12 Blood

Health-care workers wear personal protective equipment to shield themselv from body fluids containing disease-causing viruses.

Universal precautions. Blood can consist of more than cells, nutrients, proteins, and water—a single drop from an infected individual can harbor billions of viruses. In the wake of the AIDS epidemic, in 1988 the U.S. Centers for Disease Control and Prevention (CDC) devised "universal precautions," which are specific measures that health-care workers should take to prevent transmission of bloodborne infectious agents in the workplace. The CDC singled out HIV and the hepatitis B virus. The guidelines grew out of earlier suggestions for handling patients suspected to have been exposed to viruses. The term *universal* refers to the assumption that *any* patient may have been exposed to a pathogen that can be transmitted in a body fluid.

Attention to safety in the health-care setting can prevent transmission of infectious diseases. The World Health Organization estimates that 4–7% of new infections worldwide are transmitted via unsafe injections. Specific recommendations include:

- Use of personal protective equipment, such as gloves, goggles, and masks
- Engineering controls, such as fume hoods and sharps containers
- Work-practice controls, such as enforcing handwashing before and after performing procedures

Universal precautions were designed for, and work well in, preventing transmission of viral illnesses in settings that are already relatively safe, such as clinics. This isn't the case for outbreaks, natural disasters, and combat zones. For example, several pediatric nurses who aided neighbors infected with the Marburg virus in the isolated town of Uige in Angola, South Africa, in 2005 died from this hemorrhagic fever along with hundreds of others.

Headache, fever, vomiting, and diarrhea begin three to nine d after exposure to the virus. Then the person bleeds from all bc openings, internally, and under the skin. Plummeting blood press kills most infected individuals within a week, and anyone contact their blood is in danger of infection. Infected individuals must be i lated and not touched, but the scourge spreads because many fan members become infected while tending their loved ones.

In the 2005 outbreak, contaminated medical equipment caus the rapid and deadly spread of the infection. Untrained clinic work reused needles, and some people reused needles and intravenc equipment in their homes. However, even universal precautions mi not have contained this outbreak because the infected body flu were so copious. Universal precautions are critical for containing o breaks under less dire circumstances.

Learning Outcomes

After studying this chapter, you should be able to do the following:

12.1 Introduction

1. Describe the general characteristics of blood, and discuss its major functions. (p. 319)
2. Distinguish among the formed elements and liquid portion of blood. (p. 319)

12.2 Blood Cells

3. Explain the significance of red blood cell counts. (p. 321)
4. Summarize the control of red blood cell production. (p. 321)
5. Distinguish among the five types of white blood cells, and give the function(s) of each type. (p. 325)

12.3 Blood Plasma

6. Describe the functions of each of the major components of plasma. (p. 328)

12.4 Hemostasis

7. Define *hemostasis,* and explain the mechanisms that help achieve it. (p. 33
8. Review the major steps in blood coagu tion. (p. 331)

12.5 Blood Groups and Transfusions

9. Explain blood typing and how it is used to avoid adverse reactions following blood transfusions. (p. 334)
10. Describe how blood reactions may occur between fetal and maternal tissues. (p. 337)

Module 9: Cardiovascular System

Aids to Understanding Words

(Appendix A on page 564 has a complete list of Aids to Understanding Words.)

agglutin- [to glue together] *agglutination*: Clumping of red blood cells.

bil- [bile] *bilirubin*: Pigment excreted in the bile.

embol- [stopper] *embolism*: Obstruction of a blood vessel.

erythr- [red] *erythrocyte*: Red blood cell.

hema- [blood] *hematocrit*: Percentage of red blood cells in a given volume of blood.

hemo- [blood] *hemoglobin*: Red pigment responsible for the color of blood.

leuko- [white] *leukocyte*: White blood cell.

-osis [abnormal condition] leukocyt*osis*: Condition in which white blood cells are overproduced.

-poie [make, produce] erythr*opoietin*: Hormone that stimulates the production of red blood cells.

-stasis [halt] hemo*stasis*: Arrest of bleeding from damaged blood vessels.

thromb- [clot] *thrombocyte*: Blood platelet involved in the formation of a blood clot.

12.1 INTRODUCTION

Blood signifies life, and for good reason—it has many vital functions. This complex mixture of cells, cell fragments, and dissolved biochemicals transports nutrients, oxygen, wastes, and hormones; helps maintain the stability of the interstitial fluid; and distributes heat. The blood, heart, and blood vessels form the cardiovascular system and link the body's internal and external environments.

