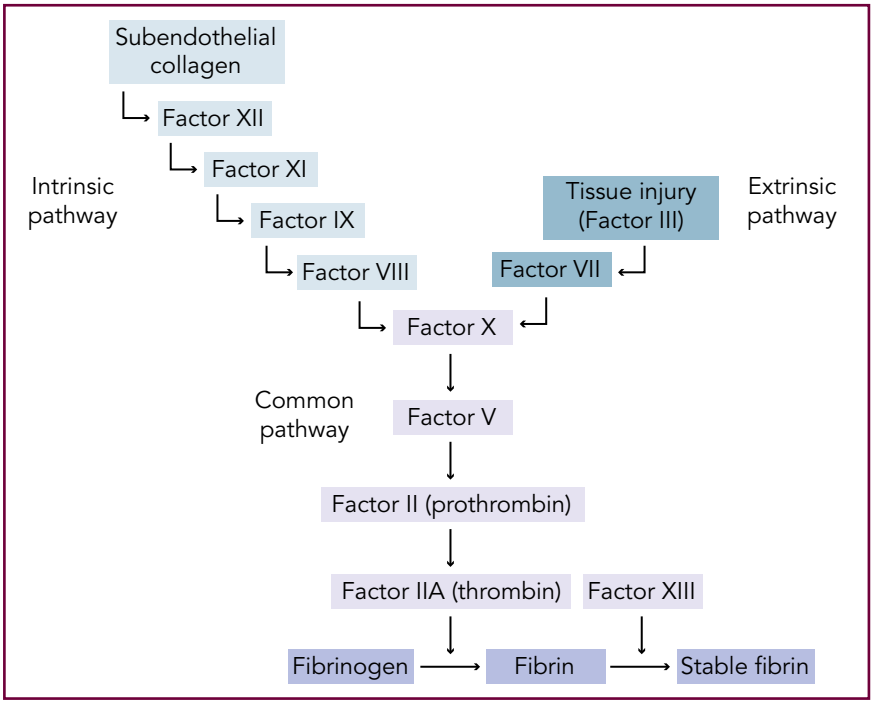
You see, even though platelet aggregation has formed a platelet plug, the plug is not enough to completely stop blood from leaking out of the blood vessel. A tighter seal must form. A real blood clot must be made. This is accomplished with the aid of plasma proteins known as *clotting factors*.

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.