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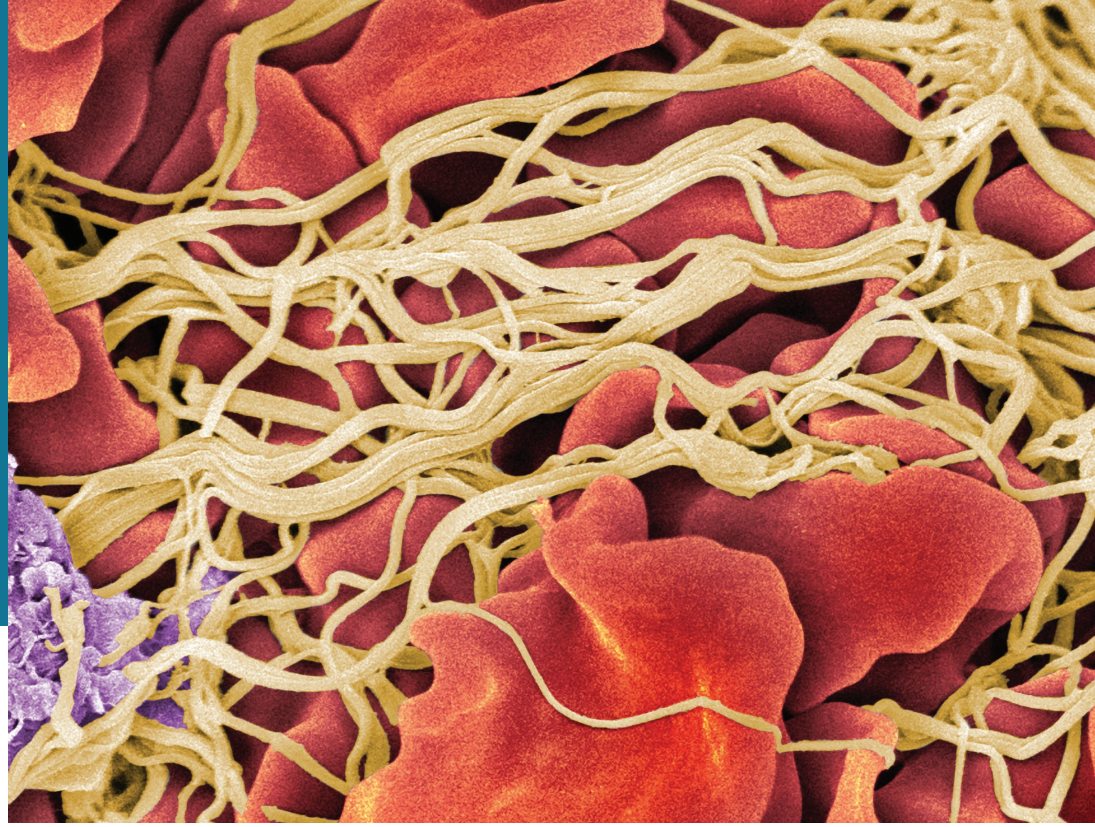


Photo: Colorized scanning electron micrograph of a blood clot. The red discs are red blood cells, the purple particles are platelets, and the yellow strands are fibrin. ©Steve Gschmeissner/Science Source

Learn to Predict

Frankie didn't have time to be sick. So at first she attributed her extreme tiredness to the stress of being a 40-year-old single mother of two teenagers while working full-time and attending school part-time. However, when she started experiencing significant abdominal pain, she consulted her doctor, who ordered several tests. The results indicated a low red blood cell (RBC) count with microcytic RBCs, a high reticulocyte count, low hemoglobin and hematocrit levels, and evidence of hemoglobin in her feces. **After reading this chapter and recalling what you learned about the endocrine system in chapters 17 and 18, explain Frankie's symptoms and test results.**

Cardiovascular System

BLOOD

Historically, many cultures around the world, both ancient and modern, have believed in the magical qualities of blood. Some societies consider blood the "essence of life" because the uncontrolled loss of it can result in death. Blood has also been thought to define character and emotions. For example, people from prominent families are sometimes described as "bluebloods," whereas criminals are said to have "bad blood." Common expressions allege that anger causes the blood to "boil" and that fear results in blood "curdling." The scientific study of blood reveals characteristics as fascinating as any of these fantasies. Blood performs many functions essential to life and can often reveal much about our health.

Blood is one component of the **cardiovascular system,** which also consists of the heart and the blood vessels. The cardiovascular system connects the various tissues of the body. The heart pumps blood through a network of blood vessels extending throughout the body. This network of blood vessels is often referred to as the *circulatory system*. As it flows through the circulatory system, the blood delivers nutrients and picks up waste products at the body tissues. This chapter focuses on the blood, whereas chapters 20 and 21 discuss the heart and the blood vessels, respectively.

19.1 Functions of Blood

LEARNING OUTCOME

After reading this section, you should be able to

A. **List and explain the ways blood helps maintain homeostasis in the body.**

The blood acts as a transport fluid carrying many substances to various parts of the body. By acting this way, blood is vital for maintaining homeostasis throughout the body. Blood helps maintain homeostasis in several ways:

1. *Transport of gases, nutrients, and waste products*. Oxygen enters the blood in the lungs and is carried to the cells. Carbon dioxide, produced by the cells, is carried in the blood to the lungs, where it is exhaled. The blood transports ingested nutrients, ions, and water from the digestive tract to the cells, and the blood transports the cells' waste products to the kidneys for elimination.
2. *Transport of processed molecules*. Many substances are produced in one part of the body and transported in the blood to another part, where they are modified. For example, the precursor to vitamin D is produced in the skin (see chapter 5) and transported by the blood to the liver and then to the kidneys for processing into active vitamin D. The blood then transports active vitamin D to the small intestine, where it promotes the uptake of calcium. Another example involves lactate produced by skeletal muscles during anaerobic respiration (see chapter 9). The blood carries lactate to the liver, where it is converted into glucose.
3. *Transport of regulatory molecules*. Regulatory molecules include chemical messengers, such as hormones, that regulate the activities of many physiological processes. Enzymes that are important for normal metabolism are also considered regulatory molecules. The blood carries the hormones and many of the enzymes that regulate body processes from one part of the body to another.
4. *Regulation of pH and osmosis*. Buffers (see chapter 2), which help keep the blood's pH within its normal range of 7.35–7.45, are in the blood. The osmotic composition of blood is also critical for maintaining normal fluid and ion balance throughout the body (see chapter 27).
5. *Maintenance of body temperature*. Body temperature regulation involves several mechanisms, including the movement of warm blood from the interior of the body to its surface, where heat is released.
6. *Protection against foreign substances*. Certain cells and chemicals in the blood make up an important part of the immune system, protecting against foreign substances, such as microorganisms and toxins.
7. *Clot formation*. Blood clotting protects against excessive blood loss when blood vessels are damaged. The blood clot that forms in damaged tissue is also the first step in tissue repair and the restoration of normal function (see chapter 4).

ASSESS YOUR PROGRESS

Answers to these questions are found in the section you have just completed. Re-read the section if you need help in answering these questions.

1. *List the ways that blood helps maintain homeostasis in the body.*
2. *What substances are transported by the blood?*
3. *What is the normal pH range of the blood?*
4. *How does the blood provide protection?*

19.2 Composition of Blood

LEARNING OUTCOMES

After reading this section, you should be able to

A. **List the components of blood.**

B. **Relate the average total blood volume for females and for males.**

Blood is a type of connective tissue consisting of a liquid matrix containing cells and cell fragments. **Plasma** is the liquid matrix, and the **formed elements** are the cells and cell fragments. The plasma makes up 55% of the total blood volume, and the formed elements make up 45% (figure 19.1). The total blood volume in the average adult female is about 4–5 L. The total blood volume in the average adult male is 5–6 L. Blood makes up about 8% of the total weight of the body.

ASSESS YOUR PROGRESS

5. *What are the two major components of blood? What portion of the total blood volume does each compose?*
6. *What is the average total blood volume for females and for males?*

19.3 Plasma

LEARNING OUTCOMES

After reading this section, you should be able to

A. **Name the components of blood plasma.**

B. **List the three major plasma proteins and describe their functions.**

Plasma (plaz′mă) is the liquid matrix of blood. It is a pale yellow fluid that consists of about 91% water and 9% other substances, such as proteins, ions, nutrients, gases, waste products, and regulatory substances (table 19.1). Plasma is a **colloid** (kol′oyd), which is a liquid containing suspended substances that do not settle out of solution. Most of the suspended substances are plasma proteins, which make up about 7% of the volume of plasma (figure 19.1). Based on molecular size and charge, the plasma proteins can be classified into three groups: albumin, globulins, and fibrinogen.

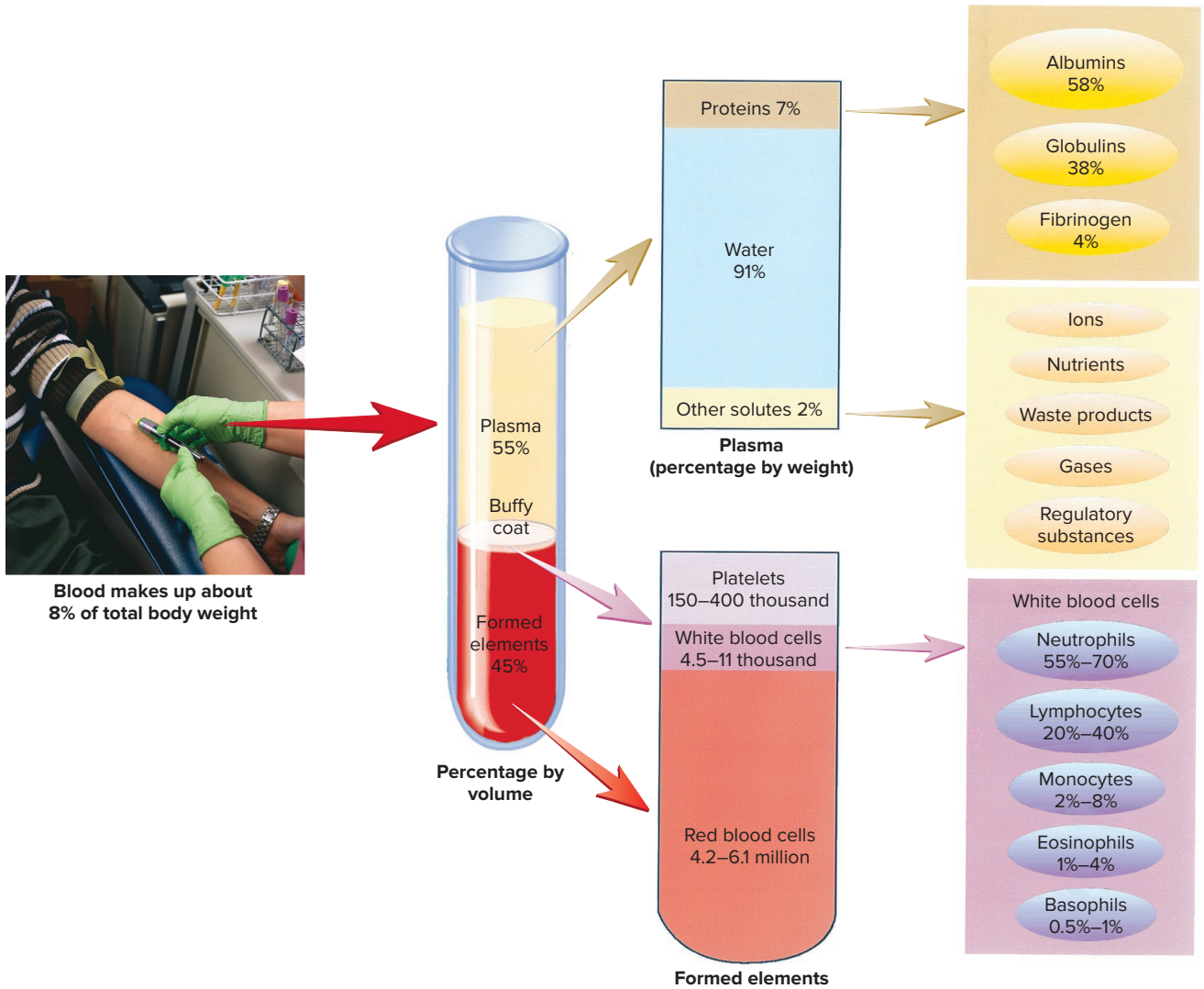


FIGURE 19.1 Composition of Blood
Approximate values for the components of blood in a normal adult. ©liquidlibrary/Getty Images AP|R

Almost all of the plasma proteins are produced by the liver or blood cells, a notable exception being protein hormones.

1. **Albumin** (al-bū′min) makes up 58% of the plasma proteins and is important in regulating the movement of water between the tissues and the blood. Albumin does not pass easily from the blood into tissues. As such, it plays an important role in maintaining blood colloid osmotic pressure (see chapters 21 and 26). Recall from chapter 3 that osmosis, the diffusion of water, occurs when solutes cannot easily move across a selectively permeable barrier and that osmotic pressure is the tendency for water to move across that barrier. Albumins also bind and transport other molecules in the blood, such as fatty acids, bilirubin, and thyroid hormones.
2. **Globulins** (glob′ū-linz) account for 38% of the plasma proteins. The globulins are subdivided into α, β, and γ globulins. Globulins function in transporting many substances in the blood. **Antibodies** are globulins that protect against microorganisms (table 19.1; see chapter 22).
3. **Fibrinogen** (fī-brin′ō-jen) constitutes 4% of the plasma proteins and is responsible for the formation of blood clots (see section 19.5). **Serum** (ser′um; whey) is plasma without the clotting factors.

Plasma composition remains relatively constant, even though material is constantly moving between the blood and the cells. Various homeostatic control mechanisms function to maintain plasma composition. The levels of water, proteins, and other substances in the blood, such as ions, nutrients, waste products, gases, and regulatory substances, are maintained within narrow limits. Normally, the amount of water taken in through the digestive tract closely matches the amount of water lost through the kidneys, lungs, digestive tract, and skin. Therefore, plasma volume also remains relatively constant. Suspended or dissolved substances in the blood come from the liver, kidneys, intestines, endocrine glands, and immune tissues, such as the lymph nodes and spleen. Oxygen enters the blood in the lungs and leaves the blood as it

TABLE 19.1 Composition of Plasma

Components	Function
Water	Acts as a solvent and suspending medium for blood components
Plasma Proteins	
Albumin	Partly responsible for blood viscosity and osmotic pressure; acts as a buffer; transports fatty acids, free bilirubin, and thyroid hormones
Globulins	
α	Protect tissues from damage by inflammation (alpha-1 antitrypsin); transport thyroid hormones (thyroid-binding globulin), cortisol (transcortin), and testosterone and estrogen (sex hormone–binding globulin); transport lipids (e.g., cholesterol in high-density lipoproteins); convert ferrous iron (Fe^{2+}) to ferric iron (Fe^{3+}), which promotes iron transport by transferrin (ceruloplasmin); transport hemoglobin released from damaged red blood cells (haptoglobin)
β	Transport iron (transferrin); transport lipids (beta-lipoproteins), especially cholesterol in low-density lipoproteins; involved with immunity (complement); prevent blood loss (coagulation proteins)
γ	Involved in immunity (most antibodies are γ globulins, but some are β or α globulins)
Fibrinogen	Functions in blood clotting
Ions	
Sodium, potassium, calcium, magnesium, chloride, iron, phosphate, hydrogen, hydroxide, bicarbonate	Involved in osmosis, membrane potentials, and acid-base balance
Nutrients	
Glucose, amino acids, triglycerides, cholesterol	Source of energy and basic "building blocks" of more complex molecules
Vitamins	Promote enzyme activity
Waste Products	
Urea, uric acid, creatinine, ammonia salts	Breakdown products of protein metabolism; excreted by the kidneys
Bilirubin	Breakdown product of red blood cells; excreted as part of the bile from the liver into the small intestine
Lactate	End product of anaerobic respiration; converted to glucose by the liver
Gases	
Oxygen	Necessary for aerobic respiration; terminal electron acceptor in electron-transport chain
Carbon dioxide	Waste product of aerobic respiration; as bicarbonate, helps buffer blood
Nitrogen	Inert
Regulatory Substances	Enzymes catalyze chemical reactions; hormones stimulate or inhibit many body functions

flows through tissues. Carbon dioxide enters the blood from the tissues and leaves the blood as it flows through the lungs.

ASSESS YOUR PROGRESS

7. *What is plasma, and what does it consist of? Why is plasma a colloid?*
8. *What are the three major plasma proteins, and what roles do they play in the blood?*
9. *Explain how plasma volume remains relatively constant.*

19.4 Formed Elements

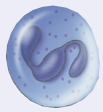
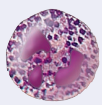
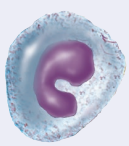
LEARNING OUTCOMES

After reading this section, you should be able to

A. **List the three kinds of formed elements using both their common and technical names.**
B. **Describe the origin and production of the formed elements.**
C. **Describe the structure and function of hemoglobin and relate which gases associate with hemoglobin and how.**
D. **Compare fetal and adult hemoglobin as to structure and affinity for oxygen.**
E. **Discuss the life history of red blood cells.**
F. **Compare the structures and functions of the five types of white blood cells.**
G. **Describe the origin and structure of platelets.**
H. **Relate the functions of platelets in preventing blood loss.**

The **formed elements** of blood consist of cells and cell fragments. The cells include red blood cells and white blood cells. Cell fragments are more commonly called **platelets.** Recall that the formed elements make up 45% of the total blood volume.