Blood is a type of connective tissue whose cells are suspended in a liquid extracellular matrix. Blood is vital in transporting substances between body cells and the external environment, thereby promoting homeostasis.

Whole blood is slightly heavier and three to four times more viscous than water. Its cells, which form mostly in red bone marrow, include red blood cells that transport gases and white blood cells that fight disease. Blood also contains cellular fragments called blood platelets that help control blood loss. Together, the cells and platelets are termed "formed elements" of the blood, in contrast to the liquid portion, which is called **plasma** (plaz'mah) (fig. 12.1).

A blood sample is usually about 45% red blood cells by volume. This percentage is called the **hematocrit (HCT).** The white blood cells and platelets account for less than 1% of blood volume. The remaining blood sample, about 55%, is the plasma, a clear, straw-colored liquid. Plasma is a complex mixture of water, amino acids, proteins, carbohydrates, lipids, vitamins, hormones, electrolytes, and cellular wastes (fig. 12.2).

Blood volume varies with body size, changes in fluid and electrolyte concentrations, and the amount of adipose tissue. An average-size adult has a blood volume of about 5 liters (5.3 quarts).

Men have more blood than women. On average, men have 5–6 liters (1.500 gallons), compared to 4–5 liters (0.875 gallons) for women.

Practice

1. What are the major components of blood?
2. What factors affect blood volume?

12.2 BLOOD CELLS

Red Blood Cells

Red blood cells, or **erythrocytes** (ĕ-rith'ro-sītz), are biconcave discs. This shape is an adaptation for transporting gases; it increases the surface area through which gases can diffuse (fig. 12.3). The red blood cell's shape also places the cell membrane closer to oxygen-carrying **hemoglobin** in the cell.

Each red blood cell is about one-third hemoglobin by volume. This protein imparts the color of blood. When hemoglobin binds oxygen, the resulting *oxyhemoglobin* is bright red, and when oxygen is released, the resulting *deoxyhemoglobin* is darker. Blood rich in deoxyhemoglobin may appear bluish when it is viewed through blood vessel walls.

Prolonged oxygen deficiency (hypoxia) causes *cyanosis*, in which the skin and mucous membranes appear bluish due to an abnormally high blood concentration of deoxyhemoglobin. Exposure to low temperature may also cause cyanosis, by constricting superficial blood vessels. This slows blood flow, allowing removal of more oxygen than usual from the blood flowing through the vessels.

Red blood cells have nuclei during their early stages of development, but the cells extrude the nuclei as they mature, providing more space for hemoglobin. Because they lack nuclei, mature red blood cells cannot synthesize proteins or divide. Because they also lack mitochondria, red blood cells produce ATP

