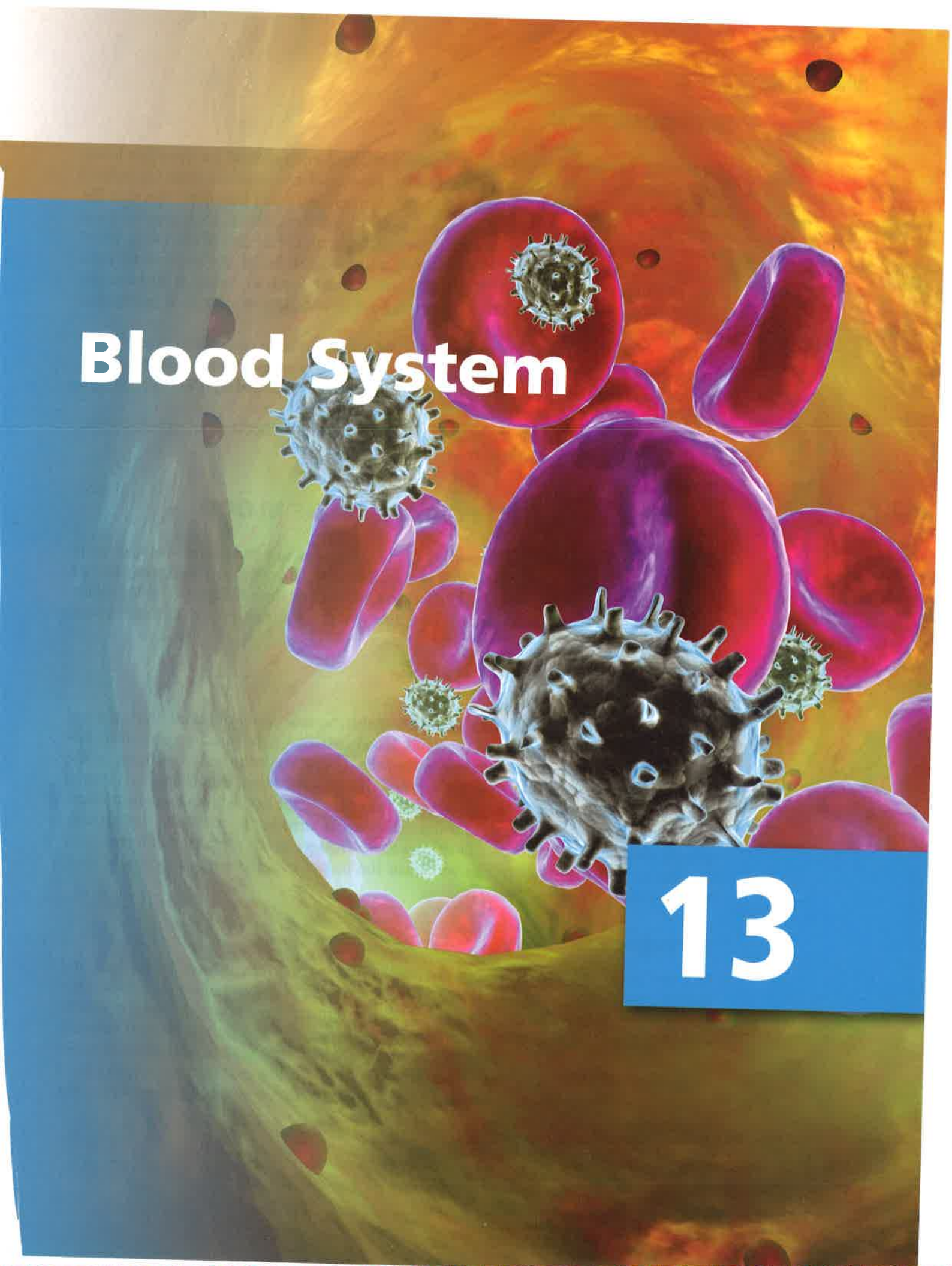

Blood System

13

INTRODUCTION

The primary function of blood is to maintain a constant environment for the other living tissues of the body. Blood transports nutrients, gases, and wastes to and from the cells of the body. Nutrients from food, digested in the stomach and small intestine, pass into the bloodstream through the lining cells of the small intestine. Blood then carries these nutrients to all body cells. Oxygen enters the body through the air sacs of the lungs. Blood cells then transport the oxygen to cells throughout the body. Blood also helps remove the waste products released by cells. It carries gaseous waste (such as carbon dioxide) to the lungs to be exhaled. It carries chemical waste, such as urea, to the kidneys to be excreted in the urine.

Blood transports chemical messengers called hormones from their sites of secretion in glands, such as the thyroid or pituitary, to distant sites where they regulate growth, reproduction, and energy production. These hormones are discussed later in the endocrine chapter.

Finally, blood contains proteins, white blood cells and antibodies that fight infection, and platelets (thrombocytes) that help the blood to clot.

COMPOSITION AND FORMATION OF BLOOD

Blood is composed of **cells,** or formed elements, suspended in a clear, straw-colored liquid called **plasma.** The cells constitute 45% of the blood volume and include **erythrocytes** (red blood cells), **leukocytes** (white blood cells), and **platelets** or **thrombocytes** (clotting cells). The remaining 55% of blood is plasma, a solution of water, proteins, sugar, salts, hormones, and vitamins.

CELLS

Beginning at birth, all blood cells originate in the marrow cavity of bones. Both the red blood cells that carry oxygen and the white blood cells that fight infection arise from the same blood-forming or **hematopoietic stem cells.** Under the influence of proteins in the bloodstream and bone marrow, stem cells change their size and shape to become specialized, or **differentiated.** In this process, the cells change in size from large (immature cells) to small (mature forms), and the cell nucleus shrinks (in red cells, the nucleus actually disappears). Figure 13-1 illustrates these changes in the formation of blood cells. Use Figure 13-1 as a reference as you learn the names of mature blood cells and their earlier forms.

ERYTHROCYTES

As a red blood cell matures (from erythroblast to erythrocyte), it loses its nucleus and assumes the shape of a biconcave disk. This shape (a depressed or hollow surface on each side of the cell, resembling a cough drop with a thin central portion) allows for a large surface area so that absorption and release of gases (oxygen and carbon dioxide) can take place (Figure 13-2). Red cells contain the unique protein **hemoglobin,** composed of **heme** (iron-containing pigment) and **globin** (protein). Hemoglobin enables the erythrocyte to carry oxygen. The combination of oxygen and hemoglobin (oxyhemoglobin) produces the bright red color of blood.

