THE CARDIOVASCULAR SYSTEM: BLOOD

did you know?

The American Red Cross calls blood donation "The Gift of Life." But many people receiving a blood donation, or transfusion, worry about the safety of the blood they will receive. Many viruses can be transmitted easily from donor to patient through a transfusion. Because the blood supply is carefully screened for the presence of viruses such as HIV (the virus that causes AIDS) and the viruses that cause Hepatitis B and Hepatitis C, the risk of receiving unsafe blood is extremely low. For example, the risk of receiving a unit of HIV-positive blood is 1 in 1.5 million.

Focus on Wellness, page 359

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The ***cardiovascular system*** (*cardio-* = heart; *-vascular* = blood or blood vessels) consists of three interrelated components: blood, the heart, and blood vessels. The focus of this chapter is blood; the next two chapters will cover the heart and blood vessels, respectively.

Functionally, the cardiovascular system transports substances to and from body cells. To perform its functions, blood must circulate throughout the body. The heart serves as the pump for circulation, and blood vessels carry blood from the heart to body cells and from body cells back to the heart.

The branch of science concerned with the study of blood, blood-forming tissues, and the disorders associated with them is ***hematology*** (hēm-a-TOL-ō-jē; *hemo-* or *hemato-* = blood; *-logy* = study of).

looking back to move ahead . . .

- **Blood Tissue (page 90)**
- **Positive Feedback System (page 8)**
- **Phagocytosis (page 51)**

FUNCTIONS OF BLOOD

OBJECTIVE • List and describe the functions of blood.

Blood, a liquid connective tissue, has three general functions: transportation, regulation, and protection.

1. **Transportation.** Blood transports oxygen from the lungs to cells throughout the body and carbon dioxide (a waste product of cellular respiration; see Chapter 20) from the cells to the lungs. It also carries nutrients from the gastrointestinal tract to body cells, heat and waste products away from cells, and hormones from endocrine glands to other body cells.
2. **Regulation.** Blood helps regulate the pH of body fluids. The heat-absorbing and coolant properties of the water in blood plasma (see page 30) and its variable rate of flow through the skin help adjust body temperature. Blood osmotic pressure also influences the water content of cells.
3. **Protection.** Blood clots (becomes gel-like) in response to an injury, which protects against its excessive loss from the cardiovascular system. In addition, white blood cells protect against disease by carrying on phagocytosis and producing proteins called antibodies. Blood contains additional proteins, called interferons and complement, that also help protect against disease.

■ CHECKPOINT

1. Name several substances transported by blood.
2. How is blood protecting?

COMPONENTS OF WHOLE BLOOD

OBJECTIVE • Discuss the formation, components, and functions of whole blood.

Blood is denser and more viscous (thicker) than water. The temperature of blood is about 38°C (100.4°F). Its pH is slightly alkaline, ranging from 7.35 to 7.45. Blood constitutes about 8% of the total body weight. The blood volume is 5 to 6 liters (1.5 gal) in an average-sized adult male and 4 to 5 liters (1.2 gal) in an average-sized adult female. The difference in volume is due to differences in body size.

Whole blood is composed of two portions: (1) *blood plasma*, a liquid that contains dissolved substances, and (2) *formed elements*, which are cells and cell fragments. If a sample of blood is centrifuged (spun at high speed) in a small glass tube, the cells sink to the bottom of the tube and the lighter-weight blood plasma forms a layer on top (Figure 14.1a). Blood is about 45% formed elements and 55% plasma. Normally, more than 99% of the formed elements are red blood cells (RBCs). The percentage of total blood volume occupied by red blood cells is termed the ***hematocrit*** (he-MAT-ō-krit). Pale, colorless white blood cells (WBCs) and platelets occupy less than 1% of total blood volume. They form a very thin layer, called the *buffy coat*, between the packed RBCs and blood plasma in centrifuged blood. Figure 14.1b shows the composition of blood plasma and the numbers of the various types of formed elements in blood.

Blood Plasma

When the formed elements are removed from blood, a straw-colored liquid called ***blood plasma*** (or simply ***plasma***) remains. Plasma is about 91.5% water, 7% proteins, and 1.5% solutes other than proteins. Proteins in the blood, the *plasma proteins*, are synthesized mainly by the liver. The most plentiful plasma proteins are the ***albumins***, which account for about 54% of all plasma proteins. Among other functions, albumins help maintain proper blood osmotic pressure, which is an important factor in the exchange of fluids across capillary walls. ***Globulins***, which compose 38% of plasma proteins, include ***antibodies***, defensive proteins produced during certain immune responses. ***Fibrinogen*** makes up about 7% of plasma proteins and is a key protein in formation of blood clots. Other solutes in plasma include electrolytes, nutrients, gases, regulatory substances such as enzymes and hormones, vitamins, and waste products.

Formed Elements

The ***formed elements*** of the blood are the following (see Figure 14.2 on page 348):

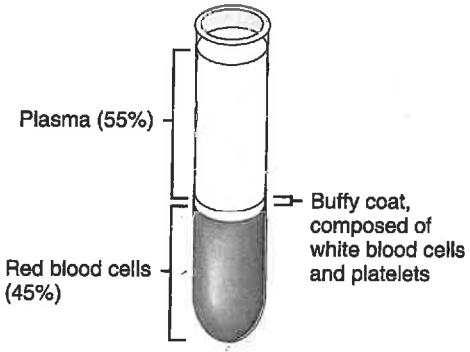
- I. Red blood cells
- II. White blood cells
  - A. Granular leukocytes (contain conspicuous granules that are visible under a light microscope after staining)
    1. Neutrophils
    2. Eosinophils
    3. Basophils
  - B. Agranular leukocytes (no granules are visible under a light microscope after staining)
    1. T and B lymphocytes and natural killer cells
    2. Monocytes
- III. Platelets

Formation of Blood Cells

The process by which the formed elements of blood develop is called ***hemopoiesis*** (hē-mō-poy-Ē-sis; *-poiesis* = making)

Figure 14.1 Components of blood in a normal adult.