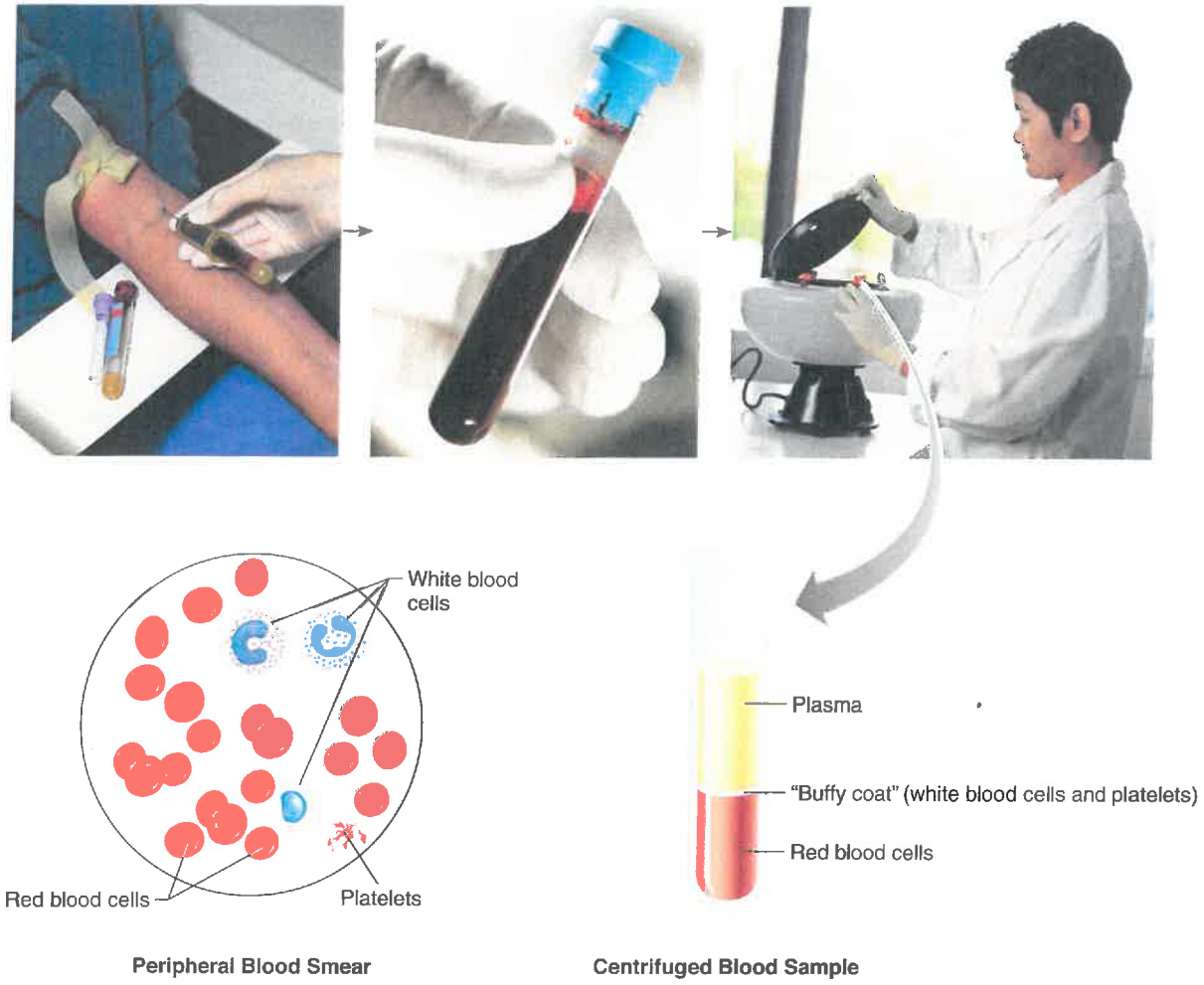


Figure 12.1 AP|R

Blood consists of a liquid portion called plasma and a solid portion (the formed elements) that includes red blood cells, white blood cells, and platelets. (Note: When blood components are separated by centrifugation, the white blood cells and platelets form a thin layer, called the "buffy coat," between the plasma and the red blood cells, which accounts for about 1% of the total blood volume.) Blood cells and platelets can be seen under a light microscope when a blood sample is smeared onto a glass slide.