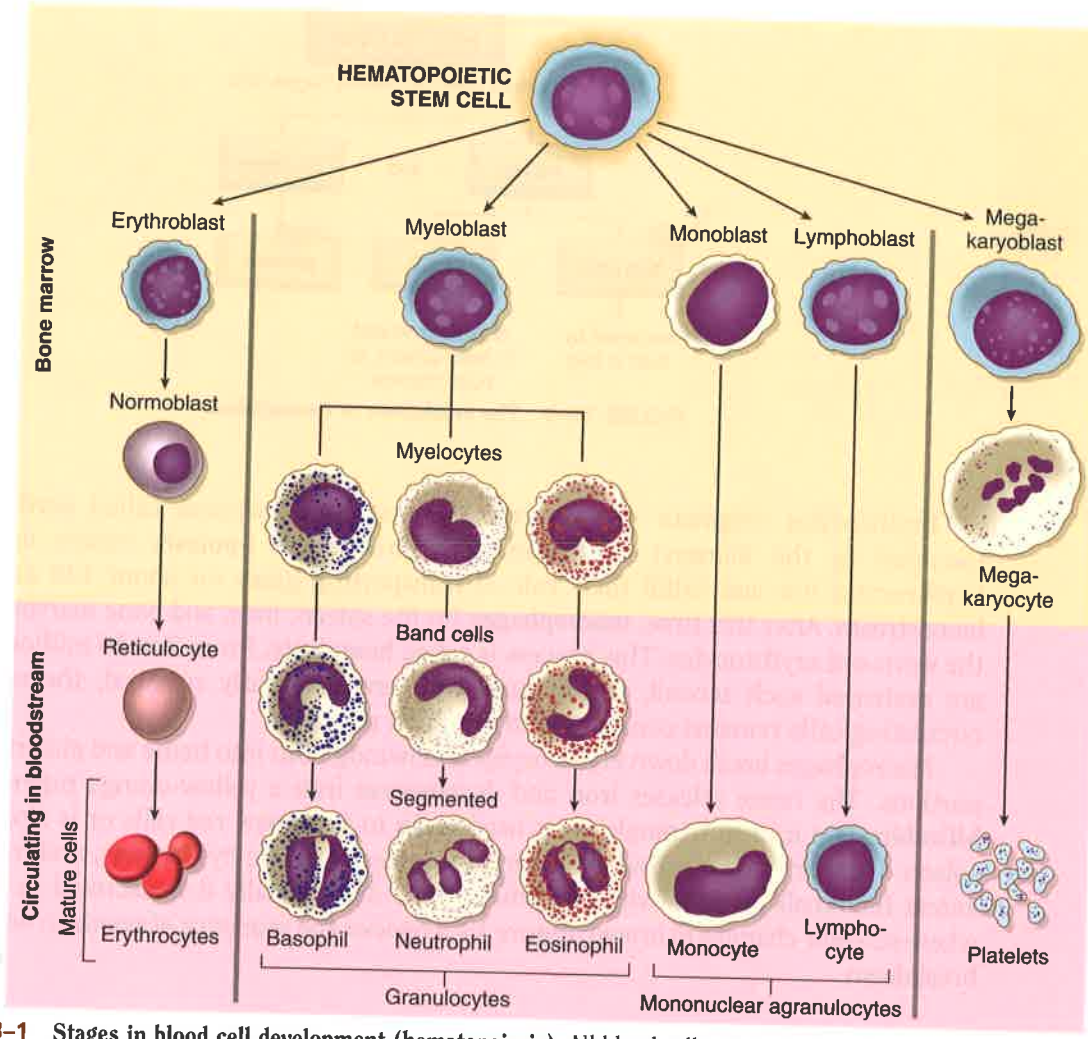

FIGURE 13–1 Stages in blood cell development (hematopoiesis). All blood cells originate from **hematopoietic stem cells.** Notice that the suffix **-blast** indicates immature forms of all cells. Band cells are identical to segmented granulocytes except that the nucleus is U-shaped and its lobes are connected by a band rather than by a thin thread as in segmented forms.

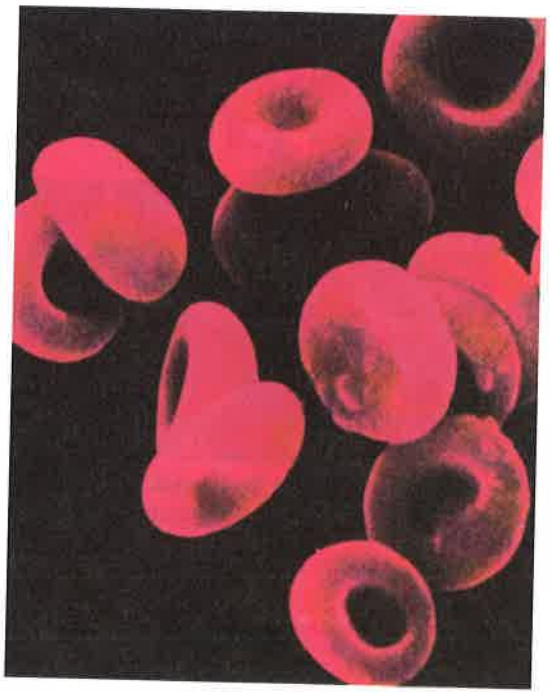

FIGURE 13–2 Normal **erythrocytes** (red blood cells). (From Thibodeau GA, Patton KT: Anatomy & Physiology, 6th ed., St. Louis, Mosby, 2007, p. 650.)

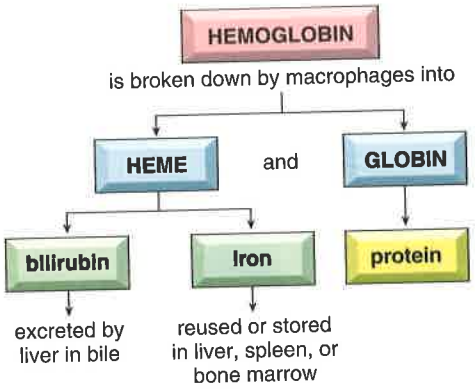

FIGURE 13–3 The breakdown of hemoglobin.

Erythrocytes originate in the bone marrow. The hormone called **erythropoietin** (secreted by the kidneys) stimulates their production (**-poiesis** means formation). Erythrocytes live and fulfill their role of transporting gases for about 120 days in the bloodstream. After this time, **macrophages** (in the spleen, liver, and bone marrow) destroy the worn-out erythrocytes. This process is called **hemolysis.** From 2 to 10 million red cells are destroyed each second, but because they are constantly replaced, the number of circulating cells remains constant (4 to 6 million per μL).

Macrophages break down erythrocytes and hemoglobin into heme and globin (protein) portions. The heme releases iron and decomposes into a yellow-orange pigment called **bilirubin.** The iron in hemoglobin is used again to form new red cells or is stored in the spleen, liver, or bone marrow. Bilirubin is excreted into bile by the liver, and from bile it enters the small intestine via the common bile duct. Finally it is excreted in the stool, where its color changes to brown. Figure 13-3 reviews the sequence of events in hemoglobin breakdown.

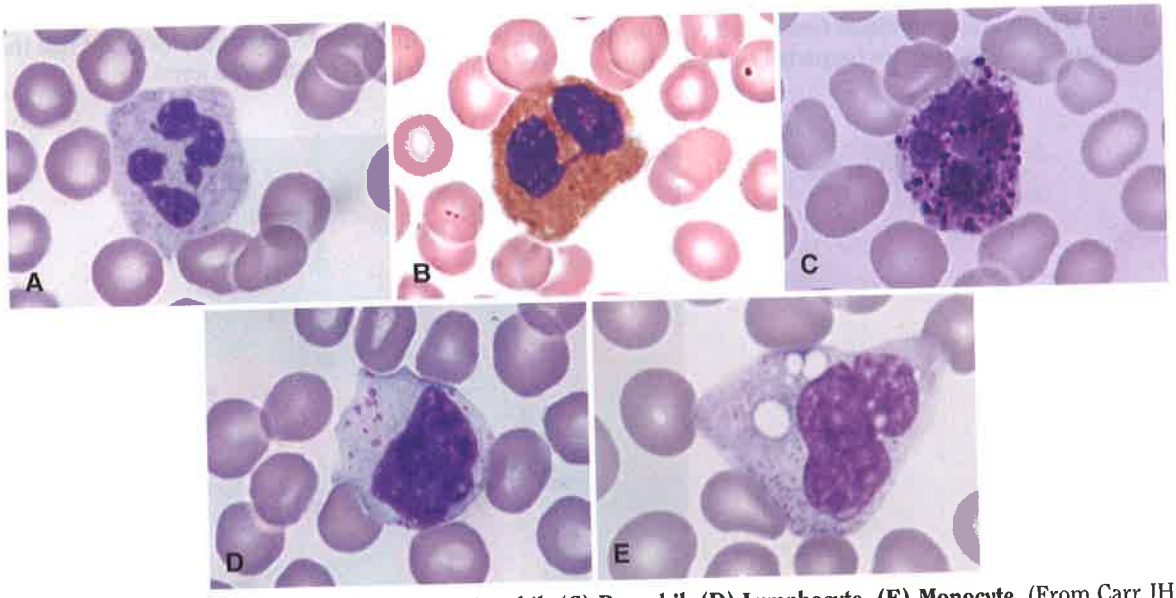

FIGURE 13–4 Leukocytes. (A) Neutrophil. (B) Eosinophil. (C) Basophil. (D) Lymphocyte. (E) Monocyte. (From Carr JH, Rodak BF: Clinical Hematology Atlas, 2nd ed., St. Louis, Mosby, 2004.)

LEUKOCYTES

White blood cells (7000 to 9000 cells per μL) are less numerous than erythrocytes, but there are five different types of mature leukocytes, shown in Figure 13-4. These are three polymorphonuclear granulocytic leukocytes (neutrophil, eosinophil, and basophil) and two mononuclear agranulocytic leukocytes (lymphocyte and monocyte).

The **granulocytes,** or **polymorphonuclear leukocytes (PMNs),** are the most numerous (about 60%). **Basophils** contain granules that stain dark blue with a basic (alkaline) dye. These granules contain heparin (an anticlotting substance) and histamine (a chemical released in allergic responses). **Eosinophils** contain granules that stain with eosin, a red acidic dye. These granules increase in allergic responses and engulf substances that trigger the allergies. **Neutrophils** contain granules that are neutral; they do not stain intensely and show only a pale color. Neutrophils are **phagocytes** (**phag/o** means to eat or swallow) that accumulate at sites of infection, where they ingest and destroy bacteria. Figure 13-5 shows phagocytosis by a neutrophil.

Specific proteins called **colony-stimulating factors** (CSFs) promote the growth of granulocytes in bone marrow. **G-CSF** (granulocyte CSF) and **GM-CSF** (granulocyte-macrophage CSF) are given to restore granulocyte production in cancer patients. **Erythropoietin,** like CSFs, can be produced by recombinant DNA techniques. It stimulates red blood cell production (erythropoiesis).

Although all granulocytes are **polymorphonuclear** (they have multilobed nuclei), the term **polymorphonuclear agranulocytes ("poly")** often describes the **neutrophil,** which is the most numerous of the granulocytes.

Mononuclear (containing one large nucleus) leukocytes do not have large numbers of granules in their cytoplasm, but they may have a few granules. These are **lymphocytes** and **monocytes** (see Figure 13-1). Lymphocytes are made in bone marrow and lymph nodes and circulate both in the bloodstream and in the parallel circulating system, the lymphatic system.