TABLE 19.2 Formed Elements of the Blood

Cell Type	Illustration	Description	Function	Abundance (cells/μL)*
Red Blood Cell		Biconcave disc; no nucleus; contains hemoglobin, which colors the cell red; 7.5 μm in diameter	Transports O_2 and CO_2	4.2–5.4 million (females) 4.7–6.1 million (males)
White Blood Cells		Spherical cells with a nucleus	Five types of white blood cells, each with specific functions	4500–11,000
Granulocytes				
Neutrophil		Nucleus with two to five lobes connected by thin filaments; cytoplasmic granules stain a light pink or reddish-purple; 10–12 μm in diameter	Phagocytizes microorganisms and other substances	55–70% of WBC
Eosinophil		Nucleus often bilobed; cytoplasmic granules stain orange-red or bright red; 11–14 μm in diameter	Attacks certain worm parasites; releases chemicals that modulate inflammation; negatively impacts airways during asthma attacks	1–4% of WBC
Basophil		Nucleus with two indistinct lobes; cytoplasmic granules stain blue-purple; 10–12 μm in diameter	Releases histamine, which promotes inflammation, and heparin, which prevents clot formation	0.5–1% of WBC
Agranulocytes				
Lymphocyte		Round nucleus; cytoplasm forms a thin ring around the nucleus; 6–14 μm in diameter	Produces antibodies and other chemicals responsible for destroying microorganisms; contributes to allergic reactions, graft rejection, tumor control, and regulation of the immune system	20–40% of WBC
Monocyte		Nucleus round, kidney-shaped, or horseshoe-shaped; contains more cytoplasm than lymphocyte does; 12–20 μm in diameter	Phagocytic cell in the blood; leaves the blood and becomes a macrophage, which phagocytizes bacteria, dead cells, cell fragments, and other debris within tissues	2–8% of WBC
Platelet		Cell fragment surrounded by plasma membrane and containing granules; 2–4 μm in diameter	Forms platelet plugs; releases chemicals necessary for blood clotting	150,000–400,000

*White blood cell counts are listed as percentage of total white blood cells.

Red blood cells, or *erythrocytes* (ĕ-rith′rō-sītz), are the most abundant blood cell type, making up about 95% of the volume of the formed elements. The remaining 5% consists of white blood cells, or *leukocytes* (loo′kō-sītz), and platelets, or *thrombocytes* (throm′bō-sītz). Table 19.2 illustrates the formed elements of the blood. In healthy adults, white blood cells are the only formed elements possessing nuclei; red blood cells and platelets lack nuclei.

Predict 1

Using table 19.1, develop a diagram that illustrates the order of the formed elements by size, from smallest to largest. *Note:* Ranges are provided for several of the formed elements.

Production of Formed Elements

The process of blood cell production is called **hematopoiesis** (hē′mă-tō-poy-ē′sis, hem′ă-to-poy-ē′sis), or *hemopoiesis* (hē′mō-poy-ē′sis). In the embryo and fetus, hematopoiesis occurs in many different tissues such as the yolk sac of the embryo, liver, thymus, spleen, lymph nodes, and red bone marrow. After birth, hematopoiesis is confined primarily to red bone marrow, though some white blood cells, specifically lymphocytes, complete their development in lymphatic tissue (see chapter 22). In young children, nearly all the bone marrow is red bone marrow. In adults, however, red bone marrow is confined to the ribs, sternum, vertebrae, pelvis, proximal femur, and proximal humerus. Yellow bone marrow replaces red bone marrow in other body locations (see chapter 6).

All the formed elements of the blood are derived from a single population of stem cells called **hemocytoblasts,** located in the red bone marrow. Hemocytoblasts are precursor cells capable of dividing to produce daughter cells that can differentiate into various types of blood cells (figure 19.2). When a hemocytoblast divides, one daughter cell remains a hemocytoblast while the other daughter cell differentiates to form one of two types of intermediate stem cells: a **myeloid stem cell** or a **lymphoid stem cell.** Red blood cells, platelets, and most of the white blood cells develop from myeloid stem cells. Myeloid stem cells give rise to several

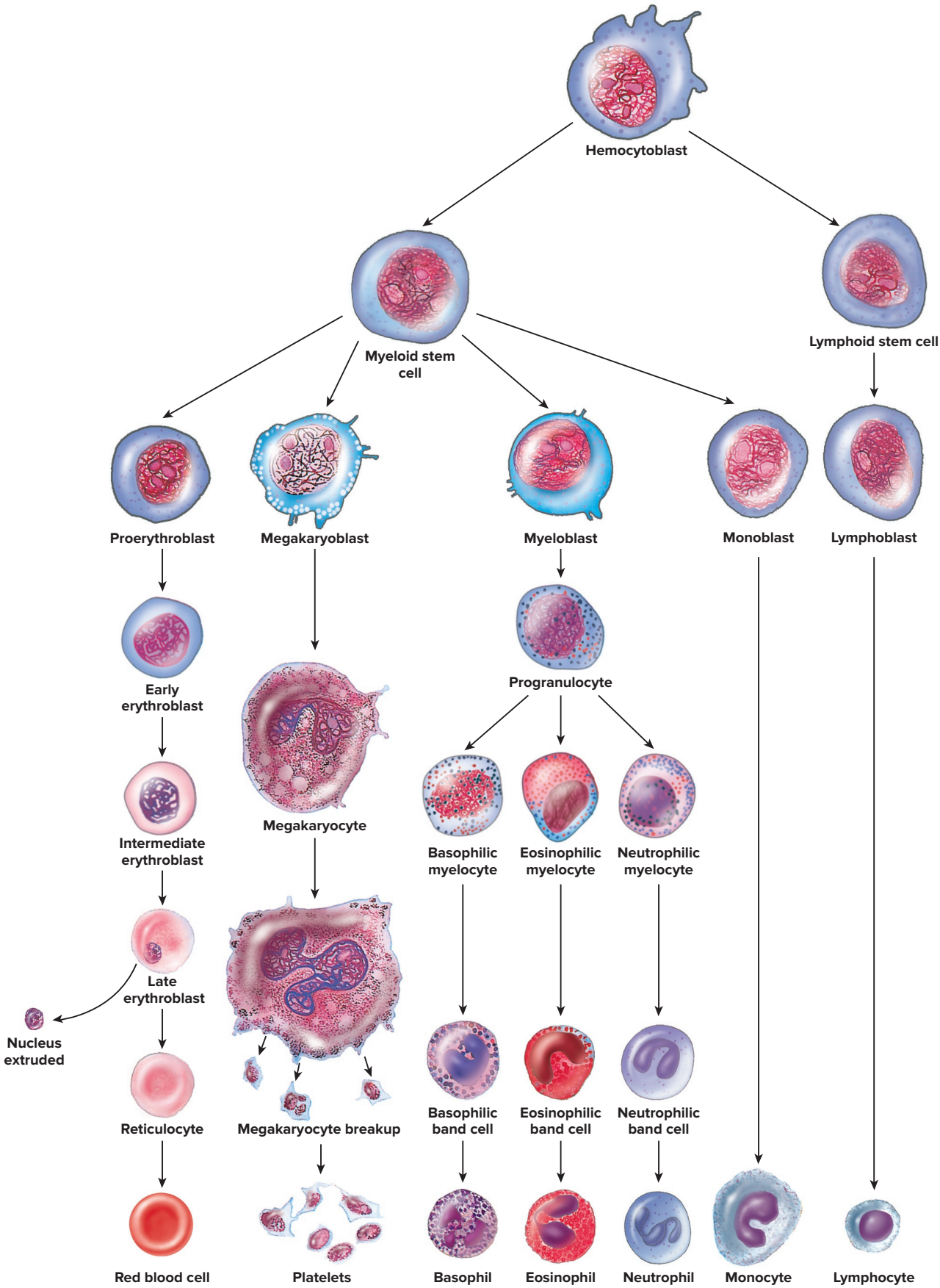


FIGURE 19.2 Hematopoiesis

Stem cells give rise to the cell lines that produce the formed elements. The production of red blood cells (far left column) is called erythropoiesis. AP|R

intermediate cell types. These intermediates include **proerythroblasts** (prō-ĕ-rith′rō-blastz), which produce red blood cells; **myeloblasts** (mī′ĕ-lō-blastz), which produce basophils, eosinophils, and neutrophils; **monoblasts** (mon′ō-blastz), which produce monocytes; and **megakaryoblasts** (meg-ă-kar′ē-ō-blastz), which produce platelets. Lymphoid stem cells give rise to lymphocytes.

Chemical signals regulate the development of the different types of formed elements. These chemical signals include **colony-stimulating factors (CSFs)** and hormones transported to the bone marrow through the blood or substances released by bone marrow cells. **Erythropoietin (EPO)** is an example of a hormone, secreted by endocrine cells of the kidneys, that stimulates myeloid stem cells to develop into red blood cells.

ASSESS YOUR PROGRESS

10. *Name the three general types of formed elements in the blood, using both their common and technical names.*
11. *What is hematopoiesis? Where does the process occur before birth? After birth? What type of stem cell are all formed elements derived from? Distinguish between myeloid stem cells and lymphoid stem cells.*
12. *What types of formed elements develop from each of the following cells: proerythroblasts, myeloblasts, lymphoblasts, monoblasts, and megakaryocytes?*

Red Blood Cells

Red blood cells (RBCs), or *erythrocytes,* are about 700 times more numerous than white blood cells and 17 times more numerous than platelets in the blood (figure 19.3*a*). Males have 4.7–6.1 million red blood cells per microliter (μL; 1 mm^3, or 10^{-6} L), whereas females have about 4.2–5.4 million/μL.

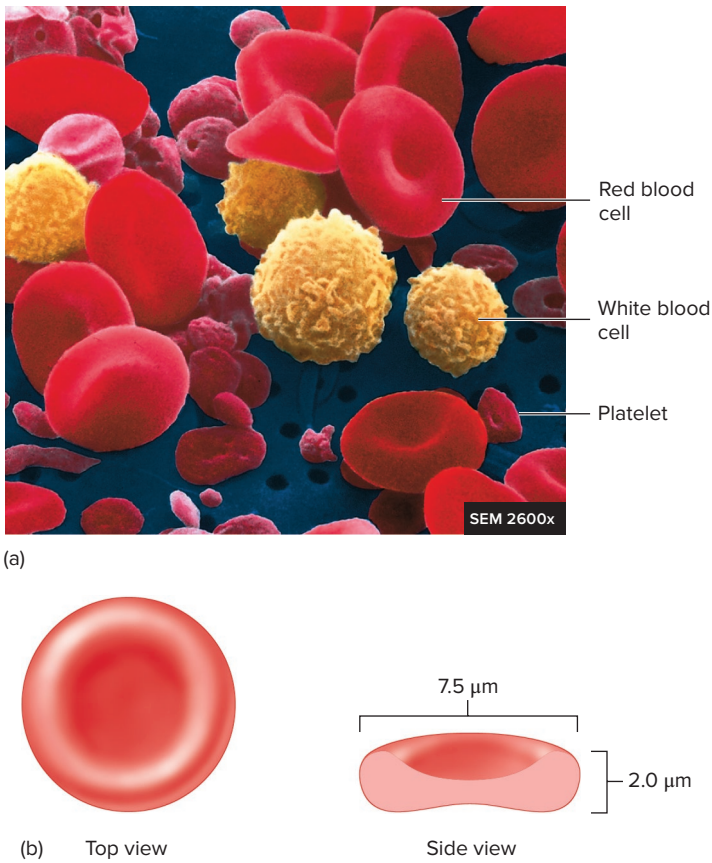
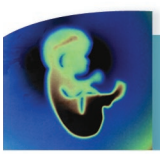


FIGURE 19.3 Formed Elements
(*a*) Color-enhanced scanning electron micrograph of formed elements: red blood cells (*red doughnut shapes*), white blood cells (*yellow*), and platelets (*red, irregular shapes*). (*b*) Shape and dimensions of a red blood cell.
(a) ©National Cancer Institute/Science Photo Library/Science Source APR

Structure

Normal red blood cells are discs about 7.5 μm in diameter, and they are biconcave, meaning that their edges are thicker than their center (figure 19.3*b*). Red blood cell structure enhances its function. Researchers have long proposed that the biconcave shape of a red blood cell increases the cell's surface area, thereby allowing gases to move into and out of the red blood cell more rapidly as compared to a flat disc of the same size. However, recent evidence suggests that this may not be as important to red blood cell function. Gases enter and exit the red blood cells most often when the cells are in small blood vessels called capillaries. As the red blood cells move through these small vessels, they change shape, so the surface area to volume association is not as obvious. But the fact that the cells change shape is of interest. Because of its biconcave shape, the red blood cell can bend or fold around its thin center, thereby decreasing its size and enabling it to pass more easily through smaller blood vessels. Research has also shown that the biconcave disc shape of red blood cells may also improve blood flow in larger vessels as well. However, red blood cells cannot move on their own; they are passively moved by forces that cause the blood to circulate.

Red blood cells are derived from specialized cells that lose their nuclei and nearly all their cellular organelles during maturation. The main component of the red blood cell is the pigmented



Clinical IMPACT 19.1

Stem Cells and Cancer Therapy

Many cancer therapies affect the type of rapidly dividing cells found in tumors. However, an undesirable side effect of such therapies can be the destruction of nontumor cells that are dividing, such as the stem cells and their derivatives in red bone marrow. After being treated for cancer, some patients are prescribed growth factors to stimulate the rapid regeneration of the red bone marrow. Although not a cure for cancer, the growth factors can speed recovery from the side effects of cancer therapy.

Some types of leukemia and genetic immune deficiency diseases can be treated with a bone marrow transplant that provides stem cells to the patient. To avoid tissue rejection, families with a history of these disorders can freeze the umbilical cord blood of their newborn children. The cord blood, which contains many stem cells, can be used instead of bone marrow.

protein **hemoglobin** (hē-mō-glō′bin). Hemoglobin occupies about one-third of the total volume of a red blood cell and accounts for its red color. Other red blood cell contents include lipids, adenosine triphosphate (ATP), and the enzyme carbonic anhydrase, which is important in the regulation of blood pH (see chapters 23 and 26).

Functions

The primary functions of red blood cells are to transport O_2 from the lungs to the various body tissues and to transport CO_2 from the tissues to the lungs. Approximately 98.5% of the O_2 in the blood is transported in combination with the hemoglobin in the red blood cells. The remaining 1.5% is dissolved in the plasma.

Carbon dioxide is transported in the blood in three major ways: (1) Approximately 7% is dissolved in the plasma; (2) approximately 23% is combined with hemoglobin; and (3) 70% is converted to bicarbonate ions. The bicarbonate ions (HCO_3^-) are produced when carbon dioxide (CO_2) and water (H_2O) combine to form carbonic acid (H_2CO_3). Carbonic acid quickly dissociates to form hydrogen (H^+) and bicarbonate ions. The combination of carbon dioxide and water is catalyzed by an enzyme, **carbonic anhydrase,** which is located primarily within red blood cells.

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \overset{\text{Carbonic anhydrase}}{\rightleftarrows} \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftarrows \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$

Hemoglobin

Hemoglobin is a complex protein consisting of four subunits. Each subunit is composed of one polypeptide chain called **globin** (glō′bin) that is bound to one heme (hēm) group. Each heme is a red-pigment molecule containing one iron atom (figure 19.4). There are three forms of hemoglobin: (1) embryonic, (2) fetal, and (3) adult. Embryonic hemoglobin is the first type of hemoglobin produced during development. By the third month of development, embryonic hemoglobin has been replaced with fetal hemoglobin. At birth, 60–90% of the hemoglobin is adult hemoglobin. At 2 to 4 years of age, fetal hemoglobin makes up less than 2% of the hemoglobin, and in adulthood only traces of fetal hemoglobin can be found.

The different forms of hemoglobin have different affinities for, or abilities to bind to, O_2. Embryonic and fetal hemoglobin have a higher affinity for O_2 than adult hemoglobin does. In the embryo and fetus, hemoglobin picks up O_2 from the mother's blood at the placenta. Even though placental blood contains less O_2 than does air in the mother's lungs, adequate amounts of O_2 are picked up because of the higher affinity of embryonic and fetal hemoglobin for O_2. After birth, hemoglobin picks up O_2 from the air in the baby's lungs.

Predict 2

What would happen to a fetus if hemoglobin of the maternal blood had an affinity for O_2 that was equal to or greater than the hemoglobin of fetal blood?

Although embryonic, fetal, and adult hemoglobin each have four globins, the types of globins are different. There are nine types of globins, each produced from a different gene and each with a slightly different amino acid composition. For example, there are two types of alpha globins, which differ from each other by one amino acid. Because they are so similar, they are usually referred to simply as alpha globins. There are also a beta globin, two kinds of gamma globins, a delta globin, and three kinds of embryonic globins. The different genes are active during different developmental stages and therefore allow for the production of three unique forms of hemoglobin. Most adult hemoglobin has two alpha globins (one of each type) and two beta globins (figure 19.4). Fetal hemoglobin has two alpha globins (one of each type) and two gamma globins (one of each type).

Oxygen molecules bind to the heme group. Specifically, each O_2 molecule that is transported by hemoglobin is associated with an iron atom at the center of a heme group; therefore, iron is necessary for

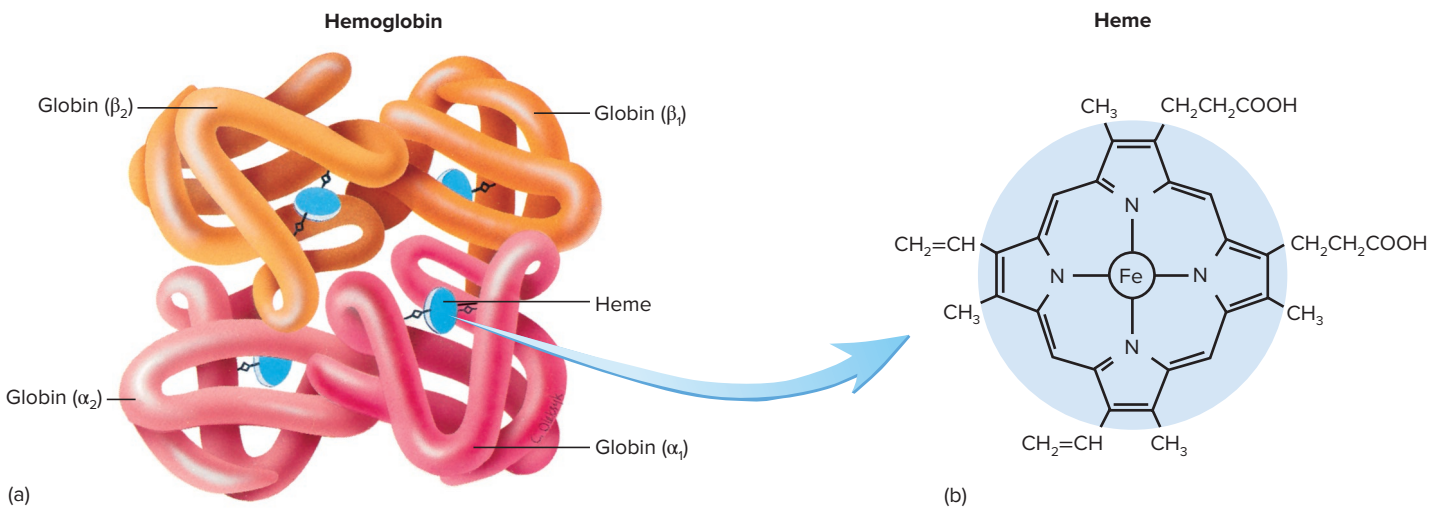


FIGURE 19.4 Hemoglobin

(*a*) Hemoglobin consists of four subunits, each with a globin and a heme. There are two alpha (α) globins and two beta (β) globins. A heme is associated with each globin. (*b*) Each heme contains one iron atom.