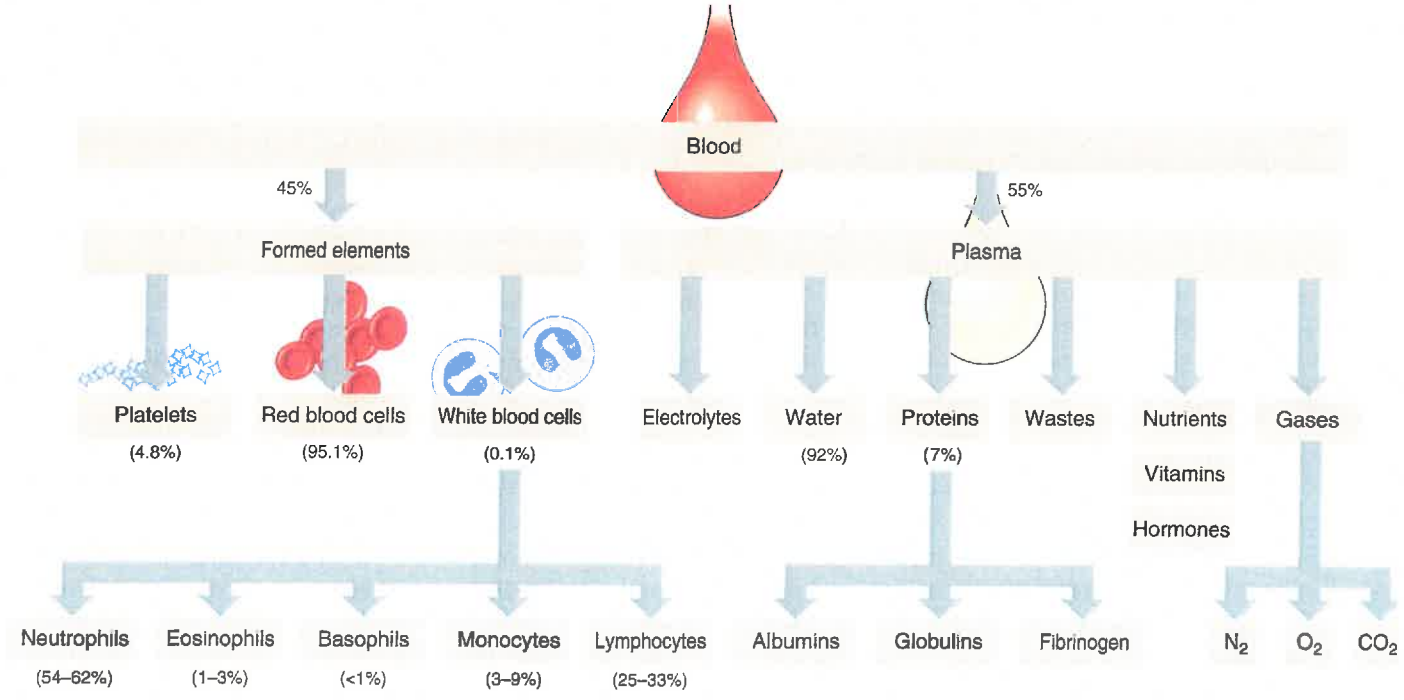


Figure 12.2

Blood composition. Blood is a complex mixture of formed elements in a liquid extracellular matrix, plasma.

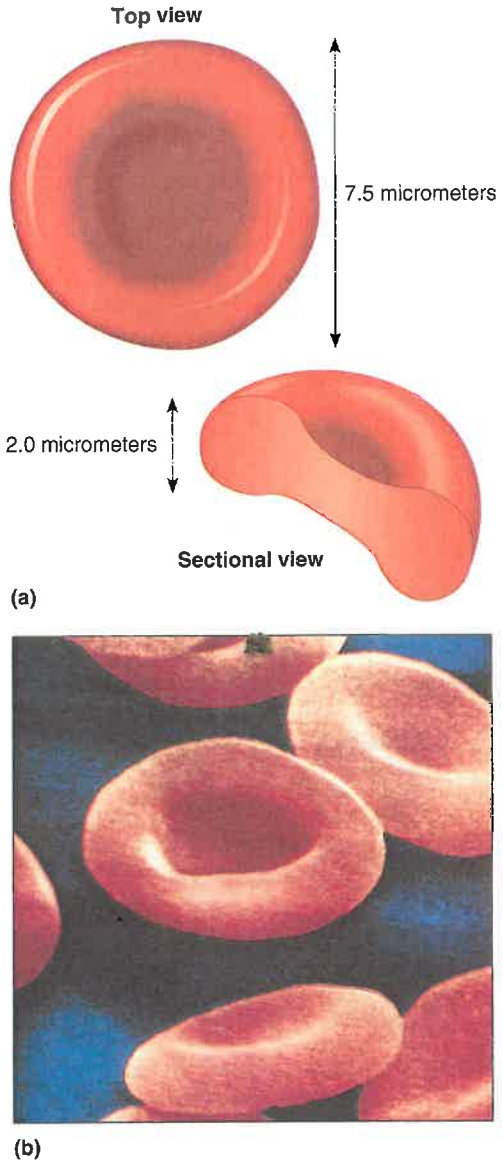


Figure 12.3
Red blood cells. **(a)** The biconcave shape of a red blood cell makes it efficient at transporting gases. **(b)** Falsely colored scanning electron micrograph of human red blood cells (5,000×).

through glycolysis only and use none of the oxygen they carry.

Red Blood Cell Counts

The number of red blood cells in a microliter (μL or mcL or 1 mm^3) of blood is called the *red blood cell count* (*RBCC* or *RCC*). Although this number varies from time to time even in healthy individuals, the typical range for adult males is 4,600,000 to 6,200,000 cells per microliter, and that for adult females is 4,200,000 to 5,400,000 cells per microliter.

Because increasing the number of circulating red blood cells increases the blood's *oxygen-carrying capacity*, changes in this number may affect health. For this reason, red blood cell counts are routinely consulted to help diagnose and evaluate the courses of various diseases.