Lymphocytes play an important role in the **immune response** that protects the body against infection. They can directly attack foreign matter and, in addition, make **antibodies** that neutralize and can lead to the destruction of foreign **antigens** (bacteria and viruses). Monocytes are phagocytic cells that also fight disease. They move from the bloodstream into tissues (as **macrophages**) and dispose of dead and dying cells and other tissue debris by phagocytosis.

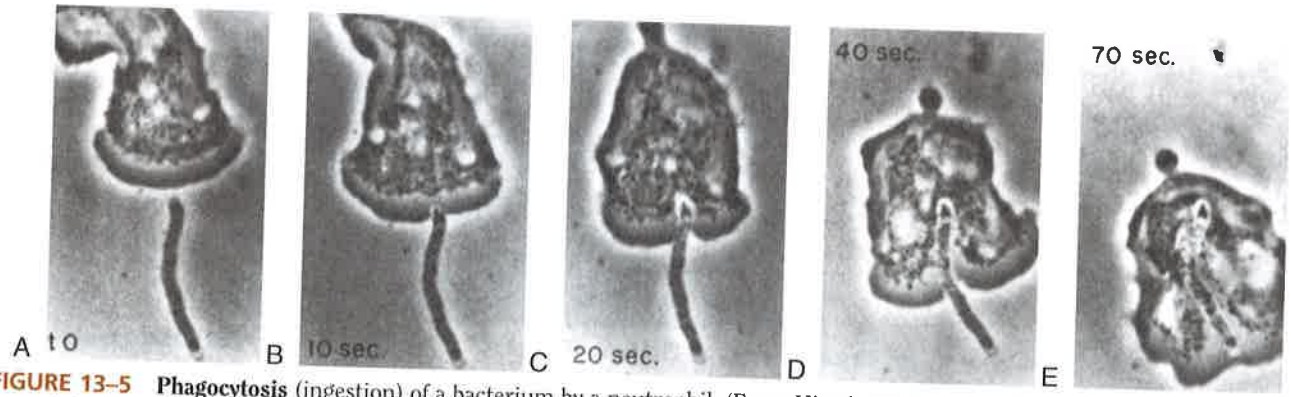

FIGURE 13–5 **Phagocytosis** (ingestion) of a bacterium by a neutrophil. (From Hirsch JG: Cinemicrophotographic observations of granule lysis in polymorphonuclear leucocytes during phagocytosis, J Exp Med 1962;116: 827, by copyright permission of Rockefeller University Press.)

TABLE 13-1 Leukocytes

Leukocyte	Normal Percentage in Blood	Function
Granulocytes		
Basophil	0-1	Contains heparin (prevents clotting) and histamine (involved in allergic responses)
Eosinophil	1-4	Phagocytic cell involved in allergic reactions
Neutrophil	50-70	Phagocytic cell that accumulates at sites of infection
Mononuclear Cells		
Lymphocyte	20-40	Controls the immune response; makes antibodies to antigens
Monocyte	3-8	Phagocytic cell that becomes a macrophage and digests bacteria and tissue debris

Table 13-1 reviews the different types of leukocytes, their numbers in the blood, and their functions.

PLATELETS (THROMBOCYTES)

Platelets, actually blood cell fragments, are formed in red bone marrow from giant cells with multilobed nuclei called **megakaryocytes** (Figure 13-6A and B). Tiny fragments of a megakaryocyte break off to form platelets. The main function of platelets is to help blood to clot. Specific terms related to blood clotting are discussed later in this chapter.

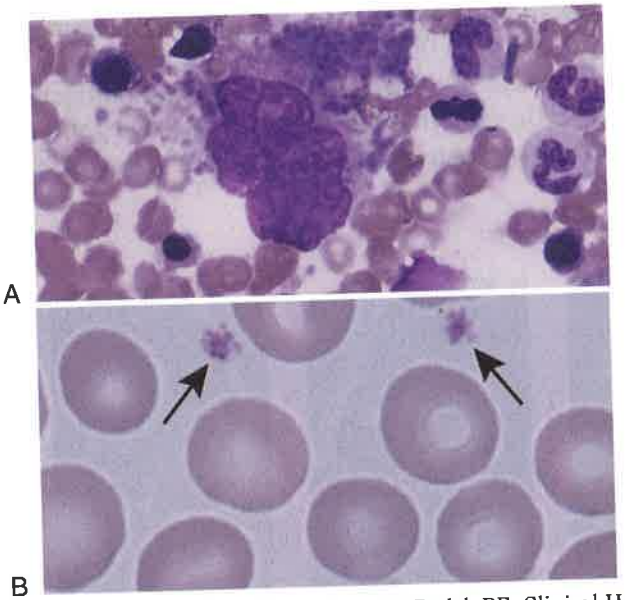

FIGURE 13–6 (A) Megakaryocyte (B) Platelets. (From Carr JH, Rodak BF: Clinical Hematology Atlas, 2nd ed., St. Louis, Mosby, 2004.)

PLASMA

Plasma, the liquid part of the blood, consists of water, dissolved proteins, sugar, wastes, salts, hormones, and other substances. The four major plasma proteins are **albumin, globulins, fibrinogen,** and **prothrombin** (the last two are clotting proteins).

Albumin maintains the proper proportion (and concentration) of water in the blood. Because albumin cannot pass easily through capillary walls, it remains in the blood and carries smaller molecules bound to its surface. It attracts water from the tissues back into the bloodstream and thus opposes the water's tendency to leave the blood and leak out into tissue spaces. **Edema** (swelling) results when too much fluid from blood "leaks" out into tissues. This happens in a mild form when a person ingests too much salt (water is retained in the blood and seeps out into tissues) and in a severe form when a person is burned in a fire. In this situation, albumin escapes from capillaries as a result of the burn injury. Then water cannot be held in the blood; it escapes through the skin, and blood volume drops.

Globulins are another component of blood and one of the plasma proteins. There are alpha, beta, and gamma globulins. The gamma globulins are **immunoglobulins,** which are antibodies that bind to and sometimes destroy antigens (foreign substances). Examples of immunoglobulin antibodies are **IgG** (found in high concentration in plasma) and **IgA** (found in breast milk, saliva, tears, and respiratory mucus). Other immunoglobulins are **IgM, IgD,** and **IgE.** Immunoglobulins are separated from other plasma proteins by **electrophoresis.** In this process, an electrical current passes through a solution of plasma. The different proteins in plasma separate as they migrate at different speeds to the source of the electricity.

Plasmapheresis (**-apheresis** means to remove) is the process of separating plasma from cells and then removing the plasma from the patient. In plasmapheresis, the entire blood sample is spun in a centrifuge machine, and the plasma, being lighter in weight than the cells, moves to the top of the sample.

Figure 13-7 reviews the composition of blood.

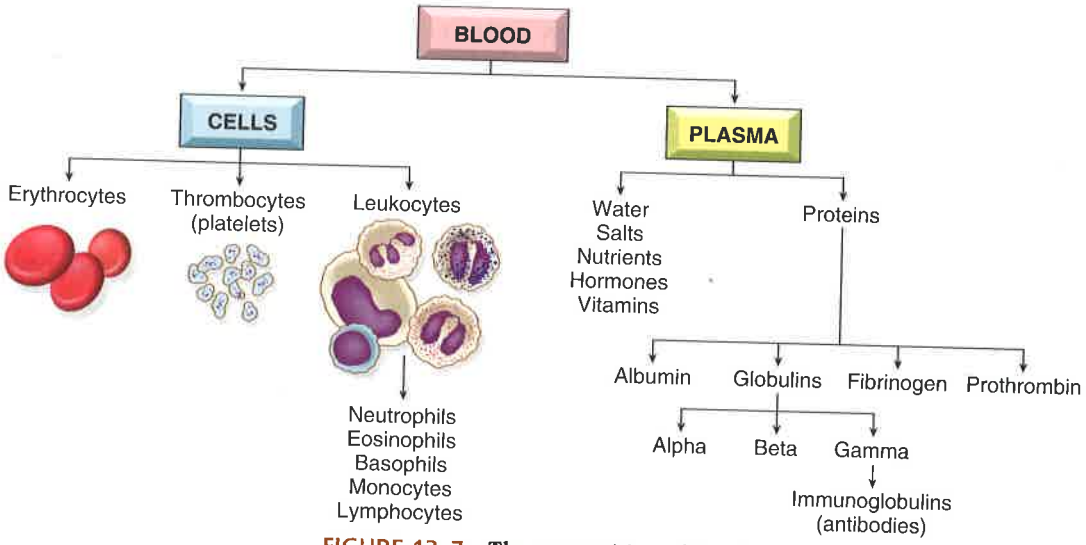

FIGURE 13–7 **The composition of blood.**

TABLE 13-2 Blood Types

Type	Percentage in Population	Red Cell Antigens	Serum Antibodies
A	41	A	Yes (anti-B)
B	10	B	Yes (anti-A)
AB	4	A and B	No (anti-A or anti-B)
O	45	No A and B	Yes (anti-A and anti-B)

BLOOD TYPES

Transfusions of whole blood (cells and plasma) are used to replace blood lost after injury, during surgery, or in severe shock. A patient who is severely anemic and needs only red blood cells will receive a transfusion of **packed red cells** (whole blood with most of the plasma removed). Human blood falls into four main types: A, B, AB, and O. These types are based on the antigens on red blood cells and antibodies found in each person's serum (Table 13-2).