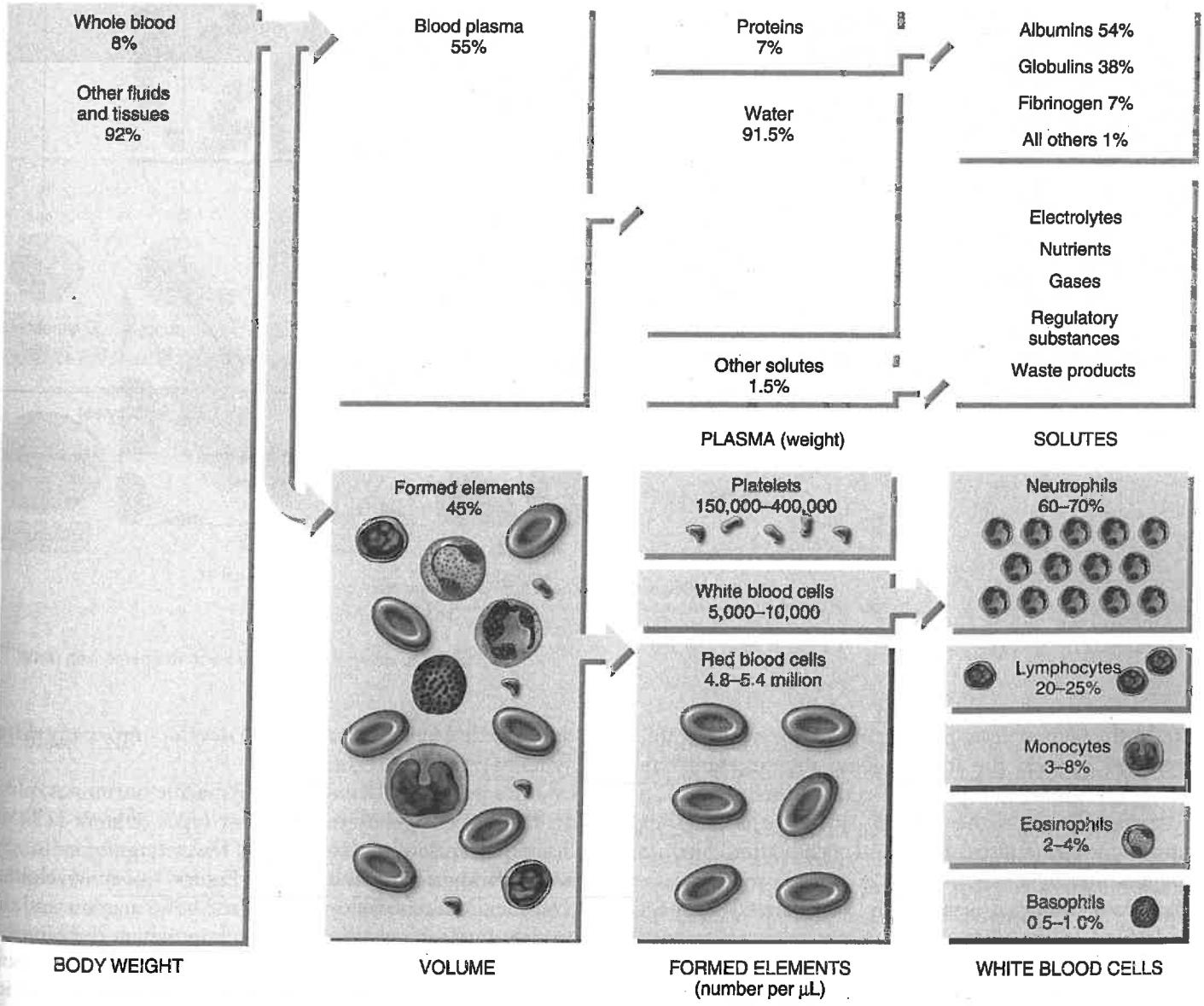
Blood is a connective tissue that consists of blood plasma (liquid) plus formed elements: red blood cells, white blood cells, and platelets.



(a) Appearance of centrifuged blood

Functions of Blood

1. Transport of oxygen, carbon dioxide, nutrients, hormones, heat, and wastes.
2. Regulation of pH, body temperature, and water content of cells.
3. Protection against blood loss through clotting
4. Protection against disease through platelets; phagocytic white blood cells; and proteins such as antibodies, complement, and interferons