Clinical GENETICS 19.1 Sickle-Cell Disease

Sickle-cell disease is a disorder in which red blood cells become sickle-shaped. It results from a mutation in the gene that codes for the beta globin chain of hemoglobin. The mutation is a change in one nucleotide in the DNA that leads to a change in one amino acid in beta globin. The single amino acid change in beta globin has a dramatic effect on hemoglobin. When blood O_2 levels decrease, as when O_2 diffuses away from hemoglobin in tissue capillaries, the abnormal hemoglobin molecules join together, causing a change in red blood cell shape (figure 19.5). When blood O_2 levels increase, as in the lungs, the abnormal hemoglobin molecules separate, and red blood cells can resume their normal shape.

Sickle-shaped red blood cells are less able to squeeze through small capillaries. Consequently, they become lodged in capillaries, blocking blood flow through them. This causes a further decrease in O_2 levels, which promotes more sickling. As O_2 levels decrease further, more capillary blockage is promoted, and so on. After repeated cycles of sickling, red blood cells lose their ability to resume their normal shape. This increases the number of sickled cells.

The major consequence of sickle-cell disease is tissue damage resulting from reduced blood flow through tissues. As tissues are deprived of blood, the most common symptom is pain, which is often severe. In addition, spleen and liver enlargement, kidney and lung damage, and stroke can occur. Priapism (prī′ă-pizm), a prolonged, painful erection due to venous blockage, can develop in men. Sickle-shaped red blood cells are also likely to rupture, which can result in hemolytic anemia (see table 19.4).

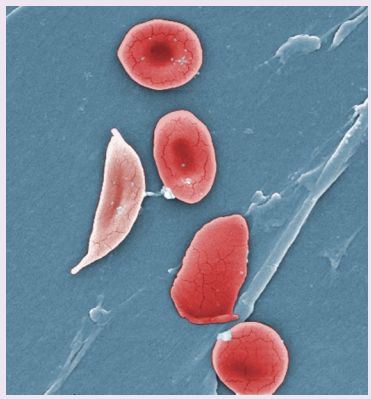


FIGURE 19.5 Sickle-Cell Disease
Red blood cells in a person with sickle-cell disease appear normal in oxygenated blood. In deoxygenated blood, hemoglobin changes shape and causes the cells to become sickle-shaped and rigid. ©CDC/Sickle Cell Foundation of Georgia: Jackie George, Beverly Sinclair/photo by Janice Haney Carr

Sickle-cell disease is an autosomal recessive disorder. Only individuals who have two mutated beta globin alleles express the disease. Individuals who are heterozygous have a normal beta globin allele and produce sufficient amounts of normal beta globin, so their red blood cells do not usually become sickle-shaped. Heterozygotes are carriers (see chapter 29) and are said to have **sickle-cell trait.**

Sickle-cell disease is an example of a genetic disorder in which the heterozygote has a better ability to survive under certain circumstances than homozygous individuals. Carriers (heterozygotes) with sickle-cell trait have increased resistance to malaria. Malaria is a disease caused by a parasitic protozoan that reproduces inside red blood cells. The parasite is usually transmitted from one person to another through the bite of a mosquito. The red blood cells of people with sickle-cell trait tend to rupture before the parasite successfully reproduces. Therefore, those people are less likely to contract malaria, and the disease is much milder if they do.

The highest percentage of people with sickle-cell trait occurs in populations exposed to malaria or whose ancestors were exposed to malaria. In certain parts of Africa where malaria is rampant, the percentage of sickle-cell carriers can be as high as 50%. In the United States, 8% of African-Americans are sickle-cell carriers, and 0.8% have sickle-cell disease. The mutant gene can also be found in other groups, but at lower frequencies.

Treatment for sickle-cell disease attempts to reduce the blockage of blood vessels, alleviate pain, and prevent infections. Hydroxyurea (hī-drok′sē-ū-rē′ă) stimulates the production of gamma (fetal) globins. When the gamma globins combine with defective beta globins, the formation of sickle-shaped cells slows. Bone marrow transplants can cure sickle-cell disease, but such transplants can be dangerous and even fatal. Gene therapy is under investigation.

normal hemoglobin function. The adult human body normally contains about 4 g of iron, two-thirds of which is associated with hemoglobin. Small amounts of iron are regularly lost from the body in waste products, such as urine and feces. Females lose additional iron as a result of menstrual bleeding and, therefore, require more dietary iron than males do. Dietary iron is absorbed into the blood from the upper part of the intestinal tract. Stomach acid and vitamin C in food increase iron absorption by converting ferric iron (Fe^{3+}) to ferrous iron (Fe^{2+}), which is more readily absorbed.

When hemoglobin is exposed to O_2, one O_2 molecule can become associated with each heme group. So one hemoglobin molecule can carry up to four oxygen molecules. This oxygenated form of hemoglobin is called **oxyhemoglobin** (ok′sē-hē-mō-glō′bin). The oxyhemoglobin in one red blood cell transports about 1 billion molecules of O_2. This estimate becomes clear when we consider that a single red blood cell contains about 280 million hemoglobin molecules, each of which carries up to four oxygen molecules. Hemoglobin not bound to O_2 is called **deoxyhemoglobin.** Interestingly, hemoglobin color changes depending on whether or not it is oxygenated. Oxyhemoglobin is bright red, whereas deoxyhemoglobin is a darker red color.

Hemoglobin also transports CO_2; however, CO_2 does not combine with the iron atoms as oxygen molecules do. Instead, CO_2 attaches to the globin molecule. This hemoglobin form is **carbaminohemoglobin** (kar-bam′i-nō-hē-mō-glō′bin). The transport of O_2 and CO_2 by the blood is discussed more fully in chapter 23.

Additionally, hemoglobin transports nitric oxide (NO), which is produced by the endothelial cells lining the blood vessels. At the same time that hemoglobin picks up O_2 in the lungs, a sulfur-containing amino acid, cysteine, in each β-globin binds with a NO molecule to form *S*-nitrosothiol (nī-trōs′ō-thī-ol; SNO). When O_2 is released in tissues, so is the NO, where it functions as a chemical messenger that induces the relaxation of the smooth muscle of blood vessels. By affecting the amount of NO in tissues, hemoglobin

may play a role in regulating blood pressure because the relaxation of blood vessels results in decreased blood pressure (see chapter 21).

Various types of poisons affect the hemoglobin molecule. Carbon monoxide (CO), which is produced by the incomplete combustion of gasoline, binds very strongly to the iron of hemoglobin to form the relatively stable compound **carboxyhemoglobin** (kar-bok′sē-hē-mō-glō′bin). As a result of the stable binding of CO, hemoglobin cannot transport O_2. Nausea, headache, unconsciousness, and death are possible consequences of prolonged exposure to CO. Interestingly, CO is found in cigarette smoke, and the blood of smokers can contain 5–15% carboxyhemoglobin.

Life History of Red Blood Cells

Under normal conditions, about 2.5 million red blood cells are destroyed every second. This loss seems staggering, but it represents only 0.00001% of the total 25 trillion red blood cells contained in the normal adult circulation. Homeostasis is maintained by replacing the 2.5 million cells lost every second with an equal number of new red blood cells. Thus, approximately 1% of the total number of red blood cells is replaced each day.

The process by which new red blood cells are produced is called **erythropoiesis** (ĕ-rith′rō-poy-ē′sis; see figure 19.2). The time required to produce a single red blood cell is about 4 days. Myeloid stem cells, derived from hemocytoblasts, give rise to **proerythroblasts.** After several mitotic divisions, proerythroblasts become **early erythroblasts.** These cells are also called *basophilic erythroblasts* because they stain with a basic dye. The dye binds to the large number of ribosomes necessary for the production of hemoglobin, giving the cytoplasm a purplish color. Early erythroblasts give rise to **intermediate erythroblasts.** These cells are also called *polychromatic erythroblasts* because they stain different colors with basic and acidic dyes. For example, when an acidic dye is used, intermediate erythroblasts stain a reddish color when it interacts with the hemoglobin accumulating in the cytoplasm. Intermediate erythroblasts continue to produce hemoglobin, and then most of their ribosomes and other organelles degenerate. The resulting **late erythroblasts** have a reddish color because about one-third of the cytoplasm is hemoglobin.

The late erythroblasts lose their nuclei to become immature red blood cells, called **reticulocytes** (re-tik′ū-lō-sīts). *Reticulocyte* refers to a reticulum, or network, that can be observed in the cytoplasm when a special staining technique is used. The reticulum is artificially produced by the reaction of the dye with the few remaining ribosomes in the reticulocyte. Reticulocytes are released from the bone marrow into the circulating blood. A normal reticulocyte level is 0.5–2% of circulating red blood cells. Reticulocyte counts are clinically useful to monitor red blood cell production, particularly when monitoring treatments for anemia. Also, reticulocyte counts can provide information about the health of the hemocytoblasts in the red bone marrow. Within 2 days, the ribosomes in the reticulocytes degenerate, and the reticulocytes become mature red blood cells.

Predict 3

During a local Red Cross blood drive, Juan donated one unit of blood (about 500 mL). Predict how his reticulocyte count changed during the week after he donated blood, and explain why the change occurred.

Cell division requires the B vitamins folate and B_{12}, which are necessary for the synthesis of DNA (see chapter 3). Hemoglobin production requires iron. Consequently, adequate amounts of folate, vitamin B_{12}, and iron are necessary for normal red blood cell production.

Red blood cell production is stimulated by low blood O_2 levels, which result from several conditions: decreased numbers of red blood cells, decreased or defective hemoglobin, diseases of the lungs, high altitude, inability of the cardiovascular system to deliver blood to tissues, and increased tissue demands for O_2—for example, during endurance exercises.

Red blood cell production is regulated by the glycoprotein **erythropoietin** (ĕ-rith-rō-poy′ĕ-tin), a hormone produced mostly by the kidneys (figure 19.6). Erythropoietin secretion increases when blood O_2 levels are low, a condition known as **hypoxia.** This stimulates red bone marrow to produce more red blood cells by increasing the number of proerythroblasts formed and by decreasing the time required for red blood cells to mature. Thus, when blood O_2 levels decrease, erythropoietin production increases, which increases red blood cell production. The greater number of red blood cells increases the blood's ability to transport O_2. This negative-feedback mechanism returns blood O_2 levels to normal and maintains homeostasis by increasing the delivery of O_2 to tissues. Conversely, if blood O_2 levels rise, less erythropoietin is released, and red blood cell production decreases.

Predict 4

Cigarette smoke produces carbon monoxide. If a nonsmoker smoked a pack of cigarettes a day for a few weeks, what would happen to the number of red blood cells in the person's blood? Explain.

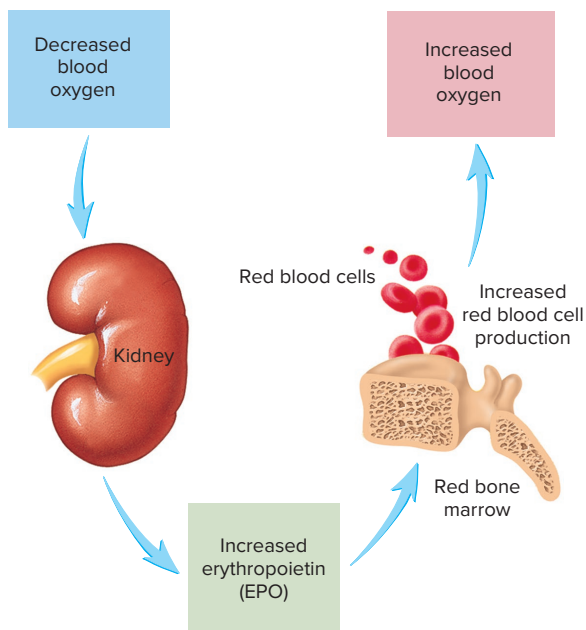
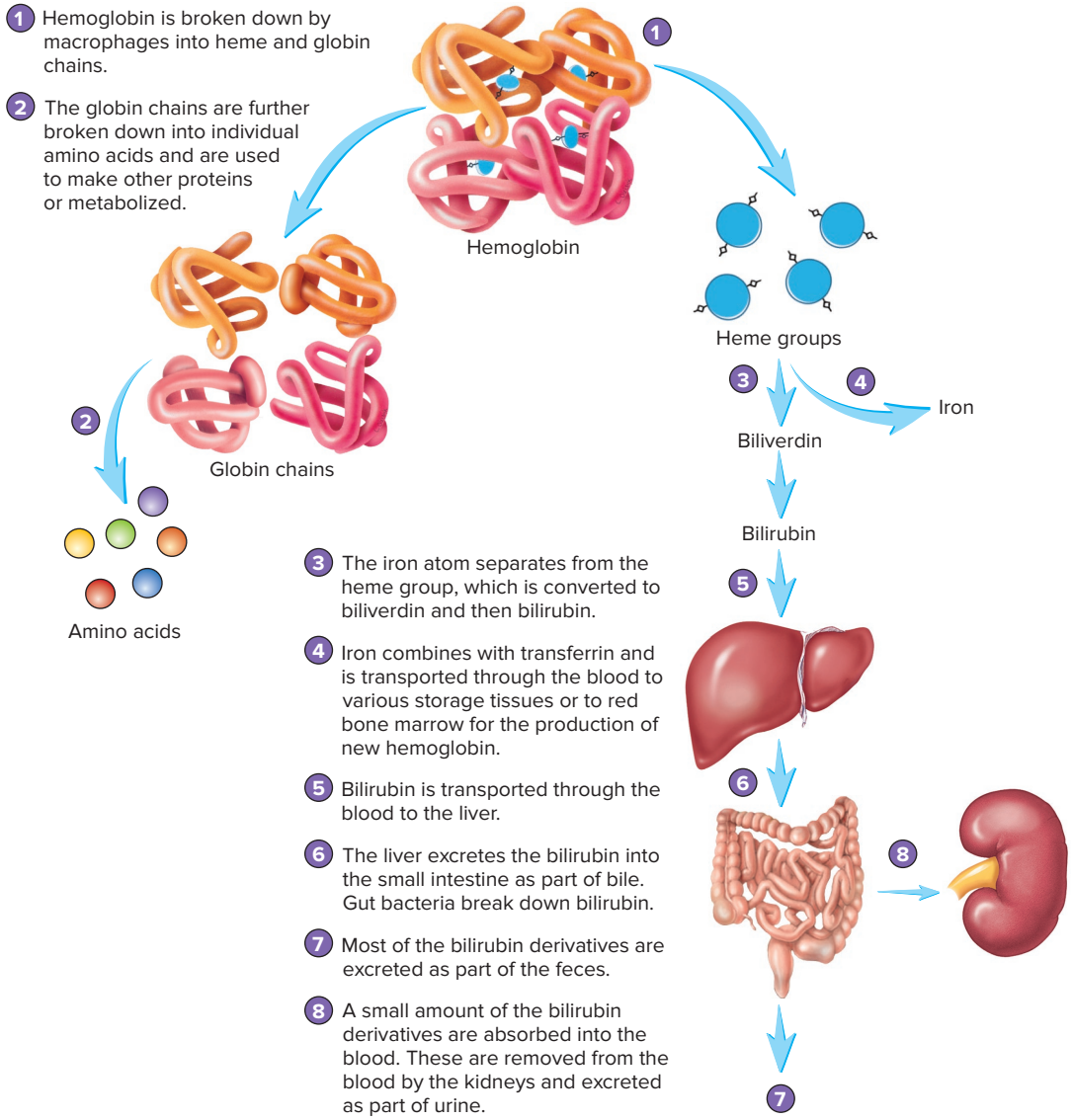


FIGURE 19.6 Red Blood Cell Production
In response to decreased blood oxygen, the kidneys release erythropoietin into the bloodstream. The increased erythropoietin stimulates red blood cell production in the red bone marrow. This process increases blood oxygen levels, restoring homeostasis.



PROCESS FIGURE 19.7 Hemoglobin Breakdown

Macrophages break down hemoglobin, and the breakdown products are used or excreted. AP|R

? *Some forms of anemia result from fewer, smaller red blood cells. These individuals produce feces that are light or white in color. Explain why this is expected.*

The normal lifespan of a red blood cell is about 120 days in males and 110 days in females. These cells have no nuclei and therefore cannot produce new proteins or divide. As their existing proteins, enzymes, plasma membrane components, and other structures degenerate, the red blood cells are less able to transport O_2, and their plasma membranes become more fragile. Eventually, the red blood cells rupture as they squeeze through a tight spot in the circulation. **Hemolysis** (hē-mol′i-sis) occurs when red blood cells rupture and the hemoglobin is released into the plasma. Hemoglobin released into the plasma will denature as the molecules change shape in a new environment (see chapter 2). Hemolysis occurs as old red blood cells rupture or as a result of hemolytic anemia (see table 19.4), transfusion reactions, hemolytic disease of the newborn, and malaria.