There are harmful effects of transfusing blood from a donor of one blood type into a recipient who has blood of another blood type. Therefore, before blood is transfused, both the blood donor and the blood recipient are tested, to make sure that the transfused blood will be compatible with the recipient's blood type. During transfusion, if blood is not compatible, then **hemolysis** (breakdown of red blood cells) occurs. This may be followed by excessive clotting in blood vessels **(disseminated intravascular coagulation,** or **DIC),** which is a life-threatening condition.

Besides A and B antigens, many other antigens are located on the surface of red blood cells. One of these is called the **Rh factor** (named because it was first found in the blood of a rhesus monkey). The term Rh-positive (Rh+) refers to a person who is born with the Rh antigen on his or her red blood cells. An Rh-negative (Rh−) person does not have the Rh antigen. In clinical practice, blood types are named to indicate both Rh and ABO antigen status: If a woman has an A+ (A-positive) blood type, for example, this means that she was born with both A antigen and Rh antigen on her red blood cells. If a man has a B− (B-negative) blood type, this means he was born with the B antigen on his red blood cells but not Rh antigen.

BLOOD CLOTTING

Blood clotting, or **coagulation,** is a complicated process involving many different substances and chemical reactions. The final result (usually taking less than 15 minutes) is the formation of a **fibrin clot** from the plasma protein **fibrinogen.** Platelets are important in beginning the process following injury to tissues or blood vessels. The platelets become

Why Is Type O the Universal Donor?

Type O blood does not contain A or B red cell antigens and therefore will not react with antibodies in any recipient's bloodstream. Anti-A and Anti-B antibodies present in type O blood become diluted in the recipient's bloodstream and do not cause an adverse reaction.

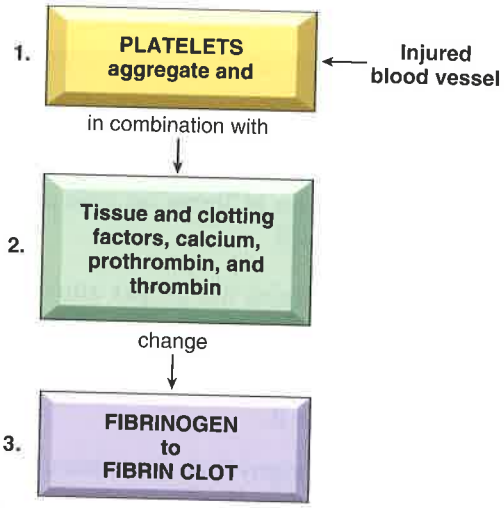

FIGURE 13–8 **The sequence of events in blood clotting.**

sticky and collect, or aggregate, at the site of injury. Then, in combination with tissue and clotting factors, plus calcium, prothrombin, and thrombin, fibrinogen is converted to fibrin to form a clot (Figure 13-8). One of the important clotting factors is factor VIII. It is missing in some people who are born with hemophilia. Other hemophiliacs are missing factor IX.

The fibrin threads form the clot by trapping red blood cells (Figure 13-9 shows a red blood cell trapped by fibrin threads). Then the clot retracts into a tight ball, leaving behind a clear fluid called **serum.** Normally, clots (thrombi) do not form in blood vessels unless the vessel is damaged or the flow of blood is impeded. **Anticoagulant substances** in the bloodstream inhibit blood clotting, so clots do not form. **Heparin,** produced by tissue cells (especially in the liver), is an example of an anticoagulant. Other drugs such as **warfarin (Coumadin)** are given to patients with thromboembolic diseases to prevent the formation of clots.

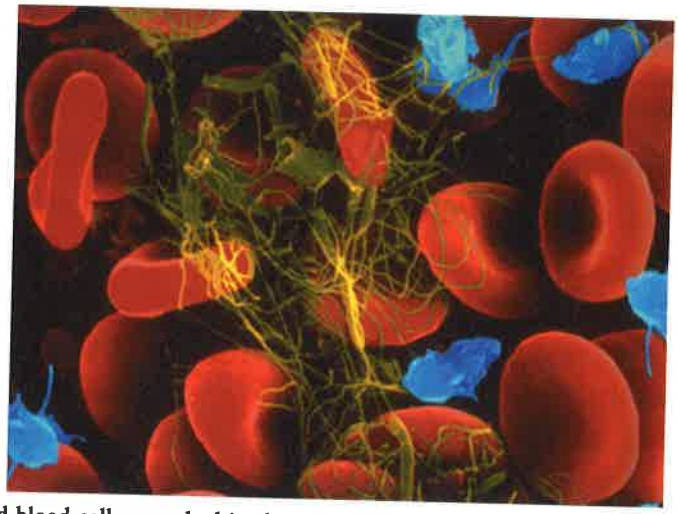

FIGURE 13–9 **A red blood cell enmeshed in threads of fibrin.** (From Thibodeau GA, Patton KT: Anatomy & Physiology, 6th ed., St. Louis, Mosby, 2007, p. 663.)

VOCABULARY

This list reviews many of the new terms introduced in the text. Short definitions reinforce your understanding of the terms. Refer to the Pronunciation of Terms on page 538 for help with difficult or unfamiliar words.

albumin	Protein in blood; maintains the proper amount of water in the blood.
antibody (Ab)	Protein (immunoglobulin) produced by lymphocytes in response to bacteria, viruses, or other antigens. An antibody is specific to an antigen and inactivates it.
antigen	Substance (usually foreign) that stimulates the production of an antibody.
basophil	White blood cell containing granules that stain blue; associated with release of histamine and heparin.
bilirubin	Orange-yellow pigment in bile; formed by the breakdown of hemoglobin when red blood cells die.
coagulation	Blood clotting.
colony-stimulating factor (CSF)	Protein that stimulates the growth and proliferation of white blood cells (granulocytes).
differentiation	Change in structure and function of a cell as it matures; specialization.
electrophoresis	Method of separating serum proteins by electrical charge.
eosinophil	White blood cell containing granules that stain red; associated with allergic reactions.
erythrocyte	Red blood cell. There are about 5 million per microliter (μL) or cubic millimeter (mm^3) of blood.
erythropoietin (EPO)	Hormone secreted by the kidneys that stimulates red blood cell formation.
fibrin	Protein threads that form the basis of a blood clot.
fibrinogen	Plasma protein that is converted to fibrin in the clotting process.
globulin	Plasma protein; alpha, beta, and gamma (immune) globulins are examples.
granulocyte	White blood cell with numerous dark-staining granules: eosinophil, neutrophil, and basophil.
hemoglobin	Blood protein containing iron; carries oxygen in red blood cells.
hemolysis	Destruction or breakdown of blood (red blood cells).
heparin	Anticoagulant found in blood and tissue cells.
immune reaction	Response of the immune system to foreign invasion.

immunoglobulin	Protein (globulin) with antibody activity; examples are IgG, IgM, IgA, IgE, IgD. Immun/o means protection.
leukocyte	White blood cell.
lymphocyte	Mononuclear leukocyte that produces antibodies.
macrophage	Monocyte that migrates from the blood to tissue spaces. As a phagocyte, it engulfs foreign material and debris.
megakaryocyte	Large platelet precursor cell found in the bone marrow.
monocyte	Leukocyte with one large nucleus. It is a cell that engulfs foreign material and debris. Monocytes become macrophages as they leave the blood and enter body tissues.
mononuclear	Pertaining to a cell (leukocyte) with a single round nucleus; lymphocytes and monocytes are mononuclear leukocytes.
neutrophil	Granulocytic leukocyte formed in bone marrow. It is a phagocytic tissue-fighting cell. Also called a **polymorphonuclear leukocyte.**
plasma	Liquid portion of blood; contains water, proteins, salts, nutrients, hormones, and vitamins.
plasmapheresis	Removal of plasma from withdrawn blood by centrifuge. Collected cells are retransfused back into the donor. Fresh-frozen plasma or salt solution is used to replace withdrawn plasma.
platelet	Small blood fragment that collects at sites of injury to begin the clotting process.
prothrombin	Plasma protein; converted to thrombin in the clotting process.
reticulocyte	Immature erythrocyte. A network of strands (reticulin) is seen after staining the cell with special dyes.
Rh factor	Antigen on red blood cells of Rh-positive (RH+) individuals. The factor was first identified in the blood of a rhesus monkey.
serum	Plasma minus clotting proteins and cells. Clear, yellowish fluid that separates from blood when it is allowed to clot. It is formed from plasma, but does not contain protein-coagulation factors.
stem cell	Unspecialized cell that gives rise to mature, specialized forms. A **hematopoietic stem cell** is the progenitor for all different types of blood cells.
thrombin	Enzyme that converts fibrinogen to fibrin during coagulation.
thrombocyte	Platelet.

TERMINOLOGY

Write the meanings of the medical terms in the spaces provided.