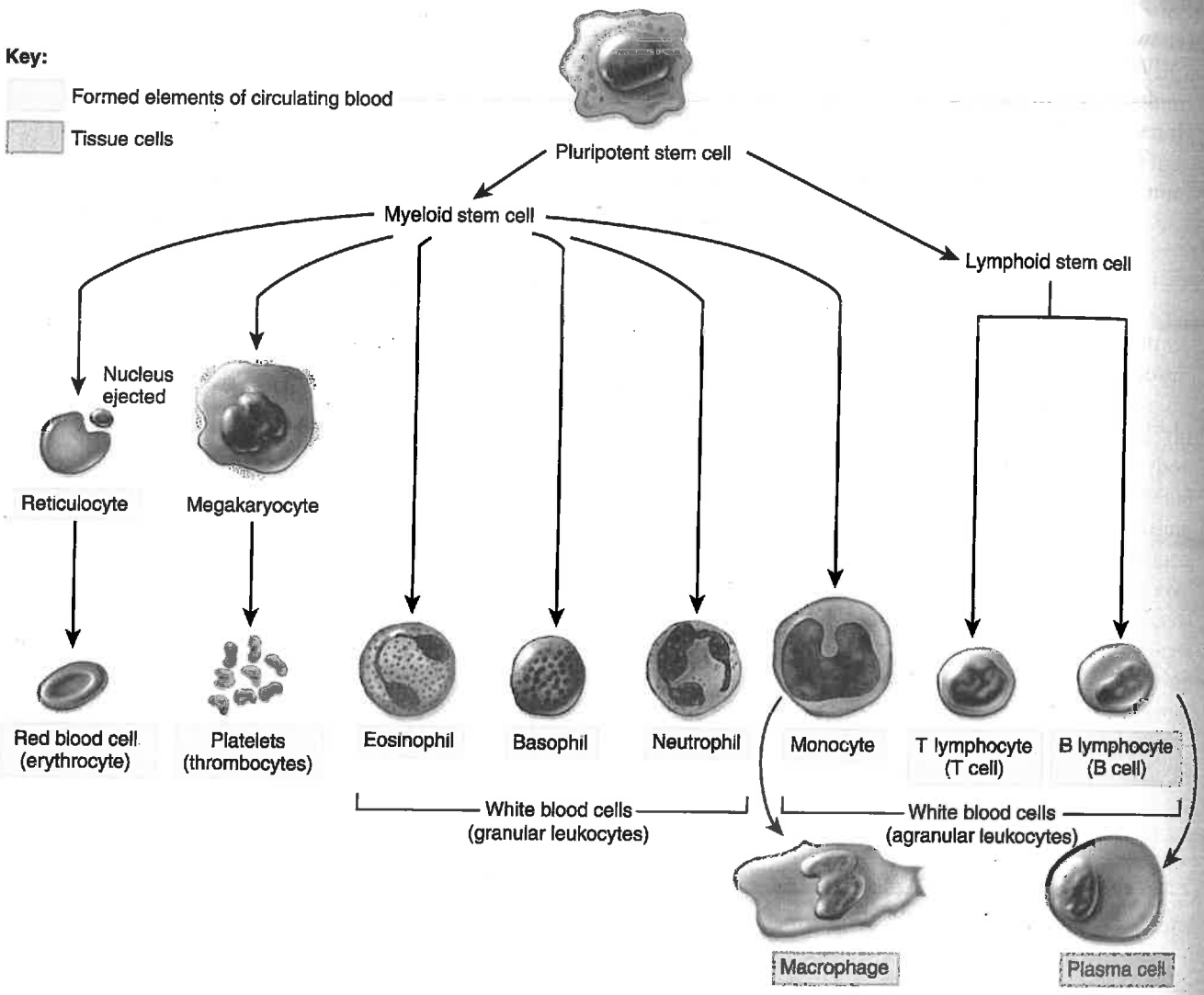


(b) Components of blood

Which formed elements of blood are most numerous?

Figure 14.2 Origin, development, and structure of blood cells. Some of the generations of some cell lines have been omitted.

Blood cell production, called hemopoiesis, occurs in red bone marrow after birth.

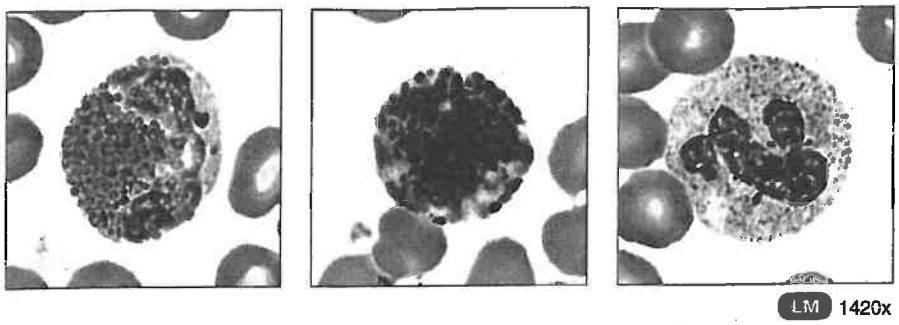


(a) Origin of blood cells from pluripotent stem cells

Before birth, hemopoiesis first occurs in the yolk sac of an embryo and later in the liver, spleen, thymus, and lymph nodes of a fetus. In the last three months before birth, red bone marrow becomes the primary site of hemopoiesis and continues as the source of blood cells after birth and throughout life.

Red bone marrow is a highly vascularized connective tissue located in the microscopic spaces between trabeculae of spongy bone tissue. It is present chiefly in bones of the axial skeleton, pectoral and pelvic girdles, and the proximal epiphyses of the humerus and femur. About 0.05–0.1% of red bone marrow cells are cells called ***pluripotent stem cells*** (ploo-RIP-ō-tent; *pluri-* = several). Pluripotent stem cells are cells that have the capacity to develop into many different types of cells (Figure 14.2a).

In response to stimulation by specific hormones, pluripotent stem cells generate two other types of stem cells which have the capacity to develop into fewer types of cells: *myeloid stem cells* and *lymphoid stem cells* (Figure 14.2a). Myeloid stem cells begin their development in red bone marrow and differentiate into several types of cells from which red blood cells, platelets, eosinophils, basophils, neutrophils, and monocytes develop. Lymphoid stem cells begin their development in red bone marrow but complete it in lymphatic tissues. They differentiate into cells from which the T and B lymphocytes develop.



(b) Photomicrographs

What percentage of body weight is made up of blood?

Red Blood Cells

RBC STRUCTURE ***Red blood cells (RBCs)*** or ***erythrocytes*** (e-RITH-rō-sīts; *erythro-* = red; *-cyte* = cell) contain the oxygen-carrying protein ***hemoglobin***, which is a pigment that gives whole blood its red color. Hemoglobin also transports about 23% of the carbon dioxide in the blood. A healthy adult male has about 5.4 million red blood cells per microliter (μL) of blood, and a healthy adult female has about 4.8 million. (One drop of blood is about 50μL.) Again this difference reflects differences in body size. To maintain normal numbers of RBCs, new mature cells must enter the circulation at the astonishing rate of at least 2 million per second, a pace that balances the equally high rate of RBC destruction. RBCs are biconcave (concave on both sides) discs averaging about 8μm* in diameter. Mature RBCs lack a nucleus and other organelles and can neither reproduce nor carry on extensive metabolic activities. However, all of their internal space is available for oxygen and carbon dioxide transport. Essentially, RBCs consist of a selectively permeable plasma membrane, cytosol, and hemoglobin.