Macrophages located in the spleen, liver, and other lymphatic tissue take up the hemoglobin released from ruptured red blood cells (figure 19.7). Within a macrophage, lysosomal enzymes digest the hemoglobin to yield amino acids, iron, and bilirubin.

- The globin part of hemoglobin is broken down into its component amino acids. Most of the amino acids are reused to produce other proteins.
- The heme groups are broken down, releasing the iron atoms. Iron atoms released from heme are carried by the blood to red bone marrow, where they are incorporated into new hemoglobin molecules.

- After the removal of the iron atoms, the non-iron part of the heme groups is first converted to **biliverdin** (bil-i-ver′din) and then to **bilirubin** (bil-i-roo′bin). The bilirubin is then released into the plasma, where it binds to albumin and is transported to liver cells. This bilirubin, called **free bilirubin,** is taken up by the liver cells and conjugated, or joined, to glucuronic acid to form **conjugated bilirubin,** which is more water-soluble than free bilirubin. The conjugated bilirubin becomes part of the **bile,** which is the fluid secreted from the liver into the small intestine. In the intestine, bacteria convert bilirubin into the pigments that give feces its characteristic brownish color. Some of these pigments are absorbed from the intestine, modified in the kidneys, and excreted in the urine, thus contributing to the characteristic yellowish color of urine.

Jaundice (jawn′dis) is a yellowish staining of the skin and the sclerae of the eyes caused by a buildup of bile pigments in the blood and some tissues. Any process that causes increased destruction of red blood cells can cause jaundice, such as damage by toxins, genetic defects in red blood cell plasma membranes, infections, and immune reactions. Other causes of jaundice are dysfunction or destruction of liver tissue and blockage of the duct system that drains bile from the liver (see chapter 24).

ASSESS YOUR PROGRESS

13. *What is the normal amount of red blood cells in a male? In a female?*
14. *How does the shape of red blood cells enable them to exchange gases and move through blood vessels more easily?*
15. *What is the main component of a red blood cell? What is the primary function of red blood cells?*
16. *Give the percentage for each of the ways that oxygen and carbon dioxide are transported in the blood. What is the function of carbonic anhydrase?*
17. *Describe the two basic parts of a hemoglobin molecule. Which part is associated with iron? What gases are transported by each part?*
18. *What is the significance of fetal hemoglobin's difference from adult hemoglobin?*
19. *Describe the process of erythropoiesis, beginning with hemocytoblasts in the red bone marrow.*
20. *What is erythropoietin, where is it produced, what causes it to be produced, and what effect does it have on red blood cell production?*
21. *How long do red blood cells normally stay in circulation? Where are red blood cells removed from the blood? List the three breakdown products of hemoglobin, and explain what happens to them.*

White Blood Cells

When the components of blood are separated from each other (see figure 19.1), **white blood cells (WBCs),** or *leukocytes,* form a thin, white layer of cells between the plasma and the red blood cells. This layer is often referred to as the *buffy coat*. White blood cells have a nucleus. In stained preparations, white blood cells attract stain, whereas red blood cells remain relatively unstained (figure 19.8; table 19.2).

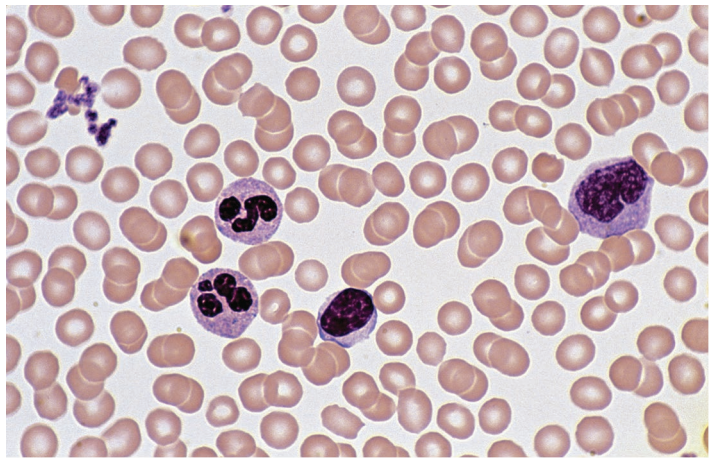


FIGURE 19.8 Standard Blood Smear
A thin film of blood is spread on a microscope slide and stained. The white blood cells have pink-colored cytoplasm and purple-colored nuclei. The red blood cells do not have nuclei. The center of a red blood cell appears whitish because light more readily shines through the thin center of the disc than through the thicker edges. The platelets are purple cell fragments. ©Ed Reschke/Getty Images

White blood cells are grouped into two categories based on their appearance in stained preparations: (1) granulocytes and (2) agranulocytes. **Granulocytes** (gran′yū-lō-sītz) are white blood cells with large cytoplasmic granules and lobed nuclei (table 19.2). Their granules stain with dyes that make the cells more visible when viewed through a light microscope. The three types of granulocytes are named according to the staining characteristics of their granules: (1) **Neutrophils** (nu′trō-filz) stain with acidic and basic dyes, (2) **eosinophils** (ē-ō-sin′ō-filz) stain red with acidic dyes, and (3) **basophils** (bā′sō-filz) stain dark purple with basic dyes. **Agranulocytes** (ă-gran′yū-lō-sītz) are white blood cells that appear to have no granules when viewed with a light microscope. Actually, agranulocytes have granules, but they are so small that they cannot be seen easily with the light microscope. The two types of agranulocytes are (1) **lymphocytes** (lim′fō-sītz) and (2) **monocytes** (mon′ō-sītz). They have nuclei that are not lobed.

White blood cells protect the body against invading microorganisms and remove dead cells and debris from the body. Three characteristics—ameboid movement, diapedesis, and chemotaxis—allow white blood cells to carry out their function of protection.

1. Most white blood cells are motile, exhibiting **ameboid movement.** This is the ability to move as an ameba does, by putting out irregular cytoplasmic projections. Ameboid movement allows white blood cells to have more directed movement, instead of moving only with the flow of blood, like red blood cells.
2. White blood cells also have the ability to leave the blood and enter other tissues. They accomplish this by the process of **diapedesis** (dī′ă-pĕ-dē′sis), in which they become thin and elongated and slip between or through the cells of blood vessel walls.
3. The white blood cells can then be attracted to foreign materials or dead cells within the tissue by **chemotaxis** (kē-mō-tak′sis; see chapter 22). At the site of an infection, white blood cells

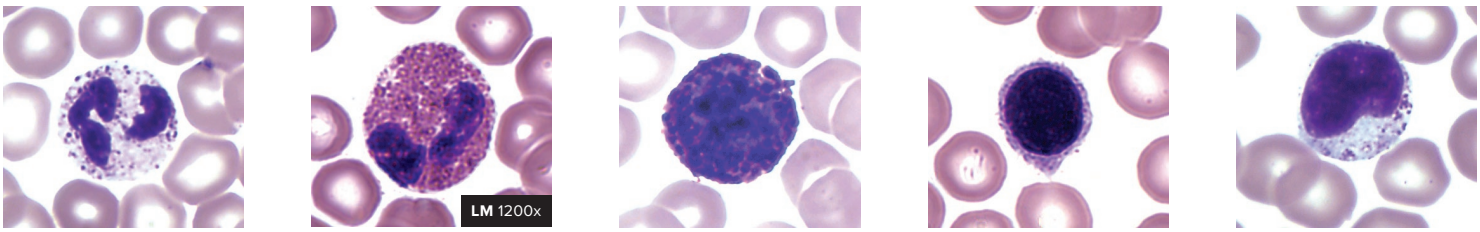


FIGURE 19.9 Types of White Blood Cells
(*a*) Neutrophil, (*b*) eosinophil, (*c*) basophil, (*d*) lymphocyte, (*e*) monocyte/macrophage. ©McGraw-Hill Education/Al Telser, photographer AP|R

accumulate and phagocytize bacteria, dirt, and dead cells; then they die. **Pus** is the accumulation of dead white blood cells and bacteria, along with fluid and cell debris.

Following are detailed descriptions of the five types of white blood cells: (1) neutrophils, (2) eosinophils, (3) basophils, (4) lymphocytes, and (5) monocytes.

Neutrophils

Neutrophils compose 55–70% of white blood cells (figure 19.9*a*; table 19.2). They have small cytoplasmic granules that stain with both acidic and basic dyes. Commonly, their nuclei are lobed, with the number of lobes varying from two to five. Neutrophils are often called *polymorphonuclear* (pol′ē-mōr-fō-noo′klē-ăr) *neutrophils,* or *PMNs,* to indicate that their nuclei can occur in more than one (*poly*) form (*morph*). Neutrophils are usually the first of the white blood cells to respond to infection. They normally remain in the blood for about 10–12 hours and then move into other tissues. Once neutrophils leave the blood, they seek out and phagocytize bacteria, antigen-antibody complexes (antigens and antibodies bound together), and other foreign matter. Neutrophils also secrete a class of enzymes called **lysozymes** (lī′sō-zīmz), which are capable of destroying certain bacteria. Neutrophils usually survive 1–2 days after leaving the blood.

Eosinophils

Eosinophils compose 1–4% of white blood cells (figure 19.9*b*; table 19.2). They contain cytoplasmic granules that stain bright red with eosin, an acidic stain. They often have a two-lobed nucleus. Eosinophils are important in the defense against certain worm parasites. Although the eosinophils are not able to phagocytize the large parasites, they attach to the worms and release substances that kill the parasites. Eosinophils also increase in number in tissues experiencing inflammation, such as during allergic reactions. Eosinophils apparently modulate the inflammatory response by producing enzymes that destroy inflammatory chemicals, such as histamine. However, research has shown that eosinophils have harmful effects on respiratory airways in certain forms of asthma.

Basophils

Basophils compose 0.5–1% of white blood cells (figure 19.9*c*; table 19.2). They contain large cytoplasmic granules that stain blue or purple with basic dyes. Basophils, like eosinophils and neutrophils, leave the blood and migrate through other tissues. They increase in number in both allergic and inflammatory reactions. Basophils contain large amounts of **histamine** (see chapter 22), which they release within tissues to increase inflammation. They also release **heparin,** which inhibits blood clotting.

Lymphocytes

Lymphocytes compose 20–40% of white blood cells (figure 19.9*d*; table 19.2). They are the smallest white blood cells, usually slightly larger in diameter than red blood cells. A lymphocyte's cytoplasm consists of only a thin, sometimes imperceptible, ring around the nucleus. Although lymphocytes originate in red bone marrow, they migrate through the blood to lymphatic tissues, where they can proliferate and produce more lymphocytes. The majority of the body's total lymphocyte population is in the lymphatic tissues: the lymph nodes, spleen, tonsils, lymphatic nodules, and thymus.

Some specific types of lymphocytes play important roles in immunity (see chapter 22). For example, **B cells** are a type of lymphocyte that can be stimulated by bacteria or toxins to divide and form cells that produce **antibodies,** a class of plasma proteins also called immunoglobulins. Antibodies can attach to bacteria and activate mechanisms that destroy the bacteria. **T cells** are another type of lymphocyte that protect against viruses and other intracellular microorganisms by attacking and destroying the cells in which they are found. In addition, T cells are involved in the destruction of tumor cells and in tissue graft rejections.

Monocytes

Monocytes compose 2–8% of white blood cells (figure 19.9*e*; table 19.2). They are typically the largest of the white blood cells. Monocytes normally remain in the blood for about 3 days. Then they leave the blood and are transformed into macrophages. Macrophages migrate through various tissues, where they phagocytize bacteria, dead cells, cell fragments, and other debris. An increase in the number of monocytes in the blood is often associated with chronic infection. Macrophages also stimulate responses from other cells in two ways: (1) by releasing chemical messengers and (2) by phagocytizing and processing foreign substances, which are then presented to lymphocytes. The responses of these other cells help protect against microorganisms and other foreign substances (see chapter 22).

ASSESS YOUR PROGRESS

22. *What are the two major functions of white blood cells? Define* ameboid movement, diapedesis, *and* chemotaxis.

23. *Describe the morphology of the five types of white blood cells.*

24. *Name the two white blood cells that function primarily as phagocytic cells. What are lysozymes?*
25. *Which white blood cell defends against parasitic worms?*
26. *Which white blood cell releases histamine and promotes inflammation?*
27. *B cells and T cells are examples of which type of white blood cell? How do these cells protect against bacteria and viruses?*

Platelets

Platelets, or *thrombocytes* (table 19.2; see figure 19.8), are minute fragments of cells. They consist of a small amount of cytoplasm surrounded by a plasma membrane. Platelets are roughly disc-shaped and average about 3 µm in diameter. Glycoproteins and proteins on their surface allow platelets to attach to other molecules, such as collagen in connective tissue. Some of these surface molecules, as well as molecules released from granules in the platelet cytoplasm, play important roles in controlling blood loss. The platelet cytoplasm also contains actin and myosin, which can cause contraction of the platelet (see section 19.5).

The life expectancy of platelets is about 5–9 days. Platelets are derived from **megakaryocytes** (meg-ă-kar′ē-ō-sitz), which are extremely large cells found in the red bone marrow. Small fragments of these cells break off and enter the blood as platelets.

Platelets play an important role in preventing blood loss by (1) forming platelet plugs that seal holes in small vessels and (2) promoting the formation and contraction of clots that help seal off larger wounds in the vessels.

ASSESS YOUR PROGRESS

28. *What is a platelet? How do platelets form?*
29. *What are the two major roles of platelets in preventing blood loss?*

19.5 Hemostasis

LEARNING OUTCOMES

After reading this section, you should be able to

A. **Explain the three processes that can lead to hemostasis: vascular spasm, platelet plug formation, and coagulation.**
B. **Describe how aspirin affects the action of platelets.**
C. **Describe the regulation of clot formation and how clots are removed.**

Hemostasis (hē′mō-stā-sis, hē-mos′tă-sis), the cessation of bleeding, is very important to the maintenance of homeostasis. If not stopped, excessive bleeding from a cut or torn blood vessel can result in a positive-feedback cycle, consisting of ever-decreasing blood volume and blood pressure that disrupts homeostasis and results in death. Fortunately, when a blood vessel is damaged, a series of events helps prevent excessive blood loss. Hemostasis involves three processes: (1) vascular spasm, (2) platelet plug formation, and (3) coagulation.

Vascular Spasm

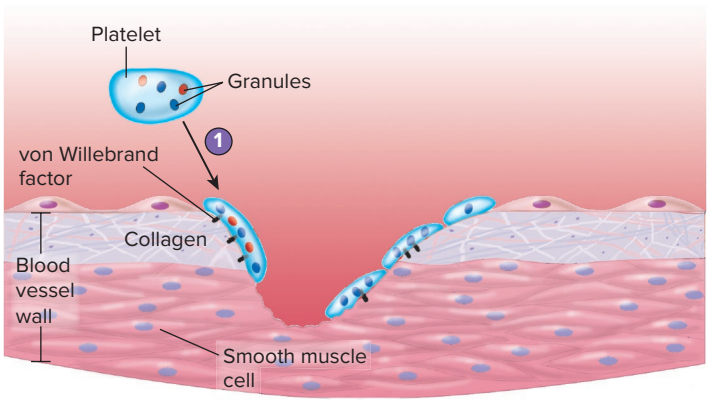
Vascular spasm is the immediate but temporary constriction of a blood vessel. Vascular spasm occurs when smooth muscle within the wall of the vessel contracts. This constriction can close small vessels completely and stop the flow of blood through them. Damage to blood vessels can activate nervous system reflexes that cause vascular spasms. Chemicals released by cells of the damaged vessel as well as platelets also stimulate vascular spasms. For example, endothelial cells release the peptide **endothelin** (en-do′the-lin), which leads to constriction of blood vessels. Also, during the formation of a platelet plug, platelets release **thromboxanes** (throm′bok-zānz), which are derived from certain prostaglandins. Thromboxanes also lead to constriction of blood vessels.

Platelet Plug Formation

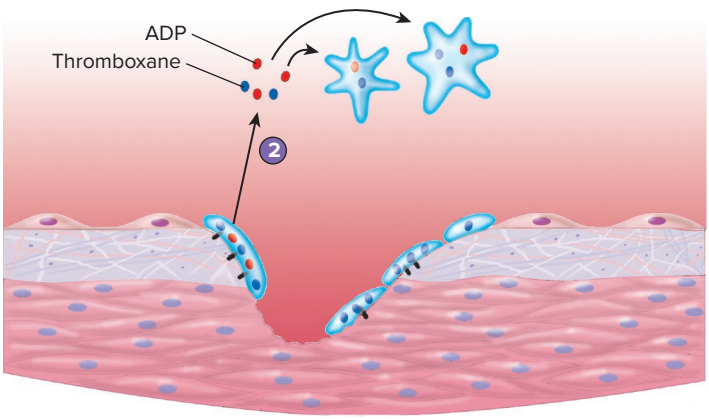
A **platelet plug** is an accumulation of platelets that can seal small breaks in blood vessels. A platelet plug is not the same thing as a blood clot, but the formation of the platelet plug is an important step in blood clot formation. Platelet plug formation is very important in maintaining the integrity of the circulatory system. Small tears occur in the smaller vessels and capillaries many times each day, and platelet plug formation quickly closes them. People who lack the normal number of platelets tend to develop numerous small hemorrhages in their skin and internal organs.