COMBINING FORMS

COMBINING FORM	MEANING	TERMINOLOGY	MEANING
bas/o	base (*alkaline*, the opposite of acid)	basophil _____ *The suffix -phil means attraction to.*	
chrom/o	color	hypochromic _____ *Hypochromic anemia is marked by a decreased concentration of hemoglobin in red blood cells.*	
coagul/o	clotting	anticoagulant _____	
		coagulopathy _____	
cyt/o	cell	cytology _____	
eosin/o	red, dawn, rosy	eosinophil _____	
erythr/o	red	erythroblast _____ *-blast means immature.*	
granul/o	granules	granulocyte _____	
hem/o	blood	hemolysis _____ *Destruction or breakdown of red blood cells. See hemolytic anemia, page 518.*	
hemat/o	blood	hematocrit _____ *The suffix -crit means to separate. The hematocrit gives the percentage of red blood cells in a volume of blood. See page 523.*	
hemoglobin/o	hemoglobin	hemoglobinopathy _____	
is/o	same, equal	anisocytosis _____ *An abnormality of red blood cells; they are of unequal (anis/o) size; -cytosis means an increase in the number of cells.*	
kary/o	nucleus	megakaryocyte _____	
leuk/o	white	leukopenia _____	
mon/o	one, single	monocyte _____ *The cell has a single, rather than a multilobed, nucleus.*	
morph/o	shape, form	morphology _____	

COMBINING FORM	MEANING	TERMINOLOGY	MEANING
myel/o	bone marrow	myeloblast	
		The suffix -blast indicates an immature cell.	
		myelodysplasia	
		This is a preleukemic condition.	
neutr/o	neutral (neither base nor acid)	neutropenia	
		This term refers to neutrophils.	
nucle/o	nucleus	polymorphonuclear	
phag/o	eat, swallow	phagocyte	
poikil/o	varied, irregular	poikilocytosis	
		Irregularity in the shape of red blood cells. Poikilocytosis occurs in certain types of anemia.	
sider/o	iron	sideropenia	
spher/o	globe, round	spherocytosis	
		In this condition, the erythrocyte has a round shape, making the cell fragile and easily able to be destroyed.	
thromb/o	clot	thrombocytopenia	

SUFFIXES

SUFFIX	MEANING	TERMINOLOGY	MEANING
-apheresis	removal, a carrying away	plasmapheresis	
		A centrifuge spins blood to remove plasma from the other parts of blood.	
		leukapheresis	
		plateletpheresis	
		Note that the a of apheresis is dropped in this term. Platelets are removed from the donor's blood (and used in a patient), and the remainder of the blood is reinfused into the donor.	
-blast	immature cell, embryonic	monoblast	

Don't confuse -apheresis with -phoresis

The suffix -apheresis, see page 516, refers to the removal of blood from a donor with a portion separated and retained and the remainder reinfused into the donor. The suffix -phoresis indicates transmission (as in **electrophoresis,** the transmission of electricity to separate substances).

SUFFIX	MEANING	TERMINOLOGY	MEANING
-cytosis	abnormal condition of cells (increase in cells)	macrocytosis	*Macrocytes are erythrocytes that are larger (macro-) than normal.*
		microcytosis	*These are erythrocytes that are smaller (micro-) than normal. Table 13-3 reviews terms related to abnormalities of red blood cell morphology.*
-emia	blood condition	leukemia	*See page 520.*
-globin	protein	hemoglobin	
-globulin		immunoglobulin	
-lytic	pertaining to destruction	thrombolytic therapy	*Used to dissolve clots.*
-oid	derived from	myeloid	
-osis	abnormal condition	thrombosis	
-penia	deficiency	granulocytopenia	
		pancytopenia	
-phage	eat, swallow	macrophage	*A large phagocyte that destroys worn-out red blood cells and foreign material.*
-philia	attraction for (an increase in cell numbers)	eosinophilia	
		neutrophilia	
-phoresis	carrying, transmission	electrophoresis	
-poiesis	formation	hematopoiesis	
		erythropoiesis	***Erythropoietin** is produced by the kidneys to stimulate erythrocyte formation.*
		myelopoiesis	
-stasis	stop, control	hemostasis	

TABLE 13-3 Abnormalities of Red Blood Cell Morphology

Abnormality	Description
Anisocytosis	Cells are **unequal** in size
Hypo**chromia**	Cells have reduced **color** (less hemoglobin)
Macrocytosis	Cells are **large**
Microcytosis	Cells are **small**
Poikilocytosis	Cells are **irregularly shaped**
Spherocytosis	Cells are **rounded**

PATHOLOGY

Any abnormal or pathologic condition of the blood generally is referred to as a blood **dyscrasia** (disease). The blood dyscrasias discussed in this section are organized in the following manner: diseases of red blood cells, disorders of blood clotting, diseases of white blood cells, and disease of the bone marrow.

DISEASES OF RED BLOOD CELLS

anemia

Deficiency in erythrocytes or hemoglobin.

The most common type of anemia is **iron deficiency anemia;** it is caused by a lack of iron, which is required for hemoglobin production (Figure 13-10).

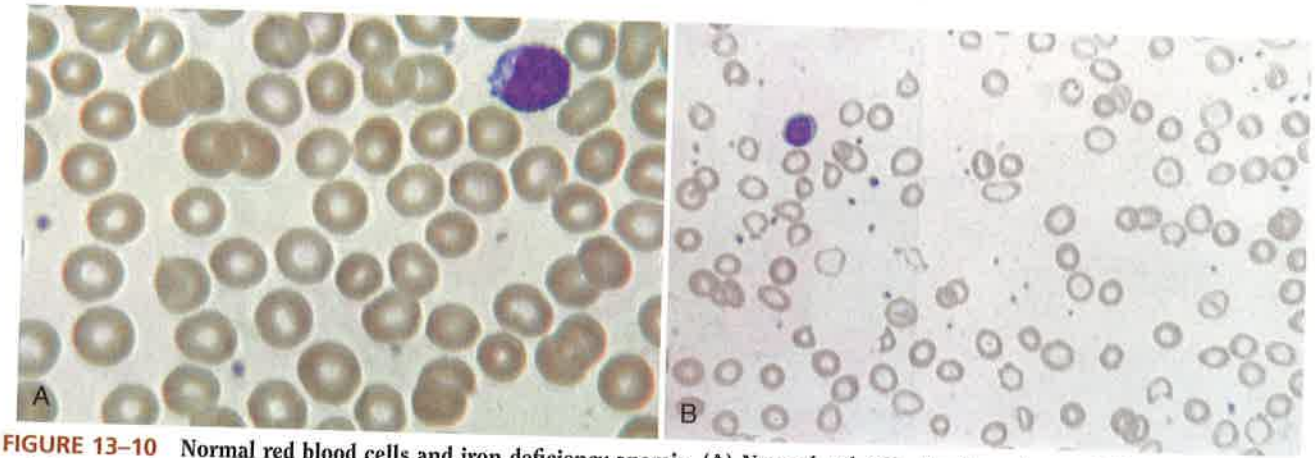

FIGURE 13–10 Normal red blood cells and iron deficiency anemia. (A) Normal red cells. Erythrocytes are fairly uniform in size and shape. The red cells are normal in hemoglobin content (normochromic) and size (normocytic). **(B) Iron deficiency anemia.** Many erythrocytes are small (microcytic) and have increased central pallor (hypochromic). Red cells in this slide show variation in size (anisocytosis) and shape (poikilocytosis). (From Tkachuk DC, Hirschmann JV, McArthur JR: Atlas of Clinical Hematology, Philadelphia, Saunders, 2002, p. 4.)

Other types of anemia include:

1. **aplastic anemia**

Failure of blood cell production in the bone marrow.

The cause of most cases of aplastic anemia is unknown (idiopathic), but some have been linked to benzene exposure and to antibiotics such as chloramphenicol. **Pancytopenia** occurs when stem cells fail to produce leukocytes, platelets, and erythrocytes. Blood transfusions prolong life, allowing the marrow time to resume its normal functioning, and antibiotics control infections. Bone marrow transplantation and regimens of drugs that inhibit the immune system are successful treatments in cases in which spontaneous recovery is unlikely.

2. **hemolytic anemia**

Reduction in red cells due to excessive destruction.

One example of hemolytic anemia is **congenital spherocytic anemia (hereditary spherocytosis).** Instead of their normal biconcave shape, erythrocytes become spheroidal. This rounded shape makes them fragile and easily destroyed (hemolysis). Shortened red cell survival results in increased reticulocytes in blood as the bone marrow compensates for hemolysis of mature erythrocytes. Because the spleen destroys red cells, removal of the spleen usually improves this anemia. Figure 13-11 shows the altered shape of erythrocytes in hereditary spherocytosis.