*1μm = 1/25,000 of an inch or 1/10,000 of a centimeter (cm), which is 1/1000 of a millimeter (mm).

Since a biconcave disc has a much greater surface area for its volume (compared to a sphere or a cube), this shape provides a large surface area for the diffusion of gas molecules into and out of a RBC.

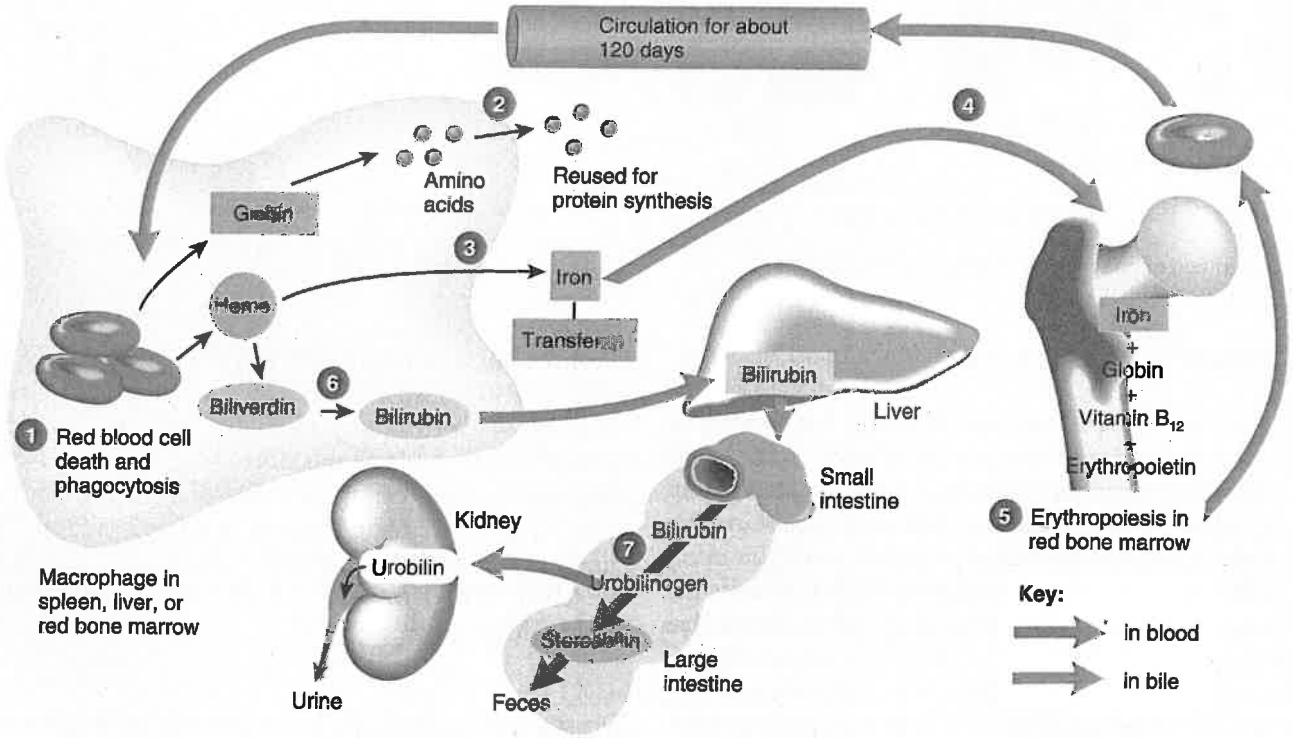
Delivery of oxygen to muscles is a limiting factor in muscular feats. As a result, increasing the oxygen-carrying capacity of the blood enhances athletic performance, especially in endurance events. Because RBCs are the main transport vehicle for oxygen, athletes have tried several means of increasing their RBC count, causing **induced polycythemia**, to gain a competitive edge. Athletes have enhanced their RBC production by injecting *Epoetin alfa* (*Procrit*® or *Epogen*®), a drug that is used to treat anemia by stimulating the production of RBCs by red bone marrow. Practices that increase the number of RBCs are dangerous because they raise the viscosity of the blood, which increases the resistance to blood flow and makes the blood more difficult for the heart to pump. Increased viscosity also contributes to high blood pressure and increased risk of stroke. During the 1980s, at least 15 competitive cyclists died from heart attacks or strokes linked to suspected use of Epoetin alfa. Although the International Olympics Committee bans Epoetin alfa use, enforcement is difficult because the drug is identical to naturally occurring EPO.

RBC LIFE CYCLE Red blood cells live only about 120 days because of wear and tear on their plasma membranes as they squeeze through blood capillaries. Worn-out red blood cells are removed from circulation as follows (Figure 14.3).

1. Macrophages in the spleen, liver, and red bone marrow phagocytize ruptured and worn-out red blood cells, splitting apart the heme and globin portions of hemoglobin.
2. The protein globin is broken down into amino acids, which can be reused by body cells to synthesize other proteins.
3. Iron removed from the heme portion associates with the plasma protein ***transferrin*** (trans-FER-in; *trans-* = across; *ferr-* = iron), which acts as a transporter.
4. The iron-transferrin complex is then carried to red bone marrow, where RBC precursor cells use it in hemoglobin synthesis. Iron is needed for the heme portion of the hemoglobin molecule, and amino acids are needed for the globin portion. Vitamin B_{12} is also needed for synthesis of hemoglobin. (The lining of the stomach must produce a protein called *intrinsic factor* for absorption of dietary vitamin B_{12} from the GI tract into the blood.)
5. Erythropoiesis in red bone marrow results in the production of red blood cells, which enter the circulation.