Practice

3. Describe a red blood cell.
4. What is the function of hemoglobin?
5. How does a red blood cell change as it matures?
6. What is the typical red blood cell count for an adult male? For an adult female?

Red Blood Cell Production and Its Control

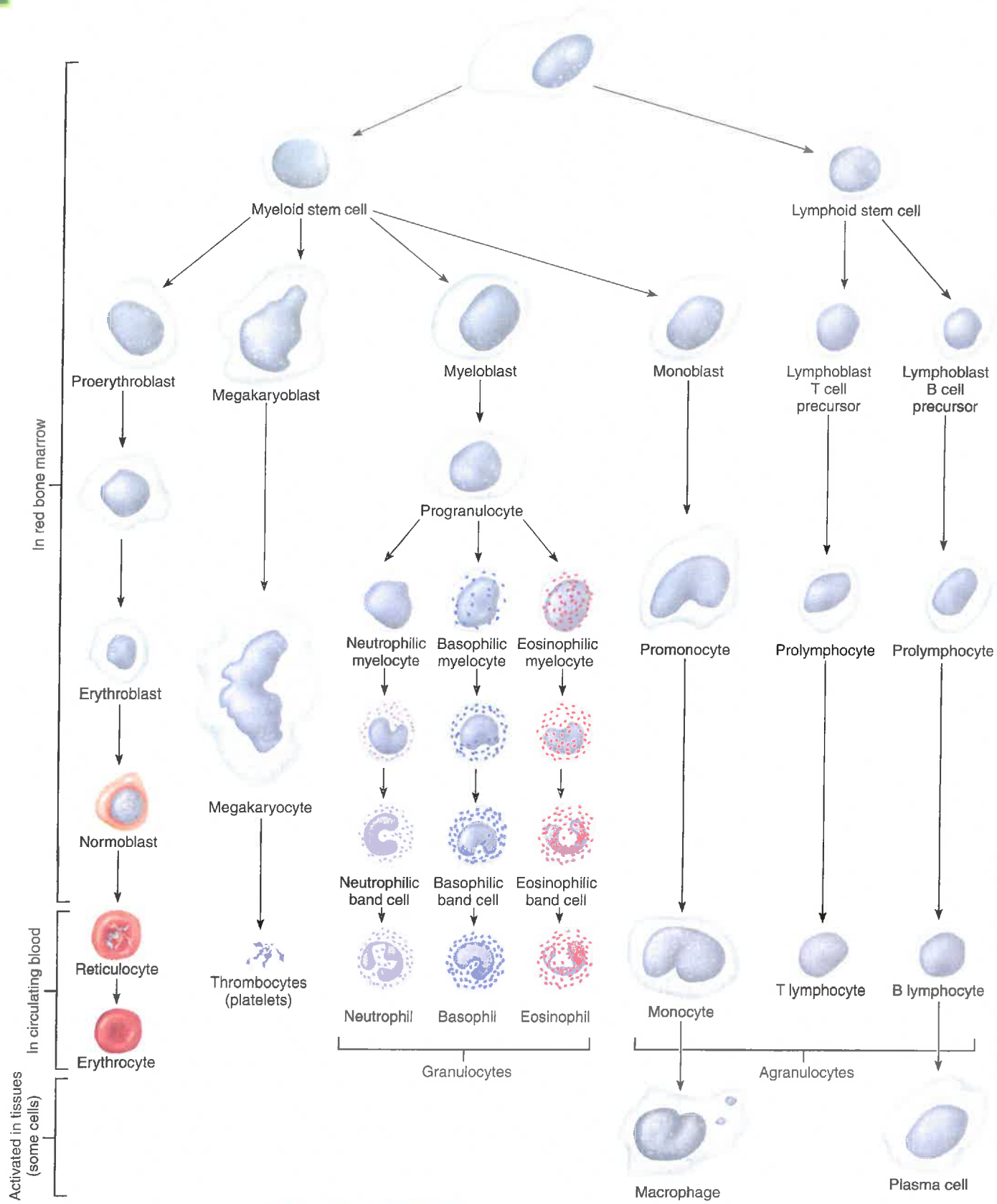
Recall from chapter 7 (p. 140) that red blood cell formation (erythropoiesis) initially occurs in the yolk sac, liver, and spleen. After birth, these cells are produced almost exclusively by tissue lining the spaces in bones, filled with red bone marrow. Figure 12.4 illustrates the stages in the formation of red blood cells from **hematopoietic** (he″mat-o-poi-et′ik) **stem cells** or *hemocytoblasts*.