The formation of a platelet plug can be described as a series of steps, but in actuality many of the steps take place simultaneously (figure 19.10):

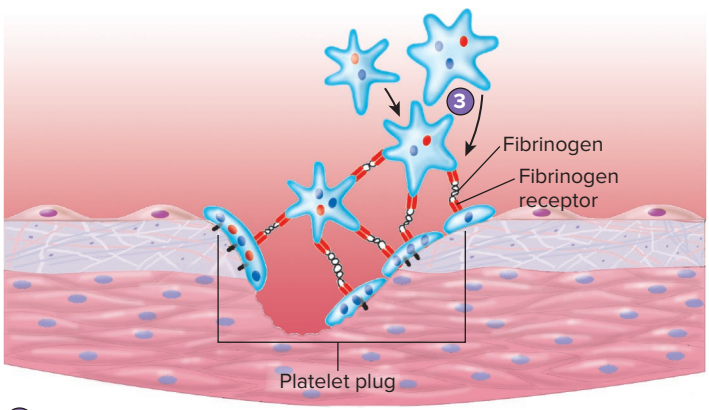
1. **Platelet adhesion** occurs when platelets bind to collagen that is exposed when a blood vessel is damaged. Most platelet adhesion is mediated through **von Willebrand factor (vWF),** a protein produced and secreted by blood vessel endothelial cells. Platelets have surface receptors on their membrane. These surface receptors bind to von Willebrand factor released from damaged blood vessels. Von Willebrand factor also binds to the exposed collagen of the damaged vessel, thereby forming a bridge between exposed collagen and platelets. In addition, other platelet surface receptors can bind directly to collagen.
2. After platelets adhere to collagen, they become activated. These activated platelets then initiate the **platelet release reaction,** in which adenosine diphosphate (ADP), thromboxanes, and other chemicals are released from the activated platelets by exocytosis. The ADP and thromboxane bind to their respective receptors on the surfaces of other platelets, activating them. These activated platelets release additional chemicals, thereby producing a cascade of chemical release by the platelets. Thus, more and more platelets become activated. This is an example of positive feedback.
3. As platelets become activated, they change shape and express fibrinogen receptors that can bind to fibrinogen, a plasma protein. In **platelet aggregation,** fibrinogen forms a bridge between the fibrinogen receptors of different platelets, resulting in a platelet plug.



1 Platelet adhesion occurs when von Willebrand factor connects exposed collagen to platelets.



2 During the platelet release reaction, ADP, thromboxanes, and other chemicals are released and activate other platelets.



3 Platelet aggregation occurs when fibrinogen receptors on activated platelets bind to fibrinogen, connecting the platelets to one another. The accumulating mass of platelets forms a platelet plug.

PROCESS FIGURE 19.10 Platelet Plug Formation

During platelet plug formation, platelets adhere to the surface of the damaged vessel and to other platelets, reducing blood loss at the injury site.

? *Among other effects, aspirin inhibits thromboxane activity. How will this affect platelet plug formation?*

In addition to forming a platelet plug, activated platelets also release phospholipids (platelet factor III) and coagulation factor V, which are important in clot formation.

Coagulation

Vascular spasms and platelet plugs alone are not sufficient to close large tears or cuts. When a blood vessel is severely damaged, **coagulation** (kō-ag-ū-lā′shŭn), or blood clotting, results in the formation of a clot. A **blood clot** is a network of threadlike protein fibers, called **fibrin,** that traps blood cells, platelets, and fluid (figure 19.11).

Blood clot formation depends on a number of **clotting factors,** or *coagulation factors,* which are proteins found within plasma (table 19.3). Normally, the clotting factors are in an inactive state and do not cause clotting. After injury, the clotting factors are activated. The activation of clotting factors is a complex process involving many chemical reactions, some of which require calcium ions (Ca^{2+}) and molecules on the surface of activated platelets, such as phospholipids and factor V.

Predict 5

Why is it advantageous for clot formation to involve molecules on the surface of activated platelets?

Clotting factors are activated in two ways: (1) the extrinsic pathway and (2) the intrinsic pathway (figure 19.12). These two pathways converge to form the common pathway, which results in the formation of a fibrin clot.

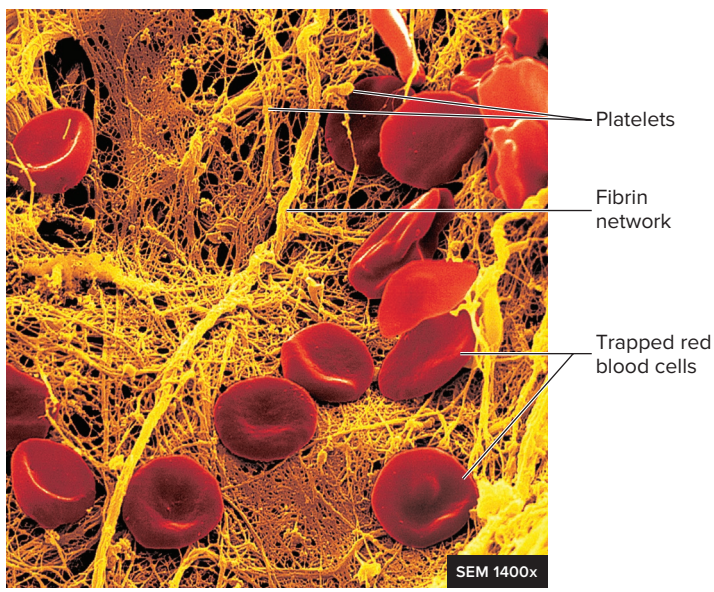
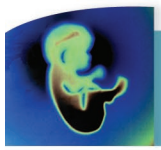


FIGURE 19.11 Blood Clot

A blood clot consists of fibrin, which traps red blood cells, platelets, and fluid.



Clinical IMPACT 19.2 Clinical Importance of Taking Aspirin

Platelet activation results in platelet plug formation and the production of chemicals, such as phospholipids, that are important for blood clotting. Alternatively, the inhibition of platelet activation reduces the formation of blood clots. Understanding how this occurs requires knowledge of the chemical behavior of the **eicosanoids,** a group that includes prostaglandins, thromboxanes, and leukotrienes, the compounds involved in platelet activation. In humans, arachidonic acid is the most common precursor molecule for the eicosanoids. The enzyme cyclooxygenase (COX) converts arachidonic acid into a prostaglandin that can be converted into thromboxane. However, the actions of COX are inhibited by aspirin, which inhibits prostaglandin and thromboxane synthesis. As a result, aspirin reduces platelet activation.

Taking aspirin can have harmful or beneficial effects, depending on the circumstances. If an expectant mother ingests aspirin near the end of pregnancy, thromboxane synthesis is inhibited and several effects are possible. The mother can experience excessive bleeding after delivery because of decreased platelet function, and the baby can exhibit numerous localized hemorrhages called **petechiae** (pe-tē′kē-ē) over the surface of its body as a result of decreased platelet function. If the quantity of ingested aspirin is large, the infant, the mother, or both may die as a result of hemorrhage.

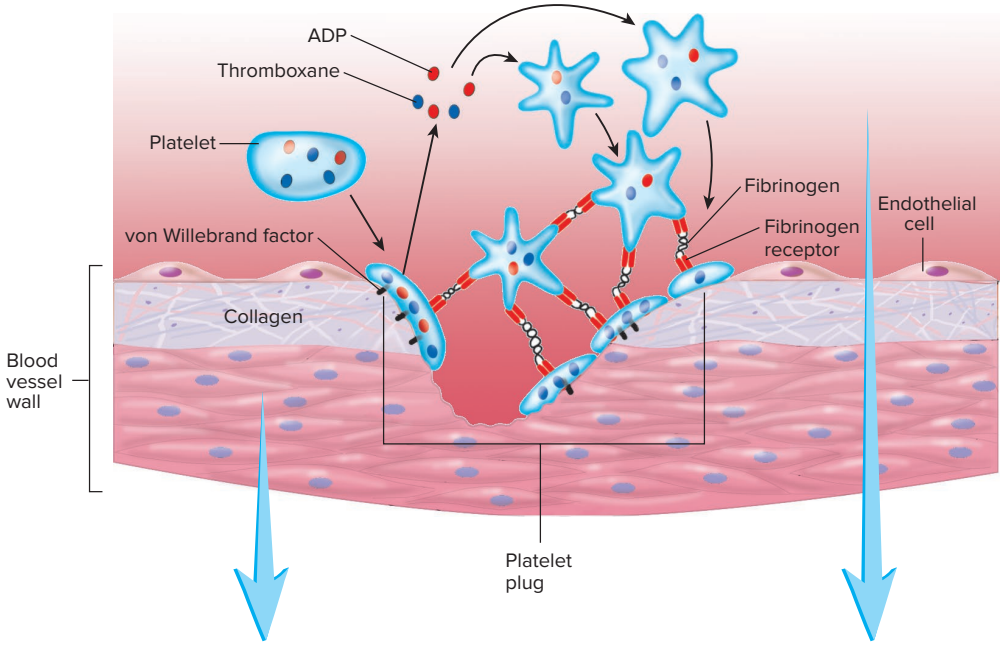
On the other hand, platelet plugs and blood clots can block blood vessels, producing heart attacks and strokes. Therefore, suspected heart attack victims are routinely given aspirin en route to the emergency room to reduce further clotting. The United States Preventive Services Task Force (USPSTF) and the American Heart Association (AHA) recommend low-dose aspirin therapy (75–160 mg/day) for all men and women at high risk for cardiovascular disease. Determining risk involves analyzing many factors and should be done in consultation with a physician. The decreased risk for cardiovascular disease from aspirin therapy must be weighed against the increased risk for hemorrhagic stroke and gastrointestinal bleeding.

The drug Plavix (clopidogrel bisulfate) reduces the activation of platelets by blocking the ADP receptors on the surface of platelets. It is used to prevent clotting and, with other anticlotting drugs, to treat heart attacks.

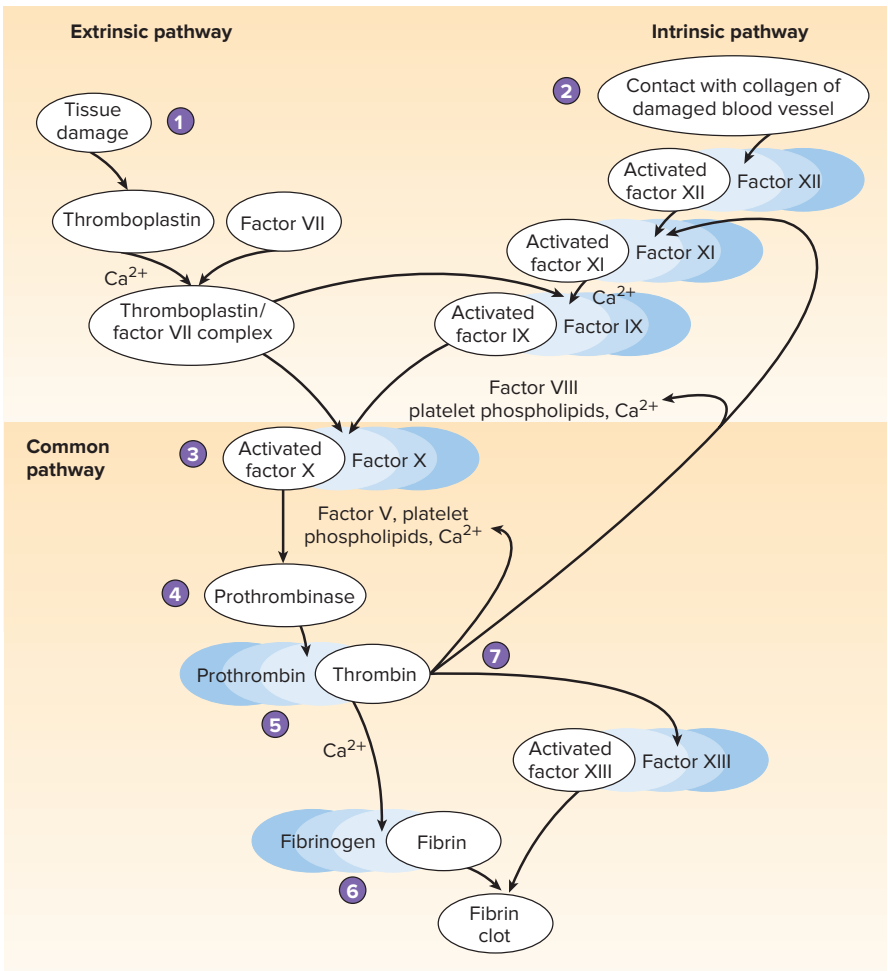
TABLE 19.3 Clotting Factors

Factor Number	Name (Synonym)	Description and Function
I	Fibrinogen	Plasma protein synthesized in the liver; converted to fibrin in the common pathway
II	Prothrombin	Plasma protein synthesized in the liver (requires vitamin K); converted to thrombin in the common pathway
III	Thromboplastin (tissue factor)	Mixture of lipoproteins released from damaged tissue; required in the extrinsic pathway
IV	Calcium ion	Required throughout the clotting sequence
V	Proaccelerin (labile factor)	Plasma protein synthesized in the liver; activated form functions in the intrinsic and extrinsic pathways
VII	Serum prothrombin conversion accelerator (stable factor, proconvertin)	Plasma protein synthesized in the liver (requires vitamin K); functions in the extrinsic pathway
VIII	Antihemophilic factor (antihemophilic globulin)	Plasma protein synthesized in megakaryocytes and endothelial cells; required in the intrinsic pathway
IX	Plasma thromboplastin component (Christmas factor)	Plasma protein synthesized in the liver (requires vitamin K); required in the intrinsic pathway
X	Stuart factor (Stuart-Prower factor)	Plasma protein synthesized in the liver (requires vitamin K); required in the common pathway
XI	Plasma thromboplastin antecedent	Plasma protein synthesized in the liver; required in the intrinsic pathway
XII	Hageman factor	Plasma protein required in the intrinsic pathway
XIII	Fibrin-stabilizing factor	Protein found in plasma and platelets; required in the common pathway
Platelet Factors		
I	Platelet accelerator	Same as plasma factor V
II	Thrombin accelerator	Accelerates thrombin and fibrin production
III		Phospholipids necessary for the intrinsic and extrinsic pathways
IV		Binds heparin, which prevents clot formation

Note: Factor VI was once thought to be involved but is no longer accepted as playing a role in clotting; apparently the same as activated factor V.



1. The extrinsic pathway of clotting is stimulated by thromboplastin, released by damaged tissue.
2. The intrinsic pathway of clotting starts when inactive factor XII, which is in the blood, is activated by coming into contact with a damaged blood vessel.
3. Activation of the extrinsic or intrinsic pathway results in the production of activated factor X.
4. Activated factor X, factor V, phospholipids, and Ca^{2+} form prothrombinase.
5. Prothrombinase converts prothrombin to thrombin.
6. Thrombin converts fibrinogen to fibrin (the clot).
7. Thrombin activates clotting factors, promoting clot formation and stabilizing the fibrin clot.



PROCESS FIGURE 19.12 Clot Formation

In a sequence of chemical reactions, activated clotting factors (*white ovals*) activate inactive clotting factors (*blue ovals*). Clot formation begins through either the extrinsic or the intrinsic pathway. The common pathway starts with factor X and results in a fibrin clot.

? *Heparin is an anticoagulant that activates an enzyme called antithrombin. Based on its name, how would antithrombin disrupt blood clotting?*

Extrinsic Pathway

The extrinsic pathway is so named because it begins with chemicals that are outside of, or extrinsic to, the blood (figure 19.12). Damaged tissues release a mixture of lipoproteins and phospholipids called **thromboplastin** (throm-bō-plas′tin), also known as *tissue factor* (*TF*) or factor III. Thromboplastin, in the presence of Ca^{2+}, forms a complex with factor VII that activates factor X, which is the clotting factor that initiates the common pathway.

Intrinsic Pathway

The intrinsic pathway is so named because it begins with chemicals that are inside, or intrinsic to, the blood (figure 19.12). Damage to blood vessels can expose collagen in the connective tissue beneath the endothelium of the blood vessel. When plasma factor XII comes into contact with collagen, factor XII is activated. Subsequently, activated factor XII stimulates factor XI, which in turn activates factor IX. Activated factor IX joins with factor VIII, platelet phospholipids, and Ca^{2+} to activate factor X, which, as stated in the extrinsic pathway description, initiates the common pathway.

Although the extrinsic and intrinsic pathways were once considered distinct, we now know that the extrinsic pathway can activate the clotting factors in the intrinsic pathway. The thromboplastin/factor VII complex from the extrinsic pathway can stimulate the formation of activated factor IX in the intrinsic pathway.

Common Pathway

On the surface of platelets, activated factor X, factor V, platelet phospholipids, and Ca^{2+} combine to form **prothrombinase,** or *prothrombin activator*. Prothrombinase converts the soluble plasma protein **prothrombin** to the enzyme **thrombin.** A major function of thrombin is to convert the soluble plasma protein fibrinogen to the insoluble protein fibrin. Fibrin is the protein that forms the fibrous network of the blood clot (see figure 19.11). In addition, thrombin also stimulates factor XIII activation, which is necessary to stabilize the clot.

Thrombin can also activate many of the clotting proteins, such as factor XI and prothrombinase. Thus, a positive-feedback system operates whereby thrombin production stimulates the production of additional thrombin. Thrombin also has a positive-feedback effect on platelet aggregation by stimulating platelet activation.

Vitamin K is required for the formation of many of the factors involved in blood clot formation (table 19.3). Humans rely on two sources for vitamin K. About half comes from the diet, and half comes from bacteria within the large intestine. Antibiotics taken to fight bacterial infections sometimes kill these intestinal bacteria, thereby reducing vitamin K levels and causing bleeding. Vitamin K supplements may be necessary for patients on prolonged antibiotic therapy. Newborns lack these intestinal bacteria; thus, they routinely receive a vitamin K injection at birth. Infants can also obtain vitamin K from food, such as milk.

The absorption of vitamin K from the large intestine requires the presence of bile because vitamin K is fat-soluble. Therefore, disorders involving an obstruction of bile flow to the intestine can interfere with vitamin K absorption and lead to insufficient blood clotting. Liver diseases that result in the decreased synthesis of clotting factors can also cause insufficient blood clotting.

Control of Clot Formation

Without control, clot formation would spread from the point of initiation through the entire circulatory system. Furthermore, blood vessels in a healthy person contain rough areas that can stimulate clot formation, and small amounts of prothrombin are constantly being converted into thrombin. To prevent unwanted clotting, the blood contains several **anticoagulants** (an′tē-kō-ag′ū-lantz). These anticoagulants prevent clotting factors from initiating clot formation under normal concentrations in the blood. Only when clotting factor concentrations exceed a given threshold in a local area does clot formation occur. At the site of injury, so many clotting factors are activated that the anticoagulants are unable to prevent clot formation. However, away from the injury site, the activated clotting factors are diluted in the blood, anticoagulants neutralize them, and clotting is prevented.