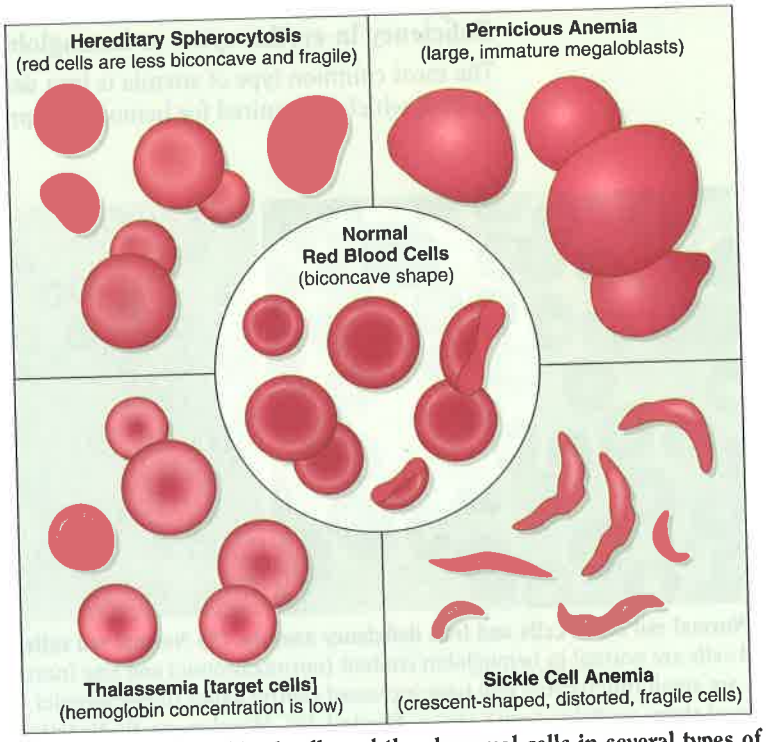

FIGURE 13–11 Normal red blood cells and the abnormal cells in several types of anemia.

3. pernicious anemia

Lack of mature erythrocytes caused by inability to absorb vitamin B_{12} into the body.

Vitamin B_{12} is necessary for the proper development and maturation of erythrocytes. Although vitamin B_{12} is a common constituent of food (liver, kidney, sardines, egg yolks, oysters), it cannot be absorbed into the bloodstream without the aid of a special substance called **intrinsic factor** that is normally found in gastric juice. People with pernicious anemia lack this factor in their gastric juice, and the result is unsuccessful maturation of red blood cells, with an excess of large, immature, and poorly functioning cells in the bone marrow and large, often oval red cells (macrocytes) in the circulation. Treatment is administration of vitamin B_{12} for life. Figure 13-11 illustrates cells in pernicious anemia. Pernicious means ruinous or hurtful.

4. sickle cell anemia

Hereditary condition characterized by abnormal sickle shape of erythrocytes and by hemolysis.

The crescent, or sickle, shape of the erythrocyte (see Figure 13-11) is caused by an abnormal type of hemoglobin (hemoglobin S) in the red cell. The distorted, fragile erythrocytes cannot pass through small blood vessels normally, leading to thrombosis and infarction (local tissue death from ischemia). Signs and symptoms include arthralgias, acute attacks of abdominal pain, and ulcerations of the extremities. The genetic defect (presence of the hemoglobin S gene) is particularly prevalent in black persons of African or African American ancestry and appears with different degrees of severity. Individuals who inherit just one gene for the trait usually do not have symptoms.

5. thalassemia

Inherited defect in the ability to produce hemoglobin, usually seen in persons of Mediterranean background.

This condition manifests in varying forms and degrees of severity and usually leads to hypochromic anemia with diminished hemoglobin content in red cells (see Figure 13-11). *Thalassa* is a Greek word meaning sea.

hemochromatosis

Excess iron deposits throughout the body.

Hepatomegaly, skin pigmentation, diabetes, and cardiac failure may occur.

polycythemia vera

General increase in red blood cells (erythremia).

Blood consistency is viscous (thick) because of greatly increased numbers of erythrocytes. The bone marrow is hyperplastic, and leukocytosis and thrombocytosis commonly accompany the increase in red blood cells. Treatment consists of reduction of red cell volume to normal levels by phlebotomy (removal of blood from a vein) and by suppressing blood cell production with myelotoxic drugs. Notice that that suffix here is -hemia, instead of -emia.

DISORDERS OF BLOOD CLOTTING

hemophilia

Excessive bleeding caused by hereditary lack of blood clotting factors (factor VIII or IX) necessary for blood clotting.

Although the platelet count of a hemophiliac patient is normal, deficiency in clotting factors (factor VIII or IX) results in a prolonged coagulation time. Treatment consists of administration of the deficient factor.

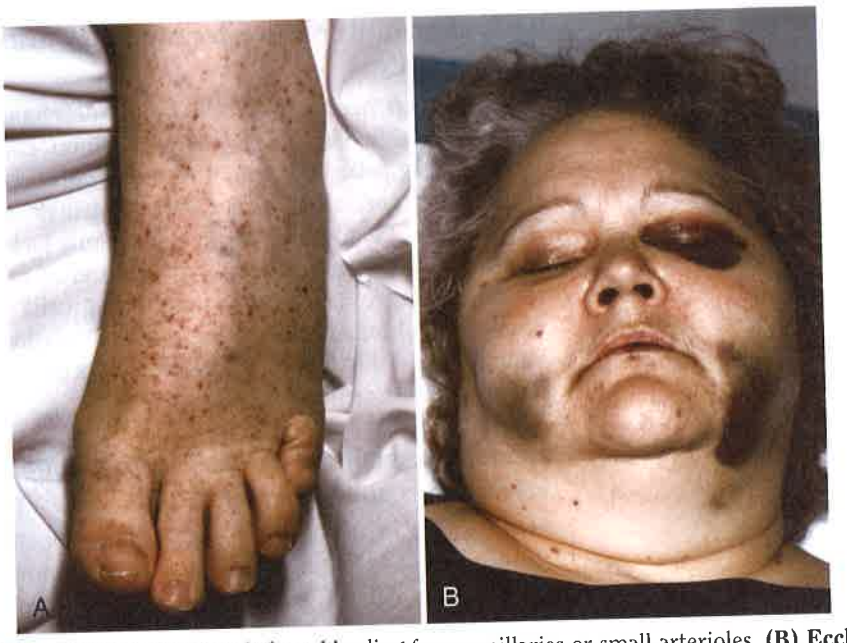

FIGURE 13–12 **(A) Petechiae** result from bleeding from capillaries or small arterioles. **(B) Ecchymoses** are larger and more extensive than petechiae. (From Gould BE: Pathophysiology for the Health Professions, 3rd ed., Philadelphia, Saunders, 2006, p. 250.)

purpura

Multiple pinpoint hemorrhages and accumulation of blood under the skin.

Hemorrhages into the skin and mucous membranes produce red-purple discoloration of the skin. **Petechiae** are tiny purple or red flat spots appearing on the skin as a result of hemorrhages. **Ecchymoses** are larger blue or purplish patches on the skin (bruises) (Figure 13-12). Purpura can be caused by having too few platelets (thrombocytopenia). The cause may be immunologic, meaning the body produces an antiplatelet factor that harms its own platelets. **Autoimmune thrombocytopenic purpura** is a condition in which a patient makes an antibody that destroys platelets. Bleeding time is prolonged; splenectomy (the spleen is the site of platelet destruction) and drug therapy with corticosteroids are common treatments.

DISEASES OF WHITE BLOOD CELLS

leukemia

Increase in cancerous white blood cells (leukocytes).

Acute leukemias have common clinical characteristics: abrupt onset of symptoms, fatigue, fever, bleeding, bone pain, lymphadenopathy, splenomegaly, and hepatomegaly. If the disease has spread to the spinal canal, CNS signs such as headache and vomiting may occur. In addition, because normal blood cells are crowded out, patients have little defense against infection.

Four types of leukemia are:

1. **Acute myelogenous (myelocytic) leukemia (AML).** Immature granulocytes (myeloblasts) predominate. Platelets and erythrocytes are diminished because of infiltration and replacement of the bone marrow by large numbers of myeloblasts (Figure 13-13A).

2. **Acute lymphocytic leukemia (ALL).** Immature lymphocytes (lymphoblasts) predominate. This form is seen most often in children and adolescents; onset is sudden (Figure 13-13B).
3. **Chronic myelogenous (myelocytic) leukemia (CML).** Both mature and immature granulocytes are present in large numbers in the marrow and bloodstream. This is a slowly progressive illness with which patients (often adults older than 55) may live for many years without encountering life-threatening problems. New therapies (such as the drug Gleevec) target abnormal proteins responsible for malignancy and produce long-term control.
4. **Chronic lymphocytic leukemia (CLL).** Abnormal numbers of relatively mature lymphocytes predominate in the marrow, lymph nodes, and spleen. This most common form of leukemia usually occurs in the elderly and follows a slowly progressive course. It often does not require immediate treatment.

All forms of leukemia are treated with chemotherapy, using drugs that prevent cell division and selectively injure rapidly dividing cells. Effective treatment can lead to a **remission** (disappearance of signs and symptoms of disease). **Relapse** occurs when disease symptoms and signs reappear, necessitating further treatment.