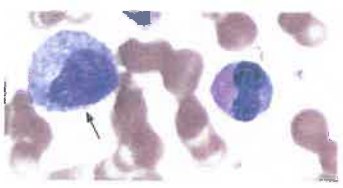
The average life span of a red blood cell is 120 days. Many of these cells are removed from the circulation each day, and yet the number of cells in the circulating blood remains relatively stable. This observation suggests a homeostatic control of the rate of red blood cell production.

The combined surface area of all the red blood cells in the human body is roughly 2,000 times as great as the body's exterior surface.

The hormone **erythropoietin** (ĕ-rith″ro-poi′ĕ-tin) controls the rate of red blood cell formation through *negative feedback*. The kidneys, and to a lesser extent the liver, release erythropoietin in response to prolonged oxygen deficiency (fig. 12.5). At high altitudes, for example, where the amount of oxygen in the air is reduced, oxygen delivery to the tissues initially decreases. This drop in oxygen triggers the release of erythropoietin, which travels via the blood to the red bone marrow and stimulates red blood cell production.

After a few days, many newly formed red blood cells appear in the circulating blood. The increased rate of production continues until the number of erythrocytes in the circulation is sufficient to supply tissues with oxygen. When the availability of oxygen returns to normal, erythropoietin release decreases, and the rate of red blood cell production returns to normal as well. An excessive increase in red blood cells is *polycythemia*. This increases blood viscosity, slowing blood flow and impairing circulation.





(b)

Figure 12.4 AP|R

Blood cells. **(a)** Development of red blood cells, white blood cells, and platelets from hematopoietic stem cells in bone marrow. **(b)** Light micrograph of a hematopoietic stem cell (arrow) in red bone marrow (500×).

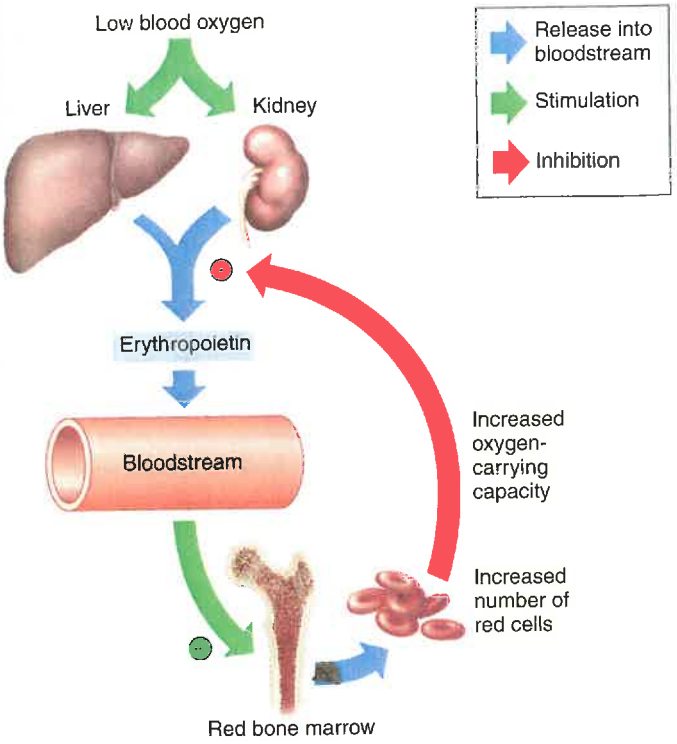


Figure 12.5
Low blood oxygen causes the kidneys and, to a lesser degree, the liver to release erythropoietin. Erythropoietin stimulates target cells in red bone marrow to increase the production of red blood cells that carry oxygen to tissues.

Dietary Factors Affecting Red Blood Cell Production

Availability of B-complex vitamins—*vitamin B_{12}* and *folic acid*—significantly influences red blood cell production. These vitamins are required for DNA synthesis, so they are necessary for the growth and division of cells. Cell division is rapid in blood-forming (hematopoietic) tissue, so this tissue is especially vulnerable to a deficiency of either of these vitamins. Hemoglobin synthesis and normal red blood cell production require iron. The small intestine absorbs iron slowly from food. The body reuses much of the iron released by the decomposition of hemoglobin from damaged red blood cells. Therefore, the diet need supply only small amounts of iron.