Figure 14.3 Formation and destruction of red blood cells, and the recycling of hemoglobin components.

The rate of RBC formation by red bone marrow equals the rate of RBC destruction by macrophages.



What substance is responsible for the brown color of feces?

6. When iron is removed from heme, the non-iron portion of heme is converted to ***biliverdin*** (bil′-i-VER-din), a green pigment, and then into ***bilirubin*** (bil′-i-ROO-bin), a yellow-orange pigment. Bilirubin enters the blood and is transported to the liver. Within the liver, bilirubin is secreted by liver cells into bile, which passes into the small intestine and then into the large intestine.
7. In the large intestine, bacteria convert bilirubin into ***urobilinogen*** (ūr-ō-bī-LIN-ō-jen). Some urobilinogen is absorbed back into the blood, converted to a yellow pigment called ***urobilin*** (ūr-ō-BĪ-lin), and excreted in urine. Most urobilinogen is eliminated in feces in the form of a brown pigment called ***stercobilin*** (ster′-kō-BĪ-lin), which gives feces its characteristic color.

Because free iron ions bind to and damage molecules in cells or in the blood, transferrin acts as a protective "protein escort" during transport of iron ions. As a result, plasma contains virtually no free iron.

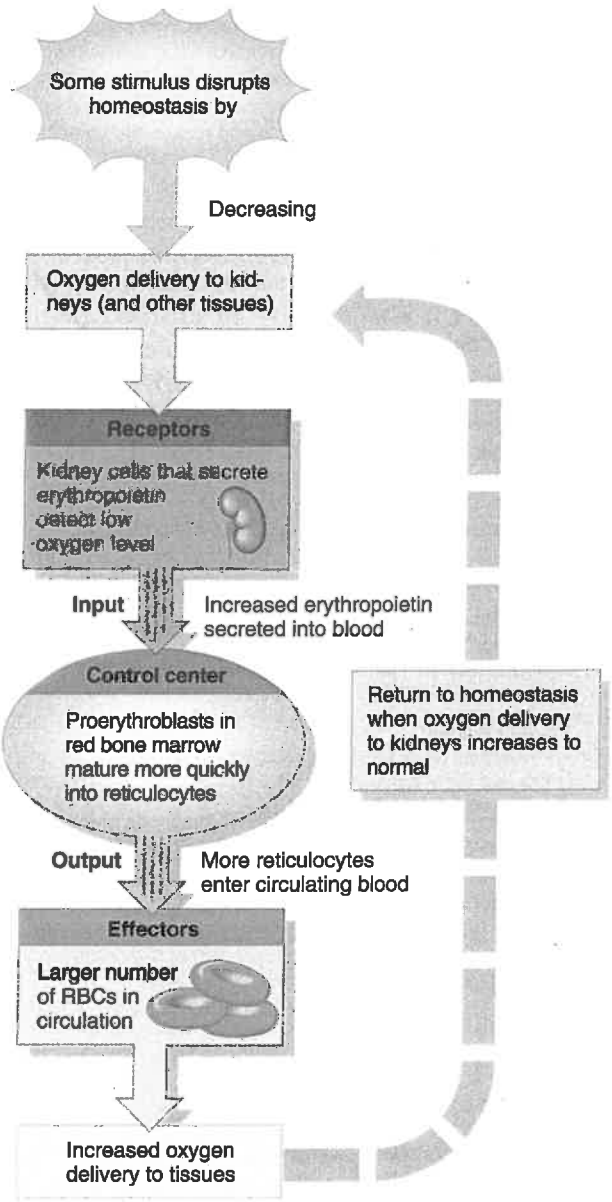
RBC PRODUCTION The formation of blood cells in general is called hemopoiesis; the formation of just RBCs is termed ***erythropoiesis*** (e-rith′-rō-poy-Ē-sis). Near the end of erythropoiesis, an RBC precursor ejects its nucleus and becomes a ***reticulocyte*** (re-TIK-ū-lō-sīt; see Figure 14.2a). Loss of the nucleus causes the center of the cell to indent, producing the RBC's distinctive biconcave shape. Reticulocytes, which are about 34% hemoglobin and retain some mitochondria, ribosomes, and endoplasmic reticulum, pass from red bone marrow into the bloodstream. Reticulocytes usually develop into mature RBCs within 1 to 2 days after their release from bone marrow.

Normally, erythropoiesis and destruction of RBCs proceed at the same pace. If the oxygen-carrying capacity of the blood falls because erythropoiesis is not keeping up with RBC destruction, RBC production increases (Figure 14.4). The controlled condition in this particular negative feedback loop is the amount of oxygen delivered to the kidneys (and thus to body tissues in general). ***Hypoxia*** (hī-POKS-ē-a), a deficiency of oxygen, stimulates increased release of ***erythropoietin*** (e-rith′-rō-POY-ē-tin), or ***EPO***, a hormone made by the kidneys. EPO circulates through the blood to the red bone marrow, where it stimulates erythropoiesis. The larger the number of RBCs in the blood, the higher the oxygen delivery to the tissues (Figure 14.4). A person with prolonged hypoxia may develop a life-threatening condition called ***cyanosis*** (sī′-a-NŌ-sis), characterized by a bluish-purple skin coloration most easily seen in the nails and mucous membranes. Oxygen delivery may fall due to ***anemia*** (a lower-than-normal number of RBCs or reduced quantity of hemoglobin) or circulatory problems that reduce blood flow to tissues.

A test that measures the rate of erythropoiesis is called a reticulocyte count. This and several other tests related to red blood cells are explained in Table 14.1.

Figure 14.4 Negative feedback regulation of erythropoiesis (red blood cell formation).