Examples of anticoagulants in the blood are antithrombin, heparin, and prostacyclin. **Antithrombin,** a plasma protein produced by the liver, slowly inactivates thrombin. Heparin, produced by basophils and endothelial cells, works with antithrombin to rapidly inactivate thrombin. **Prostacyclin** (pros-tă-sī′klin) is a prostaglandin derivative produced by endothelial cells. It counteracts the effects of thrombin by causing vasodilation and inhibiting the release of clotting factors from platelets.

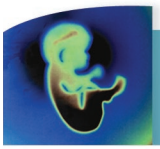
Anticoagulants are also important when blood is outside the body. They prevent the clotting of blood used in transfusions and laboratory blood tests. Besides heparin, examples include **ethylenediaminetetraacetic** (eth′il-ēn-dī′ă-mēn-tet-ră-ă-sē′tik) **acid (EDTA)** and sodium citrate. EDTA and sodium citrate prevent clot formation by binding to Ca^{2+}, thus making the ions inaccessible for clotting reactions.

Clot Retraction and Dissolution

The fibrin meshwork constituting a clot adheres to the walls of the blood vessel. Once a clot has formed, **clot retraction** occurs, a process whereby the blood clot condenses into a denser, compact structure. Platelets contain the contractile proteins actin and myosin, which operate in a similar fashion to actin and myosin in smooth muscle (see chapter 9). Platelets form extensions, which attach to fibrinogen through fibrinogen receptors (see figure 19.10). Contraction of the extensions pulls on the fibrinogen and leads to clot retraction. As the clot retracts, a fluid called **serum** (sēr′ŭm) is squeezed out of the clot. Serum is plasma from which fibrinogen and some of the clotting factors have been removed.

Clot retraction pulls the edges of the damaged blood vessel together, helping stop blood flow, reducing infection, and enhancing healing. The damaged vessel is repaired as fibroblasts move into the damaged area and new connective tissue forms. In addition, epithelial cells around the wound proliferate and fill in the torn area.

The blood clot is usually dissolved within a few days after clot formation. The process that dissolves the blood clot is called **fibrinolysis** (fī-bri-nol′i-sis). During this process, an enzyme called **plasmin** (plaz′min) hydrolyzes, or breaks, fibrin, thereby dissolving the clot. Plasmin forms from inactive plasminogen, a normal blood protein produced by the liver. Plasmin becomes part of the clot as it forms. Plasmin is activated by many substances, including thrombin, factor XII, tissue plasminogen activator (t-PA),



Clinical IMPACT 19.3

The Danger of Unwanted Clots

When platelets encounter damaged or diseased areas on the walls of blood vessels or the heart, an attached clot called a **thrombus** (throm′bŭs) may form. A thrombus that breaks loose and begins to float through the blood is called an **embolus** (em′bō-lŭs). Both thrombi and emboli can cause death if they block vessels that supply blood to essential organs, such as the heart, brain, or lungs. Abnormal clotting can be prevented or hindered by administering an anticoagulant, such as heparin, which acts rapidly. Warfarin (war′fă-rin), commonly referred to by the brand name Coumadin® (koo′mă-din), acts more slowly than heparin. Coumadin prevents clot formation by suppressing the liver's production of vitamin K–dependent clotting factors (II, VII, IX, and X). Warfarin was first used as a rat poison by causing rats to bleed to death. In small doses, Coumadin is a proven, effective anticoagulant in humans. However, caution is necessary with anticoagulant treatment because the patient can hemorrhage internally or bleed excessively when cut.

urokinase, and lysosomal enzymes released from damaged tissues. Understanding how plasmin is activated has been useful for treating some clotting disorders. In disorders resulting from a blood clot blocking normal blood flow through a vessel, such as a heart attack, dissolving the clot can restore blood flow and reduce damage to tissues. For example, t-PA, urokinase, or streptokinase (a bacterial enzyme) can be injected into the blood or introduced at the clot site by means of a catheter. These substances activate plasmin, which breaks down the clot.

Predict 6

Cedric's doctor recommended taking a small amount of aspirin each morning because Cedric has substantial atherosclerotic plaques in his coronary arteries. One morning, Cedric took his aspirin as usual, but that afternoon he was transported to the emergency room because of a coronary thrombosis. The ER team administered t-PA, and Cedric recovered quickly. What contributed to the rapid improvement in his condition?

ASSESS YOUR PROGRESS

30. *What is a vascular spasm? Name two factors that produce it. What is the source of thromboxanes and endothelin?*

31. *What is the function of a platelet plug? Describe the process of platelet plug formation. How are platelets important to clot formation?*

32. *What is a clot, and what is its function?*

33. *What are clotting factors? What vitamin is required to produce many clotting factors?*

34. *What is the difference between extrinsic and intrinsic activation of clotting? What factor is activated by both pathways?*

35. *What are the three reactions that occur in the common pathway of clotting? What ion is a necessary part of the clotting process?*

36. *What is the function of anticoagulants in blood? Name three anticoagulants in blood, and explain how they prevent clot formation.*

37. *Describe the process of clot retraction. What is serum?*

38. *What is fibrinolysis? How does it occur?*

19.6 Blood Grouping

LEARNING OUTCOMES

After reading this section, you should be able to

A. **Explain the basis of the ABO blood group system and how incompatibilities occur.**

B. **Describe the Rh blood group and its connection to hemolytic disease of the newborn (HDN).**

If large quantities of blood are lost during surgery or due to injury, the patient can go into shock and die unless red blood cells are replaced to restore the blood's oxygen-carrying capacity. In this event, a transfusion or an infusion is required. A **transfusion** is the transfer of blood or blood components from one individual to another. An **infusion,** on the other hand, is the introduction of a fluid other than blood, such as a saline or glucose solution, into the blood. It may be surprising that an infusion would be used to treat someone who has lost a large volume of blood, but in many cases the return of blood volume to normal levels is all that is necessary to prevent shock. Eventually, the body produces enough red blood cells to replace those that were lost.

Early attempts to transfuse blood from one person to another were often unsuccessful because they resulted in transfusion reactions, characterized by clotting within blood vessels, kidney damage, and death. We now know that transfusion reactions are caused by interactions between antigens and antibodies (see chapter 22). Recall from chapter 3 that cells have marker molecules on their membranes to identify them as normal cells of the body. The surfaces of red blood cells have marker molecules called **antigens** (an′ti-jenz), which identify the cells. The plasma contains proteins called **antibodies,** which bind to antigens. Antibodies are very specific, meaning that each antibody can bind only to a certain antigen. When the antibodies in the plasma bind to the antigens on the surfaces of the red blood cells, they form molecular bridges that connect the red blood cells. As a result, **agglutination** (ă-gloo-ti-nā′shŭn), or clumping, of the cells occurs. The combination of the antibodies with the antigens can also initiate reactions that cause hemolysis. Because the antigen-antibody combinations can cause agglutination, the antigens are often called **agglutinogens** (ă-gloo-tin′ō-jenz), and the antibodies are called **agglutinins** (ă-gloo′ti-ninz).

The antigens on the surface of red blood cells have been categorized into **blood groups,** and more than 35 blood groups, most of them rare, have been identified. For transfusions, the ABO and Rh blood groups are among the most important and are described in this text. Other well-known groups, not discussed in this text, are the Lewis, Duffy, MNSs, Kidd, Kell, and Lutheran groups.

ABO Blood Group

The **ABO blood group** system is used to categorize human blood based on the presence or absence of A and B antigens on the surface of red blood cells. Note that there are only two possible antigens associated with the ABO blood group: antigen A and antigen B. Type A blood has type A antigens, type B blood has type B antigens, type AB blood has both A and B antigens, and type O blood has neither A nor B antigens on the surface of red blood cells (figure 19.13). The ABO blood group is an example of codominance in that the A and B antigens can be expressed at the same time (see chapter 29).

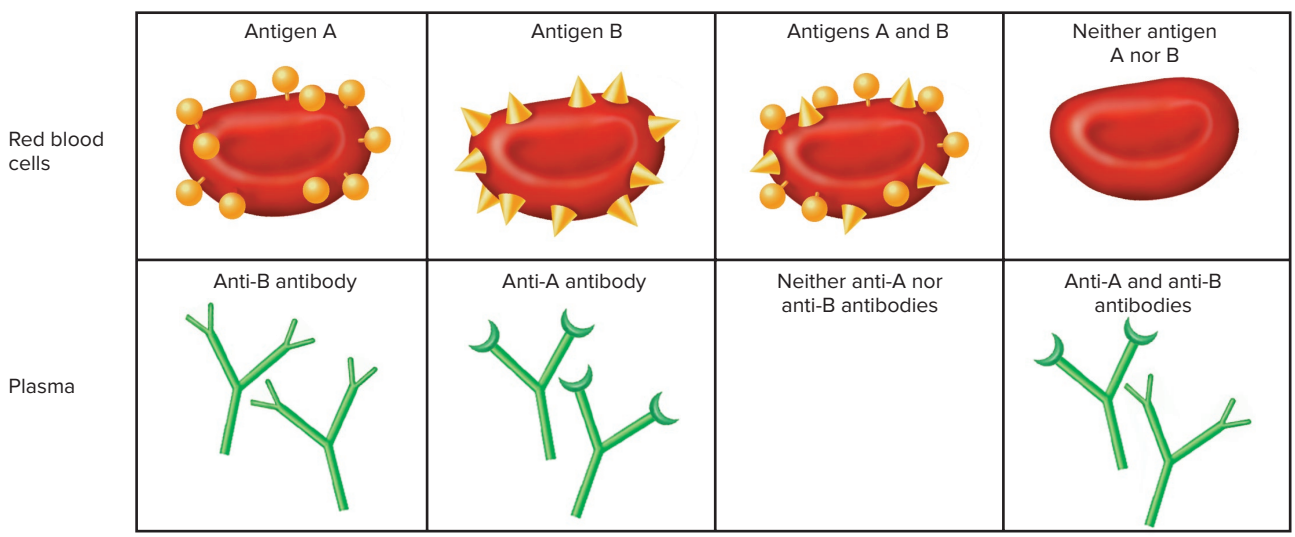
In addition to the type A and type B antigens of the ABO group, there are two types of antibodies associated with this blood group: anti-A antibody and anti-B antibody. Anti-A antibodies act against type A antigens and anti-B antibodies act against type B antigens. Because the interaction between antigens and antibodies leads to the destruction of the red blood cells, we would not expect to find matching antigens and antibodies occurring naturally in the blood. Instead, we would expect to find antibodies for the antigens that are not present. Thus, plasma from type A blood contains anti-B antibodies, and plasma from type B blood contains anti-A antibodies. Type AB blood has neither type of antibody, and type O blood has both anti-A and anti-B antibodies (see figure 19.13).

The ABO blood types do not exist in equal numbers in a population. In Caucasians in the United States, the distribution is 47% type O, 41% type A, 9% type B, and 3% type AB. Among African-Americans, the distribution is 46% type O, 27% type A, 20% type B, and 7% type AB.

Normally, antibodies do not develop against an antigen unless the body is exposed to that antigen. In the case of the antibodies associated with the ABO blood group, scientists are unsure exactly how this exposure occurs. One possible explanation for the production of anti-A and/or anti-B antibodies is that type A or B antigens on bacteria or food in the digestive tract stimulate the formation of antibodies against antigens that are different from the body's own antigens. In support of this explanation, anti-A and anti-B antibodies are not found in the blood until about 2 months after birth. It is possible that an infant with type A blood produces anti-B antibodies against the B antigens on bacteria or food. Meanwhile, an infant with A antigens does not produce antibodies against the A antigens on bacteria or food because mechanisms exist in the body to prevent the production of antibodies that react with the body's own antigens (see chapter 22).

In the event of a blood transfusion, it is very important to match the blood types of both the donor and the recipient to avoid transfusion reactions. When a blood transfusion is performed, the **donor** is the person who gives blood, and the **recipient** is the person who receives it. Usually, a recipient can successfully receive blood from a donor as long as they both have the same blood type. For example, a person with type A blood can receive blood from a person with type A blood. No ABO transfusion reaction occurs because the recipient has no anti-A antibodies against the type A antigen. On the other hand, if type A blood were donated to a person with type B blood, a transfusion reaction would occur because the person with type B blood has anti-A antibodies. These anti-A antibodies would act against the type A antigens on the red blood cells in the donated blood, causing agglutination (figure 19.14).

Type O blood is characterized by the absences of either type A or type B antigens. Because the red blood cells lack the antigens, neither anti-A nor anti-B antigens can react with these cells. People with type O blood are often called universal donors because they can usually give blood to the other ABO blood types without



Type A
Red blood cells with type A surface antigens and plasma with anti-B antibodies

Type B
Red blood cells with type B surface antigens and plasma with anti-A antibodies

Type AB
Red blood cells with both type A and type B surface antigens and neither anti-A nor anti-B plasma antibodies

Type O
Red blood cells with neither type A nor type B surface antigens but both anti-A and anti-B plasma antibodies

FIGURE 19.13 ABO Blood Groups
For simplicity, only parts of the anti-A and anti-B antibodies are illustrated. Each antibody has five identical, Y-shaped arms (see chapter 22).

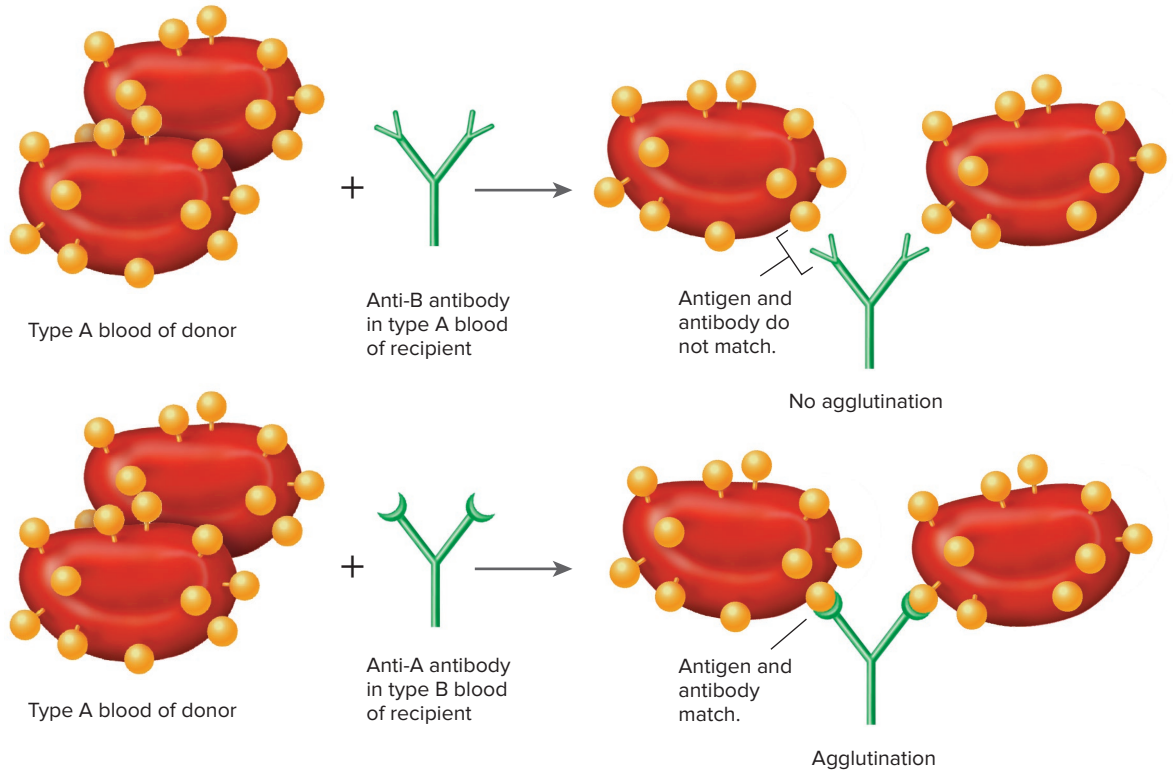


FIGURE 19.14 Agglutination Reaction

(*a*) Because the donor blood and recipient blood have the same antigens (type A) on the red blood cells, no agglutination reaction occurs. (*b*) An agglutination reaction occurs when the anti-A antibodies of the recipient attach to the type A antigens on the red blood cells in the donor blood. For simplicity, only parts of the anti-A and anti-B antibodies are illustrated. Each antibody has five identical, Y-shaped arms (see chapter 22).

causing an ABO transfusion reaction. For example, if a person with type A blood receives type O blood, the type O red blood cells do not react with the anti-B antibodies in the recipient's blood.