Transplantation of normal bone marrow from donors of similar tissue type is successful in restoring normal bone marrow function in some patients with acute leukemia. This procedure is performed after high-dose chemotherapy, which is administered to eliminate the leukemic cells.

granulocytosis

Abnormal increase in granulocytes in the blood.

An increase in neutrophils in the blood may occur in response to infection or inflammation of any type. **Eosinophilia** is an increase in eosinophilic granulocytes, seen in certain allergic conditions, such as asthma, or in parasitic infections (tapeworm, pinworm). **Basophilia** is an increase in basophilic granulocytes seen in certain types of leukemia.

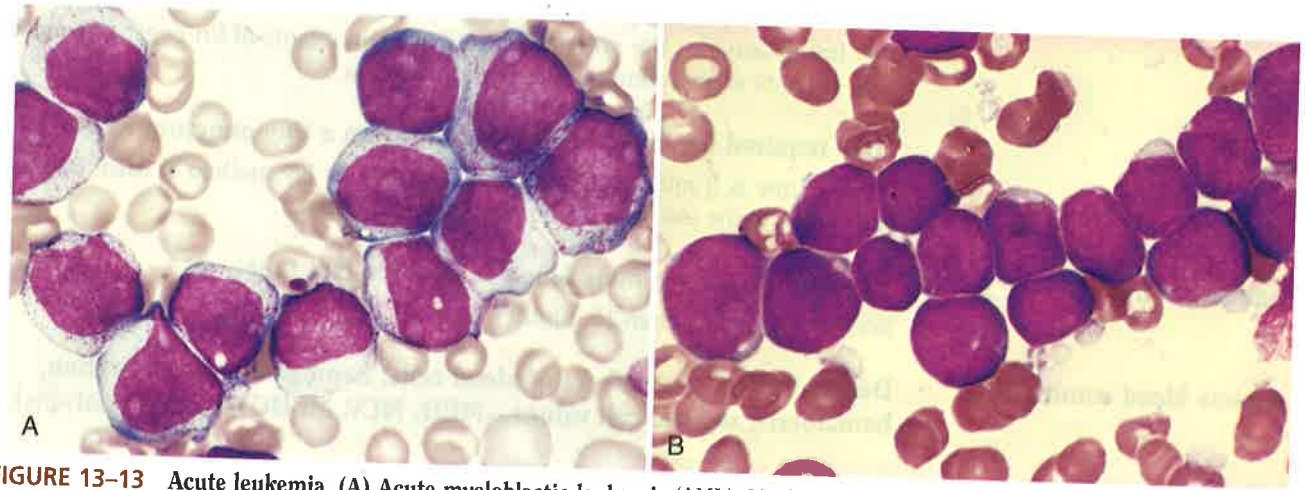

FIGURE 13–13 Acute leukemia. (A) Acute myeloblastic leukemia (AML). Myeloblasts (immature granulocytes) predominate. There are large cells with small granules in their cytoplasm. AML affects primarily adults. A majority of patients achieve remission with intensive chemotherapy, but relapse is common. Hematopoietic stem cell transplantation may be a curative therapy. **(B) Acute lymphoblastic leukemia** (ALL). Lymphoblasts (immature lymphocytes) predominate. ALL is a disease of children and young adults. Most children are cured with chemotherapy. (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas; from Kumar V et al: Robbins Basic Pathology, 8th ed., Philadelphia, Saunders, 2007, p. 448.)

mononucleosis

Infectious disease marked by increased numbers of leukocytes and enlarged cervical lymph nodes.

This disease is transmitted by the **Epstein-Barr virus (EBV).** Lymphadenitis is present, with fever, fatigue, asthenia (weakness), and pharyngitis. Atypical lymphocytes are present in the blood, liver, and spleen (leading to hepatomegaly and splenomegaly).

Mononucleosis usually is transmitted by direct oral contact (salivary exchange during kissing) and affects primarily young adults. No treatment is necessary for EBV infections. Antibiotics are not effective for self-limited viral illnesses. Rest during the period of acute symptoms and slow return to normal activities are advised.

DISEASE OF BONE MARROW CELLS

multiple myeloma

Malignant neoplasm of bone marrow.

The malignant cells (lymphocytes that produce antibodies) destroy bone tissue and cause overproduction of immunoglobulins, including **Bence Jones protein**, an immunoglobulin fragment found in urine. The condition leads to osteolytic lesions, hypercalcemia, anemia, renal damage, and increased susceptibility to infection. Treatment is with analgesics, radiotherapy, various doses of chemotherapy, and special orthopedic supports. Drugs such as thalidomide and Velcade are **palliative** (relieving symptoms) and stop disease progression, which improves the outlook for this disease. **Autologous bone marrow transplantation (ABMT),** in which the patient serves as his or her own donor for stem cells, may lead to prolonged remission.

LABORATORY TESTS AND CLINICAL PROCEDURES

LABORATORY TESTS

antiglobulin test

Test for the presence of antibodies that coat and damage erythrocytes.

This test determines the presence of antibodies in infants of Rh-negative women or in patients with autoimmune hemolytic anemia.

bleeding time

Time required for blood to stop flowing from a tiny puncture wound.

Normal time is 8 minutes or less. The Simplate or Ivy method is used. Platelet disorders and the use of aspirin prolong bleeding time.

coagulation time

Time required for venous blood to clot in a test tube.

Normal time is less than 15 minutes.

complete blood count (CBC)

Determination of numbers of blood cells, hemoglobin concentration, hematocrit, and red cell values—MCH, MCV, MCHC (see Abbreviations).

erythrocyte sedimentation rate (ESR)

Speed at which erythrocytes settle out of plasma.

Venous blood is collected into an anticoagulant, and the blood is placed in a tube in a vertical position. The distance that the erythrocytes sink in a given period of time is the sedimentation rate. The rate increases with infections, joint inflammation, and tumor, which increase the fibrinogen content of the blood. Also called sed rate for short.

hematocrit (Hct)

Percentage of erythrocytes in a volume of blood.

A sample of blood is spun in a centrifuge so that the erythrocytes fall to the bottom of the sample.

hemoglobin test (H, Hg, Hgb, HGB)

Total amount of hemoglobin in a sample of peripheral blood.

platelet count

Number of platelets per cubic millimeter (mm^3) or microliter (μL) of blood.

Platelets normally average between 150,000 and 350,000 per mm^3 (cu mm) or μL.

prothrombin time (PT)

Test of the ability of blood to clot.

Prothrombin is one of the clotting factors (factor II) made by the liver. This test is used to monitor (follow) patients taking anticoagulant drugs. Another blood clotting test, **partial thromboplastin time (PTT)**, measures other clotting factors. Both PT and PPT are often done at the same time to check for bleeding problems.

red blood cell count (RBC)

Number of erythrocytes per cubic millimeter (mm^3) or microliter (μL) of blood.

The normal number is 4 to 6 million per mm^3 (or μL).

red blood cell morphology

Microscopic examination of a stained blood smear to determine the shape of individual red cells.

Abnormal morphology includes anisocytosis, poikilocytosis, and sickle cells.

white blood cell count (WBC)

Number of leukocytes per cubic millimeter (mm^3) or microliter (μL) of blood.

Automated counting devices record numbers within seconds. Normal number of leukocytes averages between 5000 and 10,000 per mm^3 (or μL).

white blood cell differential [count]

Percentages of different types of leukocytes in the blood.

Some instruments can produce an automated differential count, but otherwise the cells are stained and counted under a microscope by a technician. Percentages of neutrophils, eosinophils, basophils, monocytes, lymphocytes, and immature cells (bands) are determined. See page 526 for the normal differential values.

The term **shift to the left** describes an increase in immature neutrophils in the blood.

Shift to the Left

The phrase "shift to the left" derives from the early practice of reporting percentages of each WBC type across the top of a page, starting with blasts (immature cells) on the left and more mature cells on the right. An increase in immature neutrophils (as seen with severe infection) would be noted on the left-hand column of a form. Thus a "shift to the left" indicates an infection and the body's effort to fight it by making more neutrophils.

CLINICAL PROCEDURES

apheresis

Separation of blood into component parts and removal of a select portion from the blood.

This procedure can remove toxic substances or autoantibodies from the blood and can collect blood cells. Leukapheresis, plateletpheresis, and plasmapheresis are examples (Figure 13-14). If plasma is removed from the patient and fresh plasma is given, the procedure is termed **plasma exchange.**

blood transfusion

Whole blood or cells are taken from a donor and infused into a patient.

Appropriate testing to ensure a match of red blood cell type (A, B, AB, or O) is essential. Tests also are performed to detect the presence of hepatitis and the acquired immunodeficiency syndrome (AIDS) virus (HIV). **Autologous transfusion** is the collection and later reinfusion of a patient's own blood or blood components. **Packed cells** are a preparation of red blood cells separated from liquid plasma and administered in severe anemia to restore levels of hemoglobin and red cells without overdiluting the blood with excess fluid.

bone marrow biopsy

Microscopic examination of a core of bone marrow removed with a needle.

This procedure is helpful in the diagnosis of blood disorders such as anemia, cell deficiencies, and leukemia. Bone marrow also may be removed by brief suction produced by a syringe, which is termed a **bone marrow aspirate.**

hematopoietic stem cell transplantation

Peripheral stem cells from a compatible donor are administered to a recipient.