The main stimulus for erythropoiesis is hypoxia, a decrease in the oxygen-carrying capacity of the blood.



What is the term for cellular oxygen deficiency?

Premature newborns often exhibit anemia, due in part to inadequate production of erythropoietin. During the first weeks after birth, the liver, not the kidneys, produces most EPO. Because the liver is less sensitive than the kidneys to hypoxia, newborns have a smaller EPO response to anemia than do adults. In addition, in infants, fetal hemoglobin is converted into adult hemoglobin; since fetal hemoglobin carries up to 30% more oxygen, the loss of fetal hemoglobin makes the anemia worse.

Table 14.1 Obtaining Blood Samples and Common Medical Tests Involving Blood

I. Obtaining Blood Samples

A. Venipuncture. This most frequently used procedure involves withdrawal of blood from a vein using a sterile needle and syringe. (Veins are used instead of arteries because they are closer to the skin, more readily accessible, and contain blood at a much lower pressure.) A commonly used vein is the median cubital vein in front of the elbow (see Figure 16.14 on page 407). A tourniquet is wrapped around the arm, which stops blood flow through the veins and makes the veins below the tourniquet stand out.

B. Fingerstick. Using a sterile needle or lancet, a drop or two of capillary blood is taken from a finger, earlobe, or heel.

C. Arterial stick. Sample is most often taken from radial artery in the wrist or femoral artery in the thigh (see Figure 16.9 on page 397).

II. Testing Blood Samples

A. Reticulocyte count (indicates the rate of erythropoiesis)

Normal value: 0.5% to 1.5%.

Abnormal values: A high reticulocyte count might indicate the presence of bleeding or hemolysis (rupture of erythrocytes), or it may be the response of someone who is iron deficient. Low reticulocyte count in the presence of anemia might indicate a malfunction of the red bone marrow, owing to a nutritional deficiency, pernicious anemia, or leukemia.

B. Hematocrit (the percentage of red blood cells in blood). A hematocrit of 40 means that 40% of the volume of blood is composed of RBCs.

Normal values:

Females: 38 to 46 (average 42)
Males: 40 to 54 (average 47)

Abnormal values: The test is used to diagnose anemia, polycythemia (an increased percentage of red blood cells), and abnormal states of hydration. Anemia may vary from mild (hematocrit of 35) to severe (hematocrit of less than 15). Athletes often have a higher-than-average hematocrit, and the average hematocrit of persons living at high altitude is greater than that of persons living at sea level.

C. Differential white blood cell count (the percentage of each type of white blood cells in a sample of 100 WBCs)

Normal values:

Type of WBC	Percentage
neutrophils	60–70
eosinophils	2–4
basophils	0.5–1
lymphocytes	20–25
monocytes	3–8

Abnormal values: A high neutrophil count might result from bacterial infections, burns, stress, or inflammation; a low neutrophil count might be caused by radiation, certain drugs, vitamin B_{12} deficiency, or systemic lupus erythematosus (SLE) (see page 93). A high eosinophil count could indicate allergic reactions, parasitic infections, autoimmune disease, or adrenal insufficiency; a low eosinophil count could be caused by certain drugs, stress, or Cushing's syndrome. Basophils could be elevated in some types of allergic responses, leukemias, cancers, and hyperthyroidism; decreases in basophils could occur during pregnancy, ovulation, stress, and hyperthyroidism. High lymphocyte counts could indicate viral infections, immune diseases, and some leukemias; low lymphocyte counts might occur as a result of prolonged severe illness, high steroid levels, and immunosuppression. A high monocyte count could result from certain viral or fungal infections, tuberculosis (TB), some leukemias, and chronic diseases; low monocyte levels rarely occur.

D. Complete blood count (CBC) (provides information about the formed elements in blood)*

Normal values:

RBC count	About 5.4 million per μL in males About 4.8 million per μL in females
Hemoglobin	14–18 g/dl in adult males 12–16 g/dl in adult females
Hematocrit	See B
WBC count	5,000–10,000 per μL
Differential white blood count	See C
Platelet count	150,000–400,000 μL

Abnormal values: Increased RBC count, hemoglobin, and hematocrit occur in polycythemia, congenital heart disease, and hypoxia; decreased RBC count, hemoglobin, and hematocrit occur in hemorrhage and certain types of anemia. Increased WBC counts may indicate acute or chronic infections, trauma, leukemia, or stress (see also above under differential white blood cell count). Decreased WBC counts could indicate anemia and viral infections (see also above under differential white blood cell count). High platelet counts may indicate cancer, trauma, or cirrhosis. Low platelet counts could indicate anemia, allergic conditions, or hemorrhage.

*Not all components of a CBC have been included.

White Blood Cells

WBC STRUCTURE AND TYPES Unlike red blood cells, ***white blood cells (WBCs)*** or ***leukocytes*** (LOO-kō-sīts; *leuko-* = white) have nuclei and do not contain hemoglobin. WBCs are classified as either granular or agranular, depending on whether they contain chemical-filled cytoplasmic granule (vesicles) that are made visible by staining when viewed through a light microscope. The *granular leukocytes* include ***neutrophils*** (NOO-trō-fils), ***eosinophils*** (ē′-ō-SIN-ō-fils), and ***basophils*** (BĀ-sō-fils). The *agranular leukocytes* include ***lymphocytes*** and ***monocytes*** (MON-ō-sīts). (See Table 14.2 for the sizes and microscopic characteristics of WBCs.)

WBC FUNCTIONS The skin and mucous membranes of the body are continuously exposed to microbes (microscopic organisms), such as bacteria, some of which are capable of invading deeper tissues and causing disease. Once microbes enter the body, some WBCs combat them by ***phagocytosis***, and others produce antibodies. Neutrophils respond first to bacterial invasion, carrying on phagocytosis and releasing enzymes such as lysozyme that destroy certain bacteria. Monocytes take longer to reach the site of infection than neutrophils, but they eventually arrive in larger numbers. Monocytes that migrate into infected tissues develop into cells called ***wandering macrophages*** (*macro-* = large; *-phages* = eaters), which can phagocytize many more microbes than neutrophils. They also clean up cellular debris following an infection.