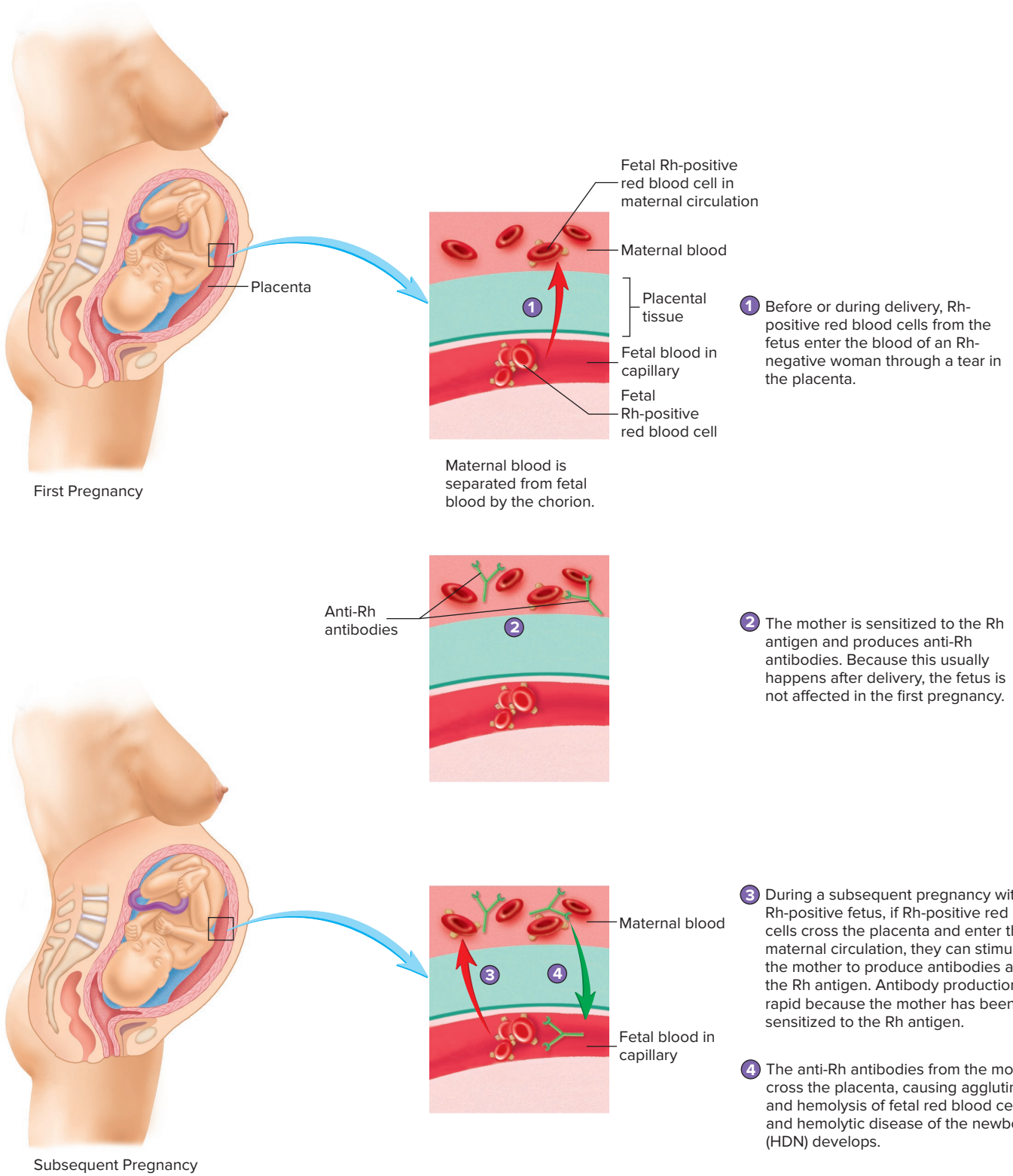
The term *universal donor* is misleading, however. Transfusion of type O blood can still produce a transfusion reaction in one of two ways: First, other blood groups can cause a transfusion reaction. Second, antibodies in the donor's blood can react with antigens in the recipient's blood. For example, type O blood has anti-A and anti-B antibodies. If type O blood is transfused into a person with type A blood, the anti-A antibodies (in the type O blood) react against the A antigens (in the type A blood). Usually, such reactions are not serious because the antibodies in the donor's blood are diluted in the larger volume of the recipient's blood, and few reactions take place. Blood banks separate donated blood into several products, such as packed red blood cells, plasma, platelets, and cryoprecipitate, which contains von Willebrand factor, clotting factors, and fibrinogen. This process allows the donated blood to be used by multiple recipients, each of whom may need only one of the blood components. Type O packed red blood cells are unlikely to cause an ABO transfusion reaction when given to a person with a different blood type because the transfusion fluid contains concentrated red blood cells with very little plasma containing anti-A and anti-B antibodies.

Rh Blood Group

A second clinically important blood group is the Rh blood group. The **Rh blood group** is so named because it was first studied in rhesus monkeys. The antigen involved in this blood group is the D antigen. People are Rh-positive if they have the D antigen on the surface of their red blood cells, and people are Rh-negative if they do not have the D antigen. About 85% of Caucasians in the United States and 88% of African-Americans are Rh-positive. The ABO blood type and the Rh blood type are usually expressed together. For example, a person designated type A in the ABO blood group and Rh-positive is said to be A-positive. The rarest combination in the United States is AB-negative, which occurs in less than 1% of the population.

Unlike the natural occurrence of anti-A and anti-B antibodies in the blood, antibodies against the Rh antigen do not develop unless an Rh-negative person is exposed to Rh-positive blood. This can occur either through a transfusion or when blood crosses the placenta to a mother from her fetus.

Rh incompatibility can pose a major problem in a pregnancy when the mother is Rh-negative and the fetus is Rh-positive. If fetal blood leaks through the placenta and mixes with the mother's blood, the mother becomes sensitized to the Rh antigen and produces anti-Rh antibodies. These antibodies can cross the placenta and enter the fetal blood. In the fetal blood, the Rh antibodies will act against the D antigens on the red blood cells and cause agglutination and hemolysis of fetal red blood cells. This disorder is called **hemolytic** (hē-mō-lit′ik) **disease of the newborn (HDN),** or *erythroblastosis fetalis* (ĕ-rith′rō-blas-tō′sis fē-ta′lis; figure 19.15). In the mother's first pregnancy, there is often no problem. The leakage of fetal blood is usually the result of a tear in the placenta that takes place



PROCESS FIGURE 19.15 Hemolytic Disease of the Newborn (HDN)

Rh incompatibility may occur in a pregnancy when the mother is Rh-negative and the fetus is Rh-positive. The concern is usually for later pregnancies, after the mother has become sensitized to the Rh antigen and is capable of producing anti-Rh antibodies at a faster and greater rate.

? *Explain why there is no concern for Rh incompatibilities in a pregnancy where the mother is Rh-positive and the fetus is Rh-negative.*

Case STUDY 19.1 Treatment of Hemolytic Disease of the Newborn

Billy was born with hemolytic disease of the newborn (HDN). He was treated with exchange transfusion, erythropoietin, and phototherapy. An exchange transfusion replaced Billy's blood with donor blood. In this procedure, as the donor's blood was transfused into Billy, his blood was withdrawn. During fetal development, the increased rate of red blood cell destruction caused by the mother's anti-Rh antibodies results in lower-than-normal numbers of red blood cells, a condition called **anemia** (ă-nē′mē-ă). It also results in increased levels of bilirubin. Although high levels of bilirubin can damage the brain by killing nerve cells, this is not usually a problem in the fetus because the bilirubin is removed by the placenta. Following birth, bilirubin levels can increase because red blood cells continue to lyse, and the newborn's liver is unable to handle the large bilirubin load. However, in phototherapy, blood that passes through the skin is exposed to blue or white lights, which break down bilirubin to less toxic compounds that the newborn's liver can remove.

Predict 7

Answer the following questions about Billy's treatment for HDN.

a. What is the purpose of giving Billy an exchange transfusion?

b. Explain the reason for giving Billy erythropoietin.

c. Just before birth, would Billy's erythropoietin levels have been higher or lower than those of a fetus without HDN?

d. After birth, but before treatment, did Billy's erythropoietin levels increase or decrease?

e. When treating HDN with an exchange transfusion, should the donor's blood be Rh-positive or Rh-negative? Explain.

f. Does giving an Rh-positive newborn a transfusion of Rh-negative blood change the newborn's blood type? Explain.

either late in the pregnancy or during delivery. Thus, there is not sufficient time for the mother to produce enough anti-Rh antibodies to harm the fetus. However, if sensitization occurs, it can cause problems in a subsequent pregnancy. First, once a woman is sensitized and produces anti-Rh antibodies, she may continue to produce the antibodies throughout her life. Thus, in a subsequent pregnancy, anti-Rh antibodies may already be present. Second, and especially dangerous in a subsequent pregnancy with an Rh-positive fetus, if any fetal blood leaks into the mother's blood, she rapidly produces large amounts of anti-Rh antibodies, resulting in HDN. Because HDN can be fatal to the fetus, the levels of anti-Rh antibodies in the mother should be monitored. If they increase to unacceptable levels, the fetus should be tested to determine the severity of the HDN. In severe cases, a transfusion to replace lost red blood cells can be performed through the umbilical cord, or the baby can be delivered if mature enough.

Prevention of HDN is often possible if the Rh-negative mother is injected with a specific type of antibody preparation, called Rh_o(D) immune globulin (RhoGAM), which contains antibodies against Rh antigens. The injection can be given during the pregnancy, before delivery, or immediately after each delivery, miscarriage, or abortion. The injected antibodies bind to the Rh antigens of any fetal red blood cells that may have entered the mother's blood. This treatment inactivates the fetal Rh antigens and prevents sensitization of the mother. However, if sensitization has already occurred, the treatment is ineffective.

ASSESS YOUR PROGRESS

39. *What are blood groups, and how do they cause transfusion reactions? What is agglutination?*

40. *What kinds of antigens and antibodies are found in each of the four ABO blood types?*

41. *Why is a person with type O blood considered a universal donor?*

42. *What does it mean to be Rh-positive?*

43. *What Rh blood types must the mother and the fetus have before HDN can occur?*

44. *Why does HDN usually not develop in the first pregnancy?*

19.7 Diagnostic Blood Tests

LEARNING OUTCOMES

After reading this section, you should be able to

A. **Describe diagnostic blood tests and the normal values for the tests.**

B. **Give examples of disorders that produce abnormal test values.**

Type and Crossmatch

To prevent transfusion reactions, blood is typed. **Blood typing** determines the ABO and Rh blood groups of the blood sample. Typically, the cells are separated from the serum and then tested with known antibodies to determine the type of antigen on the cell surface (figure 19.16). For example, if a patient's blood cells agglutinate when mixed with anti-A antibodies but do not agglutinate when mixed with anti-B antibodies, the cells have type A antigen. In a similar fashion, the serum is mixed with known cell types (antigens) to determine the type of antibodies in the serum. Normally, donor blood must match the ABO and Rh type of the recipient.

FIGURE 19.16 Blood Typing
Blood types are often determined by separating the blood cells from the plasma and then testing them with known antibodies. Agglutination, as seen in the middle and right-hand samples on the slide, indicates the presence of the antigen for the known antibody. Lack of agglutination as seen in the left-hand sample on the slide, indicates that the antigen for the known antibody is not present. ©jarun011/Getty Images

The International Society of Blood Transfusion recognizes 29 important blood groups, including the ABO and Rh groups. Because any of these blood groups can cause a transfusion reaction, a crossmatch is performed. In a **crossmatch,** the donor's blood cells are mixed with the recipient's serum, and the donor's serum is mixed with the recipient's cells. The donor's blood is considered safe for transfusion only if no agglutination occurs in either match.

Complete Blood Count

A **complete blood count (CBC)** is an analysis of blood that provides much useful information. A CBC consists of a red blood count, hemoglobin and hematocrit measurements, a white blood count, and a differential white blood count.

Red Blood Count

Blood cell counts are usually performed with an electronic instrument, but they can also be done manually with a microscope. A **red blood count (RBC)** is the number (expressed in millions) of red blood cells per microliter of blood. A normal RBC for a male is 4.7–6.1 million/μL of blood; for a female, a normal RBC is 4.2–5.4 million/μL of blood. The condition called **erythrocytosis** (ĕ-rith′rō-sī-tō′sis) is an overabundance of red blood cells (see table 19.4).

Hemoglobin Measurement

A **hemoglobin measurement** determines the amount of hemoglobin in a given volume of blood, usually expressed as grams of hemoglobin per 100 mL of blood. The normal hemoglobin count for a male is 14–17 g/100 mL of blood, and for a female it is 12–15 g/100 mL of blood. Abnormally low hemoglobin is an indication of anemia (see table 19.4).

Hematocrit Measurement

The hematocrit (hē′mă-tō-krit, hem′ă-tō-krit) is the percentage of the total blood volume that is composed of red blood cells. One way to determine hematocrit is to place blood in a tube and spin it in a centrifuge. The formed elements, which are heavier than the plasma, are forced to one end of the tube (figure 19.17). Of these, the white blood cells and platelets form a thin, whitish layer, called the buffy coat, between the plasma and the red blood cells. The red blood cells account for 40–54% of the total blood volume in males and 38–47% in females.

The number and size of red blood cells affect the hematocrit measurement. **Normocytes** (nōr′mō-sītz) are normal-sized red blood cells with a diameter of 7.5 mm. **Microcytes** (mī′krō-sītz) are smaller than normal, with a diameter of 6 μm or less, and **macrocytes** (ma′krō-sītz) are larger than normal, with a diameter of 9 μm or greater. Blood disorders can result in an abnormal hematocrit measurement because they cause red blood cell numbers to be abnormally high or low or cause the red blood cells themselves to be abnormally small or large (see table 19.4). A decreased hematocrit indicates that the volume of red blood cells is less than normal. This can result from a decreased number of normocytes or a normal number of microcytes. For example, inadequate iron in the diet can impair hemoglobin production. Consequently, during their formation, red blood cells do not fill with hemoglobin, and they remain smaller than normal.

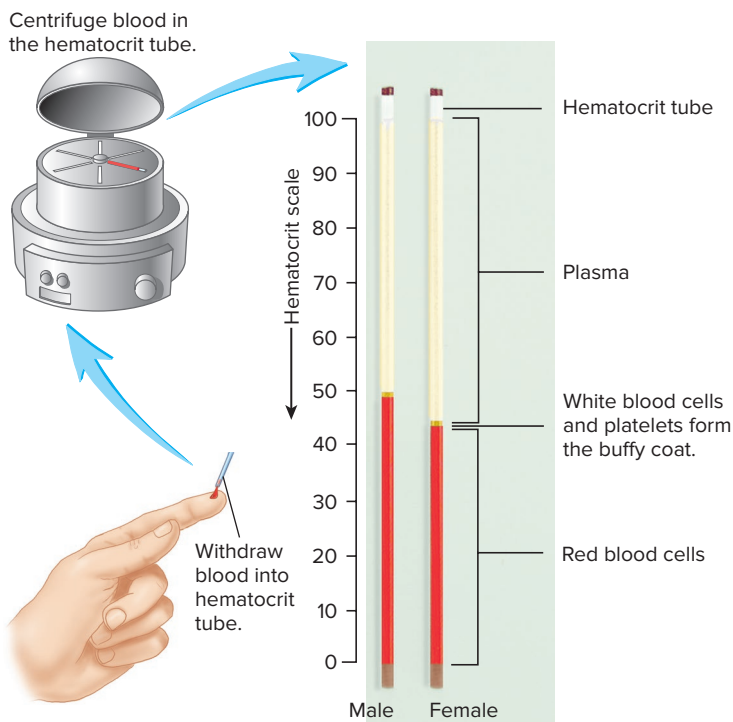


FIGURE 19.17 Hematocrit
Blood is withdrawn into a capillary tube and spun in a centrifuge. The blood is separated into plasma and red blood cells, with a narrow layer of white blood cells and platelets forming in between. The hematocrit is the percentage of the total blood volume that is composed of red blood cells. It does not include the white blood cells and platelets. Normal hematocrits for a male and a female are shown.

TABLE 19.4 Representative Diseases and Disorders of Blood

Condition	Description
Erythrocytosis	
Relative erythrocytosis	Overabundance of red blood cells due to decreased blood volume, as may result from dehydration, diuretics, or burns
Primary erythrocytosis (polycythemia vera)	Stem cell defect of unknown cause; results in overproduction of red blood cells, granulocytes, and platelets; signs include low erythropoietin levels and enlarged spleen; increased blood viscosity and blood volume can cause clogging of the capillaries and hypertension
Secondary erythrocytosis	Overabundance of red blood cells resulting from decreased O_2 supply, as occurs at high altitudes, in chronic obstructive pulmonary disease, and in congestive heart failure; decreased O_2 delivery to the kidney stimulates the secretion of erythropoietin, resulting in increased blood viscosity and blood volume that can cause clogging of the capillaries and hypertension
Anemia	Deficiency of hemoglobin in the blood
Iron-deficiency anemia	Caused by insufficient intake or absorption of iron or by excessive iron loss; leads to reduced hemoglobin production
Folate-deficiency anemia	Folate is important in DNA synthesis; inadequate folate in the diet results in a reduction in cell division and therefore a reduced number of red blood cells
Pernicious anemia	Secondary folate-deficiency anemia caused by inadequate amounts of vitamin B_{12}, which is important for folate synthesis
Hemorrhagic anemia	Results from blood loss due to trauma, ulcers, or excessive menstrual bleeding
Hemolytic anemia	Occurs when red blood cells rupture or are destroyed at an excessive rate; causes include inherited defects, exposure to certain drugs or snake venom, response to artificial heart valves, autoimmune disease, and hemolytic disease of the newborn
Aplastic anemia	Caused by an inability of the red bone marrow to produce red blood cells, usually as a result of damage to stem cells after exposure to certain drugs, chemicals, or radiation
Thalassemia	Autosomal recessive disease that results in insufficient production of globin part of hemoglobin
Leukemia	Cancers of the red bone marrow in which one or more white blood cell types is produced; cells are usually immature or abnormal and lack normal immunological functions
Thrombocytopenia	Reduction in the number of platelets that leads to chronic bleeding through small vessels and capillaries; causes include genetics, autoimmune disease, infections, and decreased platelet production resulting from pernicious anemia, drug therapy, radiation therapy, or leukemias
Clotting Disorders	
Disseminated intravascular coagulation (DIC)	Clotting throughout the vascular system, followed by bleeding; may develop when normal regulation of clotting by anticoagulants is overwhelmed, as occurs due to massive tissue damage; also caused by alteration of the lining of the blood vessels resulting from infections or snakebites
Von Willebrand disease	Most common inherited bleeding disorder; platelet plug formation and the contribution of activated platelets to blood clotting are impaired; treatments are injection of von Willebrand factor or administration of drugs that increase von Willebrand factor levels in blood, which helps platelets adhere to collagen and become activated
Hemophilia	Genetic disorder in which clotting is abnormal or absent; each of the several types results from deficiency or dysfunction of a clotting factor; most often a sex-linked trait that occurs almost exclusively in males
Infectious Diseases of Blood	
Septicemia (blood poisoning)	Spread of microorganisms and their toxins by the blood; often the result of a medical procedure, such as insertion of an intravenous tube; release of toxins by bacteria can cause septic shock, producing decreased blood pressure and possibly death
Malaria	Caused by a protozoan introduced into blood by *Anopheles* mosquito; symptoms include chills and fever produced by toxins released when the protozoan causes red blood cells to rupture
Infectious mononucleosis	Caused by Epstein-Barr virus, which infects salivary glands and lymphocytes; symptoms include fever, sore throat, and swollen lymph nodes, all probably produced by the immune system response to infected lymphocytes
Acquired immunodeficiency syndrome (AIDS)	Caused by human immunodeficiency virus (HIV), which infects lymphocytes and suppresses immune system

White Blood Count

A **white blood count (WBC)** measures the total number of white blood cells in the blood. Normally, 4500–11,000 white blood cells are present in each microliter of blood. **Leukopenia** (loo-kō-pē′nē-ă) is a lower-than-normal WBC resulting from depression or destruction of the red marrow. Viral infections, radiation, drugs, tumors, and vitamin deficiencies (B_{12} or folate) can cause leukopenia. **Leukocytosis** (loo′kō-sī-tō′sis) is an abnormally high WBC. **Leukemia** (loo-kē′mē-ă), a cancer of the red marrow, often results in leukocytosis, but the white blood cells have an abnormal structure and function as well. Bacterial infections can also cause leukocytosis by stimulating neutrophils to increase in number.