Patients with malignant hematologic disease, such as AML, ALL, CLL, CML, and multiple myeloma, are candidates for this treatment. First the donor is treated with a drug that mobilizes stem cells into the blood. Then stem cells are removed from the donor, a process like leukapheresis in Figure 13-14. Meanwhile, the patient (recipient) undergoes a conditioning process in which radiation and chemotherapy drugs are administered to kill malignant marrow cells and inactivate the patient's immune system so that subsequently infused stem cells will not be rejected. A cell suspension containing the donor's stem cells, which will repopulate the bone marrow, is then given through a vein to the recipient. **Bone**

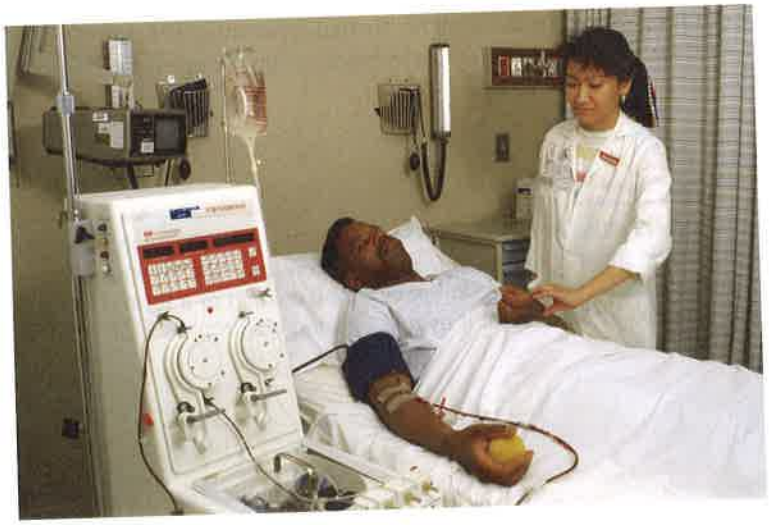

FIGURE 13–14 Leukapheresis. This machine is an automated blood cell separator that removes large numbers of white blood cells and returns red cells, platelets, and plasma to the patient. (From Black JM, Hawks JH, Keene AM: Medical-Surgical Nursing: Clinical Management for Positive Outcomes, 6th ed., Philadelphia, Saunders, 2001, p. 2170.)

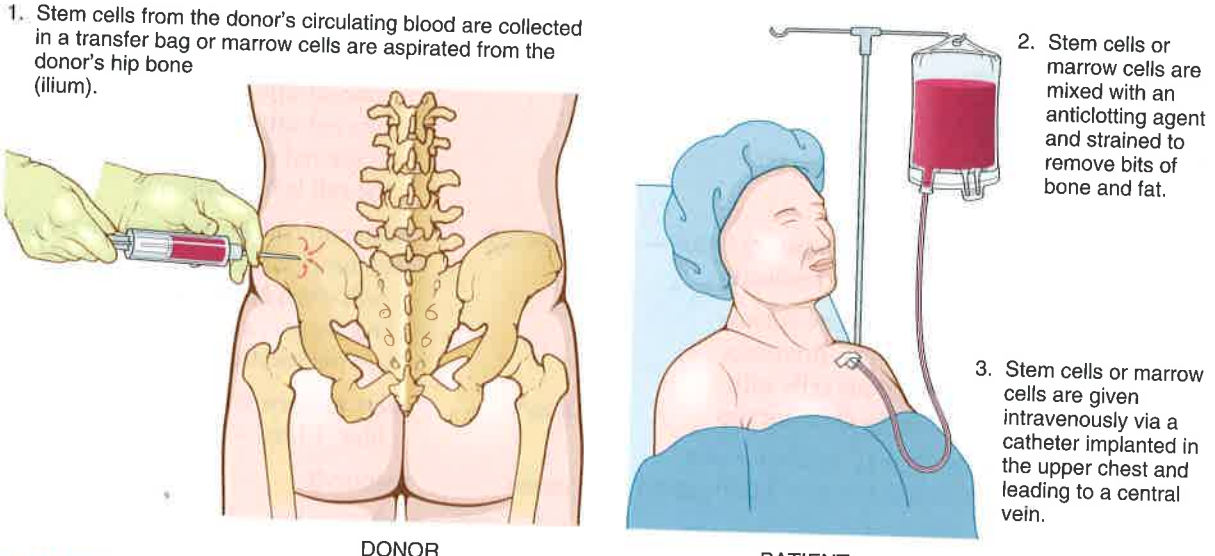

FIGURE 13–15 Hematopoietic stem cell and bone marrow transplantation. These procedures constitute **allogeneic** (all/o means other, different) **transplantation,** in which a relative or unrelated person having a close or identical HLA (human leukocyte antigen) type is the donor. It carries a high rate of morbidity (disease) and mortality (death) because of complications of incompatibility such as GVHD (graft-versus-host disease). In an **autologous transplantation,** stem cells or bone marrow cells are removed from the patient during a remission phase and given back to the patient after intensive chemotherapy (drug treatment).

marrow transplantation follows the same procedure, except that bone marrow cells are used rather than peripheral stem cells (Figure 13-15). Problems encountered subsequently may include serious infection, **graft-versus-host disease (GVHD),** and relapse of the original disease despite the treatment.

In GVHD, the immunocompetent cells in the donor's tissue recognize the recipient's tissues as foreign and attack them. Because the recipient patient is totally immunosuppressed, his or her immune system cannot defend against the attack.

ABBREVIATIONS

Ab	antibody
ABMT	autologous bone marrow transplantation—patient serves as his or her own donor for stem cells
ABO	four main blood types—A, B, AB, and O
ALL	acute lymphocytic leukemia
AML	acute myelogenous leukemia
ANC	absolute neutrophil count—this is the total WBC times a measure of the number of neutrophils present in the blood; a normal ANC is about 1500 cells (ANC of less than 500 cells is neutropenia)
ASCT	autologous stem cell transplantation
bands	immature white blood cells (granulocytes)
baso	basophils
BMT	bone marrow transplantation
CBC	complete blood count
CLL	chronic lymphocytic leukemia
CML	chronic myelogenous leukemia
DIC	disseminated intravascular coagulation—bleeding disorder marked by reduction in blood clotting factors due to their use and depletion for intravascular clotting
diff	differential count (white blood cells)
EBV	Epstein-Barr virus; cause of mononucleosis

eos	eosinophils
EPO	erythropoietin
ESR	erythrocyte sedimentation rate
Fe	iron
G-CSF	granulocyte colony-stimulating factor—promotes neutrophil production
GM-CSF	granulocyte-macrophage colony-stimulating factor—promotes myeloid progenitor cells with differentiation to granulocytes
g/dL	gram per deciliter (1 deciliter = one tenth of a liter; 1 liter = 1.057 quarts)
GVHD	graft-versus-host disease—immune reaction of donor's cells to recipient's tissue
HCL	hairy cell leukemia—abnormal lymphocytes accumulate in bone marrow, leading to anemia, thrombocytopenia, neutropenia, and infection
Hct	hematocrit
Hgb, HGB	hemoglobin
H and H	hemoglobin and hematocrit
HLA	human leukocyte antigen
IgA, IgD, IgE, IgG, IgM	immunoglobulins
lymphs	lymphocytes
MCH	mean corpuscular hemoglobin—average amount of hemoglobin per cell
MCHC	mean corpuscular hemoglobin concentration—average concentration of hemoglobin in a single red cell; when MCHC is low, the cell is hypochromic
MCV	mean corpuscular volume—average volume or size of a single red blood cell; when MCV is high, the cells are macrocytic, and when low, the cells are microcytic
mm³	cubic millimeter—one millionth of a liter; 1 liter = 1.057 quarts
mono	monocyte
polys, PMNs, PMNLs	polymorphonuclear leukocytes; neutrophils, eosinophils, basophils
PT	prothrombin time
PTT	partial thromboplastin time
RBC	red blood cell; red blood cell count
sed rate	erythrocyte sedimentation rate
segs	segmented, mature white blood cells (neutrophils)
SMAC	Sequential Multiple Analyzer Computer—an automated chemistry system that determines substances in serum
μL	microliter—one millionth of a liter; 1 liter = 1.057 quarts
WBC	white blood cell; white blood cell count
WNL	within normal limits

PRACTICAL APPLICATIONS

The cases presented here are based on data from actual medical records. Use the table of normal values to help you decide on a probable diagnosis in each case. Answers to the questions are on page 537.

Normal Laboratory Values

WBC 4,500–11,000/mm³ or μL

Differential:

Segs (polys)	54-62%
Lymphs	20-40%
Eos	1-3%
Baso	0-1%
Mono	3-7%

RBC	M:	4.5-6.0 million per mm³ or μL
	F:	4.0-5.5 million per mm³ or μL
Hct	M:	40-50%
	F:	37-47%
Hgb	M:	14-16 g/dL
	F:	12-14 g/dL

Platelets 150,000-350,000/mm³ or μL