Eosinophils leave the capillaries and enter interstitial fluid. They release enzymes that combat inflammation in allergic reactions. Eosinophils also phagocytize antigen–antibody complexes and are effective against certain parasitic worms. A high eosinophil count often indicates an allergic condition or a parasitic infection.

Basophils are also involved in inflammatory and allergic reactions. They leave capillaries, enter tissues, and can liberate heparin, histamine, and serotonin. These substances intensify the inflammatory reaction and are involved in allergic reactions.

Three types of lymphocytes—B cells, T cells, and natural killer (NK) cells—are the major combatants in immune responses, which are described in detail in Chapter 17. B cells develop into plasma cells, which produce antibodies that help destroy bacteria and inactivate their toxins. T cells attack viruses, fungi, transplanted cells, cancer cells, and some bacteria. Natural killer cells attack a wide variety of infectious microbes and certain spontaneously arising tumor cells.

White blood cells and other nucleated body cells have proteins, called ***major histocompatibility (MHC) antigens***, protruding from their plasma membrane into the extracellular fluid. These "cell identity markers" are unique for each person (except identical twins). Although RBCs (which do not possess nuclei) possess blood group antigens, they lack the MHC antigens. An incompatible tissue transplant is rejected by the recipient due, in part, to differences in donor and recipient MHC antigens. The MHC antigens are used to type tissues to identify compatible donors and recipients and thus reduce the chance of tissue rejection.

WBC LIFE SPAN Red blood cells outnumber white blood cells about 700 to 1. There are normally about 5000 to 10,000 WBCs per μL of blood. Bacteria have continuous access to the body through the mouth, nose, and pores of the skin. Furthermore, many cells, especially those of epithelial tissue, age and die daily, and their remains must be removed. However, a WBC can phagocytize only a certain amount of material before it interferes with the WBC's own metabolic activities. Thus, the life span of most WBCs is only a few days. During a period of infection, many WBCs live only a few hours. However, some B and T cells remain in the body for years.

Leukocytosis (loo′-kō-sī-TŌ-sis), an increase in the number of WBCs, is a normal, protective response to stresses such as invading microbes, strenuous exercise, anesthesia, and surgery. Leukocytosis usually indicates an inflammation or infection. Because each type of white blood cell plays a different role, determining the percentage of each type in the blood assists in diagnosing the condition. This test, called a ***differential white blood cell count***, measures the number of each kind of white cell in a sample of 100 white blood cells (see Table 14.1). An abnormally low level of white blood cells (below 5000 cells/μL), called ***leukopenia*** (loo′-kō-PĒ-nē-a), is never beneficial; it may be caused by exposure to radiation, shock, and certain chemotherapeutic agents.

WBC PRODUCTION Leukocytes develop in red bone marrow. As shown in Figure 14.2a, monocytes and granular leukocytes develop from a myeloid stem cell. T and B cells develop from a lymphoid stem cell.

Platelets

Pluripotent stem cells also differentiate into cells that produce platelets (see Figure 14.2a). Some myeloid stem cells develop into cells called *megakaryoblasts*, which in turn transform into megakaryocytes, huge cells that splinter into 2000–3000 fragments in the red bone marrow and then enter the bloodstream. Each fragment, enclosed by a piece of the megakaryocyte cell membrane, is a ***platelet***. Between 150,000 and 400,000 platelets are present in each μL of blood. Platelets are disc-shaped, have a diameter of 2–4 μm, and exhibit many vesicles but no nucleus. When blood vessels are damaged, platelets help stop blood loss by forming a platelet plug. Their vesicles also contain chemicals that promote blood clotting (both processes are described shortly). After their short life span of 5–9 days, platelets are removed by macrophages in the spleen and liver.

A **bone marrow transplant** is the replacement of cancerous or abnormal red bone marrow with healthy red bone marrow in order to establish normal blood cell counts. The defective red bone marrow is destroyed by high doses of chemotherapy and whole body radiation just before the transplant takes place. These treatments kill the cancer cells and destroy the patient's immune system in order to decrease the chance of transplant rejection. The red bone marrow from a donor is usually removed from the hip bone under general anesthesia with a syringe and is then injected into the recipient's vein, much like a blood transfusion. The injected marrow migrates to the recipient's red bone marrow cavities, and the stem cells in the marrow multiply. If all goes well, the recipient's red bone marrow is replaced entirely by healthy, noncancerous cells.

Bone marrow transplants have been used to treat aplastic anemia, certain types of leukemia, severe combined immunodeficiency disease (SCID), Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, thalassemia, sickle-cell disease, breast cancer, ovarian cancer, testicular cancer, and hemolytic anemia. However, there are some drawbacks. Since the recipient's white blood cells have been completely destroyed by chemotherapy and radiation, the patient is extremely vulnerable to infection. (It takes about 2–3 weeks for transplanted bone marrow to produce enough white blood cells to protect against infection.) In addition, transplanted red bone marrow may produce T lymphocytes that attack the recipient's tissues. Another drawback is that patients must take immunosuppressive drugs for life. Because these drugs reduce the level of immune system activity, they increase the risk of infection.

Table 14.2 presents a summary of the formed elements in blood.

■ **CHECKPOINT**

3. Briefly outline the process of hemopoiesis.
4. What is erythropoiesis? How does erythropoiesis affect hematocrit? What factors speed up and slow down erythropoiesis?
5. What functions do neutrophils, eosinophils, basophils, monocytes, B cells, T cells, and natural killer cells perform?
6. How are leukocytosis and leukopenia different? What is a differential white blood cell count?