Differential White Blood Count

A **differential white blood count** determines the percentage of each of the five kinds of white blood cells. Normally, neutrophils account for 55–70%; lymphocytes, 20–40%; monocytes, 2–8%; eosinophils, 1–4%; and basophils, 0.5–1%. A differential WBC can provide insight into a patient's condition. For example, in patients with bacterial infections the neutrophil count is often greatly increased, whereas in patients with allergic reactions the eosinophil and basophil counts are elevated.

Clotting

The blood's ability to clot can be assessed by the platelet count and the prothrombin time measurement.

Platelet Count

A normal **platelet count** is 150,000–400,000 platelets per microliter of blood. In the condition called **thrombocytopenia** (throm′bō-sī-tō-pē′nē-ă), the platelet count is greatly reduced, resulting in chronic bleeding through small vessels and capillaries. It can be caused by decreased platelet production as a result of hereditary disorders, lack of vitamin B_{12}, drug therapy, or radiation therapy.

Prothrombin Time Measurement

Prothrombin time measurement expresses how long it takes for the blood to start clotting, which is normally 9–12 seconds. Prothrombin time is determined by adding thromboplastin to whole plasma. Thromboplastin is a chemical released from injured tissues that starts the process of clotting (see figure 19.12). Prothrombin time is officially reported as the International Normalized Ratio (INR), which standardizes the time blood takes to clot based on the slightly different thromboplastins used by different labs. Because many clotting factors must be activated to form fibrin, a deficiency of any one of them can cause the prothrombin time to be abnormal. Vitamin K deficiency, certain liver diseases, and drug therapy can increase prothrombin time.

Blood Chemistry

The composition of materials dissolved or suspended in the plasma can be used to assess the functioning of many of the body's systems. For example, high blood glucose levels can indicate that the pancreas is not producing enough insulin; high blood urea nitrogen (BUN) can be a sign of reduced kidney function; increased bilirubin can indicate liver dysfunction or hemolysis; and high cholesterol levels can signify an increased risk for cardiovascular disease. A number of blood chemistry tests are routinely done when a blood sample is taken, and additional tests are available.

Predict 8

When a patient complains of acute pain in the abdomen, the physician suspects appendicitis, which is often caused by a bacterial infection of the appendix. What blood test should be done to support the diagnosis?

ASSESS YOUR PROGRESS

45. *What occurs in a type and crossmatch?*
46. *What tests are included in a CBC? Give the normal value, and name a disorder that would cause an abnormal test result for each.*
47. *What are the normal values for a platelet count and a prothrombin time measurement? Name a disorder that would cause an abnormal result for each test.*
48. *What are some examples of blood chemistry tests?*

Answer

Learn to Predict

Frankie's feeling of fatigue and her blood test results are consistent with anemia. A low red blood cell count with microcytic cells, low hemoglobin, and a low hematocrit are all indicators of iron deficiency anemia.

The increased reticulocyte count indicated an increased rate of red blood cell production. But if red blood cell production was increased, why was Frankie's red blood cell count still low? We learned in this chapter that red blood cell production is regulated by the hormone erythropoietin. Specifically, reduced red blood cell numbers, as indicated by Frankie's blood test, caused less oxygen to be transported to her kidneys. Consequently, her kidneys secreted more erythropoietin, which resulted in increased red blood cell production in the red bone marrow. Because of Frankie's iron deficiency, which caused hemoglobin synthesis to slow, the newly synthesized red blood cells were smaller than normal, or microcytic. Remember, Frankie also complained of intense abdominal pain. The evidence of hemoglobin in her feces suggested that Frankie is losing blood into her digestive tract, which, considering her abdominal pain, would be consistent with having an ulcer. Frankie's doctor would need to order additional tests to confirm the presence of ulcers before determining treatment.

Answers to the odd-numbered Predict questions from this chapter appear in appendix E.

Summary

19.1 Functions of Blood

1. Blood transports gases, nutrients, waste products, processed molecules, and regulatory molecules.
2. Blood is involved in the regulation of pH, osmosis, and body temperature.
3. Blood protects against disease and initiates tissue repair.

19.2 Composition of Blood

Blood is a type of connective tissue that consists of plasma and formed elements.

19.3 Plasma

1. Plasma is mostly water (91%) and contains proteins, such as albumin (maintains osmotic pressure), globulins (function in transport and immunity), fibrinogen (involved in clot formation), and hormones and enzymes (involved in regulation).
2. Plasma contains ions, nutrients, waste products, and gases.

19.4 Formed Elements

The formed elements are red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (cell fragments).

Production of Formed Elements

1. In the embryo and fetus, the formed elements are produced in a number of locations.
2. After birth, red bone marrow becomes the source of the formed elements.
3. All formed elements are derived from hemocytoblast, which gives rise to two intermediate stem cells: myeloid stem cells and lymphoid stem cells. Myeloid stem cells give rise to red blood cells, platelets, and most of the white blood cells. Lymphoid stem cells give rise to lymphocytes.

Red Blood Cells

1. Red blood cells are biconcave discs containing hemoglobin and carbonic anhydrase.
   - A hemoglobin molecule consists of four heme and four globin molecules. The heme molecules transport oxygen, and the globin molecules transport carbon dioxide and nitric oxide. Iron is required for oxygen transport.
   - Carbonic anhydrase is involved with the transport of carbon dioxide.
2. Erythropoiesis is the production of red blood cells.
   - Stem cells in red bone marrow eventually give rise to late erythroblasts, which lose their nuclei and are released into the blood as reticulocytes. Loss of the endoplasmic reticulum by a reticulocyte produces a red blood cell.
   - In response to low blood oxygen, the kidneys produce erythropoietin, which stimulates erythropoiesis.
3. Hemoglobin from ruptured red blood cells is phagocytized by macrophages. The hemoglobin is broken down, and heme becomes bilirubin, which is secreted in bile.

White Blood Cells

1. White blood cells protect the body against microorganisms and remove dead cells and debris.
2. Five types of white blood cells exist.
   - Neutrophils are small, phagocytic cells.
   - Eosinophils attack certain worm parasites and modulate inflammation.
   - Basophils release histamine and are involved with increasing the inflammatory response.
   - Lymphocytes are important in immunity, including the production of antibodies.
   - Monocytes leave the blood, enter tissues, and become large, phagocytic cells called macrophages.

Platelets

Platelets, or thrombocytes, are cell fragments pinched off from megakaryocytes in the red bone marrow.

19.5 Hemostasis

Hemostasis, the cessation of bleeding, is very important to the maintenance of homeostasis.

Vascular Spasm

Vasoconstriction of damaged blood vessels reduces blood loss.

Platelet Plug Formation

1. Platelets repair minor damage to blood vessels by forming platelet plugs.
   - In platelet adhesion, platelets bind to collagen in damaged tissues.
   - In the platelet release reaction, platelets release chemicals that activate additional platelets.
   - In platelet aggregation, platelets bind to one another to form a platelet plug.
2. Platelets also release chemicals involved with coagulation.

Coagulation

1. Coagulation is the formation of a blood clot.
2. The first stage of coagulation occurs through the extrinsic or intrinsic pathway. Both pathways end with the production of activated factor X.
   - The extrinsic pathway begins with the release of thromboplastin from damaged tissues.
   - The intrinsic pathway begins with the activation of factor XII.
3. Activated factor X, factor V, phospholipids, and Ca^{2+} form prothrombinase.
4. Prothrombinase converts prothrombin to thrombin.
5. Thrombin converts fibrinogen to fibrin. The insoluble fibrin forms the clot.

Control of Clot Formation

1. Heparin and antithrombin inhibit thrombin activity. Therefore, fibrinogen is not converted to fibrin, and clot formation is inhibited.
2. Prostacyclin counteracts the effects of thrombin.

Clot Retraction and Dissolution

1. Clot retraction results from the contraction of platelets, which pull the edges of damaged tissue closer together.
2. Serum, which is plasma minus fibrinogen and some clotting factors, is squeezed out of the clot.
3. Factor XII, thrombin, tissue plasminogen activator, and urokinase activate plasmin, which dissolves fibrin (the clot).

19.6 Blood Grouping

1. Blood groups are determined by antigens on the surface of red blood cells.
2. Antibodies can bind to red blood cell antigens, resulting in agglutination or hemolysis of red blood cells.

ABO Blood Group

1. Type A blood has A antigens, type B blood has B antigens, type AB blood has A and B antigens, and type O blood has neither A nor B antigens.
2. Type A blood has anti-B antibodies, type B blood has anti-A antibodies, type AB blood has neither anti-A nor anti-B antibodies, and type O blood has both anti-A and anti-B antibodies.
3. Mismatching the ABO blood group results in a transfusion reaction.

Rh Blood Group

1. Rh-positive blood has the D antigen, whereas Rh-negative blood does not.
2. Antibodies against the D antigen are produced by an Rh-negative person when the person is exposed to Rh-positive blood.
3. The Rh blood group is responsible for hemolytic disease of the newborn.

19.7 Diagnostic Blood Tests

Type and Crossmatch

Blood typing determines the ABO and Rh blood groups of a blood sample. A crossmatch tests for agglutination reactions between donor and recipient blood.

Complete Blood Count

A complete blood count consists of the following: red blood count, hemoglobin measurement (grams of hemoglobin per 100 mL of blood), hematocrit measurement (percent volume of red blood cells), white blood count, and differential white blood count (the percentage of each type of white blood cell).

Clotting

Platelet count and prothrombin time measurement assess the blood's ability to clot.

Blood Chemistry

The composition of materials dissolved or suspended in plasma (e.g., glucose, urea nitrogen, bilirubin, and cholesterol) can be used to assess the functioning and status of the body's systems.

REVIEW AND COMPREHENSION

1. Which of these is a function of blood?
   a. clot formation
   b. protection against foreign substances
   c. maintenance of body temperature
   d. regulation of pH and osmosis
   e. All of these are correct.

2. Which of these is *not* a component of plasma?
   a. nitrogen c. platelets e. urea
   b. sodium ions d. water

3. Which of these proteins is normally found in the plasma and plays an important role in maintaining the osmotic concentration of the blood?
   a. albumin c. platelets e. globulins
   b. fibrinogen d. hemoglobin

4. Red blood cells
   a. are the least numerous formed element in the blood.
   b. are phagocytic cells.
   c. are produced in the yellow marrow.
   d. do not have a nucleus.
   e. All of these are correct.

5. Given these ways of transporting carbon dioxide in the blood:
   (1) bicarbonate ions
   (2) combined with blood proteins
   (3) dissolved in plasma

   Choose the arrangement that lists them in the correct order from largest to smallest percentage of carbon dioxide transported.
   a. 1,2,3 c. 2,3,1 e. 3,1,2
   b. 1,3,2 d. 2,1,3

6. Each hemoglobin molecule can become associated with _____ oxygen molecule(s).
   a. one d. four
   b. two e. an unlimited number of
   c. three

7. Erythropoietin
   a. is produced mainly by the heart.
   b. inhibits the production of red blood cells.
   c. production increases when blood oxygen decreases.
   d. production is inhibited by testosterone.
   e. All of these are correct.

8. Which of these changes occur(s) in the blood in response to the initiation of a vigorous exercise program?
   a. increased erythropoietin production
   b. increased concentration of reticulocytes
   c. decreased bilirubin formation
   d. Both a and b are correct.
   e. All of these are correct.

9. Which of the components of hemoglobin is correctly matched with its fate following the destruction of a red blood cell?
   a. heme—reused to form a new hemoglobin molecule
   b. globin—broken down into amino acids
   c. iron—mostly secreted in bile
   d. All of these are correct.

10. The blood cells that protect against worm parasites are
    a. eosinophils. c. neutrophils. e. lymphocytes.
    b. basophils. d. monocytes.

11. The most numerous type of white blood cell, whose primary function is phagocytosis, is
    a. eosinophils. c. neutrophils. e. lymphocytes.
    b. basophils. d. monocytes.

12. Monocytes
    a. are the smallest white blood cells.
    b. increase in number during chronic infections.
    c. give rise to neutrophils.
    d. produce antibodies.

13. The smallest white blood cells, which include B cells and T cells, are
    a. eosinophils. c. neutrophils. e. lymphocytes.
    b. basophils. d. monocytes.
14. Platelets
    a. are derived from megakaryocytes.
    b. are cell fragments.
    c. have surface molecules that attach to collagen.
    d. play an important role in clot formation.
    e. All of these are correct.
15. Given these processes in platelet plug formation:
    (1) platelet adhesion (3) platelet release reaction
    (2) platelet aggregation

    Choose the arrangement that lists the processes in the correct order after a blood vessel is damaged.
    a. 1,2,3 c. 3,1,2 e. 2,3,1
    b. 1,3,2 d. 3,2,1
16. A constituent of plasma that forms the network of fibers in a clot is
    a. fibrinogen. c. platelets. e. prothrombinase.
    b. tissue factor. d. thrombin.
17. Given these chemicals:
    (1) activated factor XII (3) prothrombinase
    (2) fibrinogen (4) thrombin

    Choose the arrangement that lists the chemicals in the order they are used during clot formation.
    a. 1,3,4,2 c. 3,2,1,4 e. 3,4,2,1
    b. 2,3,4,1 d. 3,1,2,4
18. The extrinsic pathway
    a. begins with the release of thromboplastin (tissue factor).
    b. leads to the production of activated factor X.
    c. requires Ca^{2+}.
    d. All of these are correct.
19. The chemical involved in the breakdown of a clot (fibrinolysis) is
    a. antithrombin. d. plasmin.
    b. fibrinogen. e. sodium citrate.
    c. heparin
20. A person with type A blood
    a. has anti-A antibodies.
    b. has type B antigens.
    c. will have a transfusion reaction if given type B blood.
    d. All of these are correct.
21. In the United States, the most common blood type is
    a. A positive. c. O positive. e. AB negative.
    b. B positive. d. O negative.

Answers appear in appendix F.

CRITICAL THINKING

1. In hereditary hemolytic anemia, massive destruction of red blood cells occurs. Would you expect the reticulocyte count to be above or below normal? Explain why one of the symptoms of the disease is jaundice. In 1910, physicians discovered that hereditary hemolytic anemia can be treated successfully by removing the spleen. Explain why this treatment is effective.
2. Joseph, a physical education major, wanted to improve his performance in an upcoming marathon race. About 6 weeks before the race, 500 mL of blood was removed from his body, and the formed elements were separated from the plasma. The formed elements were frozen, and the plasma was reinfused into his body. Just before the competition, the formed elements were thawed and injected into his body. Explain why this procedure, called blood doping or blood boosting, would help Joseph's performance. Suggest any possible bad effects.
3. Ben has an infected prostate. His physician prescribed several antibiotics before finding one that was effective. Results of the most recent blood tests indicate that Ben is anemic. After analyzing the following measurements of Ben's blood, identify the type of anemia he has.

	Ben's Values	Normal Values
Red blood count	3.1 million RBCs/mm^3	4.6–6.2 million RBCs/mm^3
Reticulocyte count	0.4%	1–3%
Red blood cells	Normocytic, 7.5 mm	Normocytic, 7.5 mm
White blood count	2800 WBCs/mm^3	5000–10,000 WBCs/mm^3
Hemoglobin	9.0 g/100 mL	14–16.5 g/100 mL
Hematocrit	27%	40–54%
Prothrombin time	20 seconds	11–15 seconds
Platelets	200,000/mm^3	250,000–400,000 platelets/mm^3

Which of the following conclusions is most consistent with the results? Explain.
a. pernicious anemia
b. iron-deficiency anemia
c. aplastic anemia
d. hemorrhagic anemia
e. vitamin B_{12} deficiency

4. Some people habitually use barbiturates to depress feelings of anxiety. Barbiturates cause hypoventilation, a slower-than-normal rate of breathing, because they suppress the respiratory centers in the brain. What happens to the red blood count of a habitual user of barbiturates? Explain.
5. According to an old saying, "good food makes good blood." Name three substances in the diet that are essential for "good blood." What blood disorders develop if these substances are absent from the diet?
6. Grace has a plasma membrane defect in her red blood cells that makes them more susceptible to rupturing. Her red blood cells are destroyed faster than they can be replaced. Are her RBC, hemoglobin, hematocrit, and bilirubin levels below normal, normal, or above normal? Explain.
7. Pam lives in Los Angeles, not far from the beach. She traveled by plane with her fiance, Alex, to Jackson Hole, which is approximately 6000 feet above sea level. They took hikes of increasing length for each of 4 days and rested on the fifth day. On the sixth day, she and Alex hiked to the top of Table Mountain, which is approximately 11,000 feet above sea level. Which of the following was (were) apparent in Pam on the day they climbed Table Mountain? Explain.
   (1) Pam's rate of erythropoietin secretion was increasing.
   (2) Pam's erythrocyte count was increasing.
   (3) Pam's reticulocyte count was increasing.
   (4) Pam's platelet count was increasing.
   a. 1,2,3,4 c. 1,2 e. 1
   b. 1,2,3 d. 2,3

Answers to odd-numbered questions appear in appendix G.

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