HEMOSTASIS

OBJECTIVE • Describe the various mechanisms that prevent blood loss.

Hemostasis (hē′-mō-STĀ-sis; *-stasis* = standing still) is a sequence of responses that stops bleeding when blood vessels are injured. (Be sure not to confuse the two words *hemostasis* and *homeostasis*.) The hemostatic response must be quick, localized to the region of damage, and carefully controlled. Three mechanisms can reduce loss of blood from blood vessels: (1) vascular spasm, (2) platelet plug formation, and (3) blood clotting (coagulation). When successful, hemostasis prevents ***hemorrhage*** (HEM-or-ij; *-rhage* = burst forth), the loss of a large amount of blood from the vessels. Hemostasis can prevent hemorrhage from smaller blood vessels, but extensive hemorrhage from larger vessels usually requires medical intervention.

Vascular Spasm

When a blood vessel is damaged, the smooth muscle in its wall contracts immediately, a response called a ***vascular spasm***. Vascular spasm reduces blood loss for several minutes to several hours, during which time the other hemostatic mechanisms begin to operate. The spasm is probably caused by damage to the smooth muscle and by reflexes initiated by pain receptors. As platelets accumulate at the damaged site, they release chemicals that enhance vasoconstriction (narrowing of a blood vessel), thus maintaining the vascular spasm.

Platelet Plug Formation

When platelets come into contact with parts of a damaged blood vessel, their characteristics change drastically and they quickly come together to form a platelet plug that helps fill the gap in the injured blood vessel wall. Platelet plug formation occurs as follows.

Initially, platelets contact and stick to parts of a damaged blood vessel, such as collagen fibers. Then, they interact with one another and begin to liberate the chemicals. The chemicals activate nearby platelets and sustain the vascular spasm, which decreases blood flow through the injured vessel. The release of platelet chemicals makes other platelets in the area sticky, and the stickiness of the newly recruited and activated platelets causes them to stick to the originally activated platelets. Eventually, a large number of platelets forms a mass called a ***platelet plug***. A platelet plug can stop blood loss completely if the hole in a blood vessel is small enough.

Blood Clotting

Normally, blood remains in its liquid form as long as it stays within its vessels. If it is withdrawn from the body, however, it thickens and forms a gel. Eventually, the gel separates from the liquid. The straw-colored liquid, called ***serum***, is simply plasma minus the clotting proteins. The gel is called a ***clot*** and consists of a network of insoluble protein fibers called ***fibrin*** in which the formed elements of blood are trapped (see Figure 14.5).

Table 14.2 Summary of Formed Elements in Blood

Name and Appearance	Number	Characteristics*	Functions
Red Blood Cells (RBCs) or Erythrocytes 	4.8 million/μL in females; 5.4 million/μL in males.	7–8 μm diameter, biconcave discs, without a nucleus; live for about 120 days.	Hemoglobin within RBCs transports most of the oxygen and part of the carbon dixoide in the blood.
White Blood Cells (WBCs) or Leukocytes	5000–10,000/μL	Most live for a few hours to a few days.†	Combat pathogens and other foreign substances that enter the body.
Granular Leukocytes			
Neutrophils 	60–70% of all WBCs.	10–12 μm diameter; nucleus has 2–5 lobes connected by thin strands of chromatin; cytoplasm has very fine, pale lilac granules.	Phagocytosis. Destruction of bacteria with lysozyme, defensins, and strong oxidants, such as superoxide anion, hydrogen peroxide, and hypochlorite anion.
Eosinophils 	2–4% of all WBCs.	10–12 μm diameter; nucleus has 2 or 3 lobes; large, red-orange granules fill the cytoplasm.	Combat the effects of histamine in allergic reactions, phagocytize antigen–antibody complexes, and destroy certain parasitic worms.
Basophils 	0.5–1% of all WBCs.	8–10 μm diameter; nucleus has 2 lobes; large cytoplasmic granules appear deep blue-purple.	Liberate heparin, histamine, and serotonin in allergic reactions that intensify the overall inflammatory response.
Agranular Leukocytes			
Lymphocytes (T cells, B cells, and natural killer cells) 	20–25% of all WBCs.	Small lymphocytes are 6–9 μm in diameter; large lymphocytes are 10–14 μm in diameter; nucleus is round or slightly indented; cytoplasm forms a rim around the nucleus that looks sky blue; the larger the cell, the more cytoplasm is visible.	Mediate immune responses, including antigen–antibody reactions. B cells develop into plasma cells, which secrete antibodies. T cells attack invading viruses, cancer cells, and transplanted tissue cells. Natural killer cells attack a wide variety of infectious microbes and certain spontaneously arising tumor cells.
Monocytes 	3–8% of all WBCs.	12–20 μm diameter; nucleus is kidney shaped or horseshoe shaped; cytoplasm is blue-gray and has foamy appearance.	Phagocytosis (after transforming into fixed or wandering macrophages).
Platelets 	150,000–400,000/μL.	2–4 μm diameter cell fragments that live for 5–9 days; contain many vesicles but no nucleus.	Form platelet plug in hemostasis; release chemicals that promote vascular spasm and blood clotting.

*Colors are those seen when using Wright's stain.

†Some lymphocytes, called T and B memory cells, can live for many years once they are established.

The process of clot formation, called ***clotting (coagulation)***, is a series of chemical reactions that culminates in the formation of fibrin threads. If blood clots too easily, the result can be ***thrombosis***, clotting in an unbroken blood vessel. If the blood takes too long to clot, hemorrhage can result.

Clotting is a complex process in which various chemicals known as ***clotting factors*** activate each other. Clotting (coagulation) factors include calcium ions (Ca^{2+}), several enzymes that are made by liver cells and released into the blood, and various molecules associated with platelets or released by damaged tissues. Many clotting factors are identified by Roman numerals. Clotting occurs in three stages (Figure 14.5):