A deficiency of red blood cells, or a reduction in the amount of hemoglobin they contain, results in a condition called *anemia*. This reduces the oxygen-carrying capacity of the blood, and the affected person may appear pale and lack energy. A pregnant woman may become anemic if she doesn't eat iron-rich foods, because her blood volume increases due to fluid retention to accommodate the requirements of the fetus. This increased blood volume decreases the hematocrit.

In contrast to anemia, in an inherited disorder called hemochromatosis, the small intestine absorbs iron at ten times the normal rate. Iron builds up in organs, to toxic levels. Treatment is periodic blood removal, as often as every week following diagnosis. The blood is discarded.

In *sickle cell disease*, a single DNA base mutation changes one amino acid in the protein part of hemoglobin, causing hemoglobin to crystallize in a low-oxygen environment. This bends the red blood cells containing the abnormal hemoglobin into a sickle shape, which blocks circulation in small blood vessels, causing excruciating joint pain and damaging many organs.

Children with sickle cell disease are typically diagnosed at birth and receive antibiotics daily for years to prevent infection. Hospitalization for blood transfusions may be necessary for painful sickling "crises" of blocked circulation.

A drug, hydroxyurea, is used to activate production of a form of hemoglobin normally produced only in the fetus. The fetal hemoglobin slows sickling, which enables the red blood cells to reach the lungs—where fresh oxygen restores the cells' normal shapes. A bone marrow transplant or an umbilical cord stem cell transplant from a donor can completely cure sickle cell disease but have a 15% risk of fatality. The procedures are equally effective.

Practice

7. Where are red blood cells produced?
8. How is red blood cell production controlled?
9. Which vitamins are necessary for red blood cell production?
10. Why is iron required for the formation of red blood cells?

Destruction of Red Blood Cells

Red blood cells are elastic and flexible, and they readily bend as they pass through small blood vessels. With age, however, these cells become more fragile and may be damaged simply by passing through capillaries, particularly those in active muscles that must withstand contractile forces. **Macrophages** phagocytize and destroy damaged red blood cells, primarily in the liver and spleen. Recall from chapter 5, pages 102–103, that macrophages are large, phagocytic, wandering cells.

Hemoglobin molecules liberated from red blood cells break down into their four component polypeptide "globin" chains, each surrounding a *heme* group. The heme further decomposes into iron and a greenish pigment called **biliverdin.** The blood may transport the iron, combined with a protein, to the hematopoietic tissue in red bone marrow to be reused in synthesizing new hemoglobin. About 80% of the iron is stored in the liver in the form of an iron-protein complex. Biliverdin eventually is converted to an orange pigment called **bilirubin.** Biliverdin and bilirubin are excreted in the

bile as bile pigments (see chapter 15, p. 418). Figure 12.6 summarizes the life cycle of a red blood cell.

In jaundice (icterus), accumulation of bilirubin turns the skin and eyes yellowish. Newborns can develop *physiologic jaundice* a few days after birth.

Physiologic jaundice may be the result of immature liver cells that ineffectively excrete bilirubin into the bile. Treatment includes exposure to fluorescent light, which breaks down bilirubin in the tissues, and feedings that promote bowel movements. In hospital nurseries, babies being treated for physiologic jaundice lie under "bili lights," clad only in diapers and protective goggles. The healing effect of fluorescent light was discovered in the 1950s, when an astute nurse noted that jaundiced babies improved after sun exposure, except in the areas their diapers covered.

Practice

11. What happens to damaged red blood cells?
12. What are the products of hemoglobin breakdown?

White Blood Cells

White blood cells, or **leukocytes** (lu'ko-sītz), protect against disease. Leukocytes develop from hematopoietic stem cells in the red bone marrow (see fig. 12.4) in response to hormones, much as red blood cells form from precursors upon stimulation from erythropoietin. These hormones fall into two groups—**interleukins** and **colony-stimulating factors (CSFs).** Interleukins are numbered, while most colony-stimulating factors are named for the cell population they stimulate.

Blood transports white blood cells to sites of infection. White blood cells may then leave the bloodstream, as described on page 326.

Normally, five types of white blood cells are in circulating blood. They differ in size, the nature of their cytoplasm, the shape of the nucleus, and their staining characteristics, and are named for these distinctions. For example, leukocytes with granular cytoplasm are called **granulocytes,** whereas those without cytoplasmic granules are called **agranulocytes** (see fig. 12.4).

A typical granulocyte is about twice the size of a red blood cell. Members of this group include

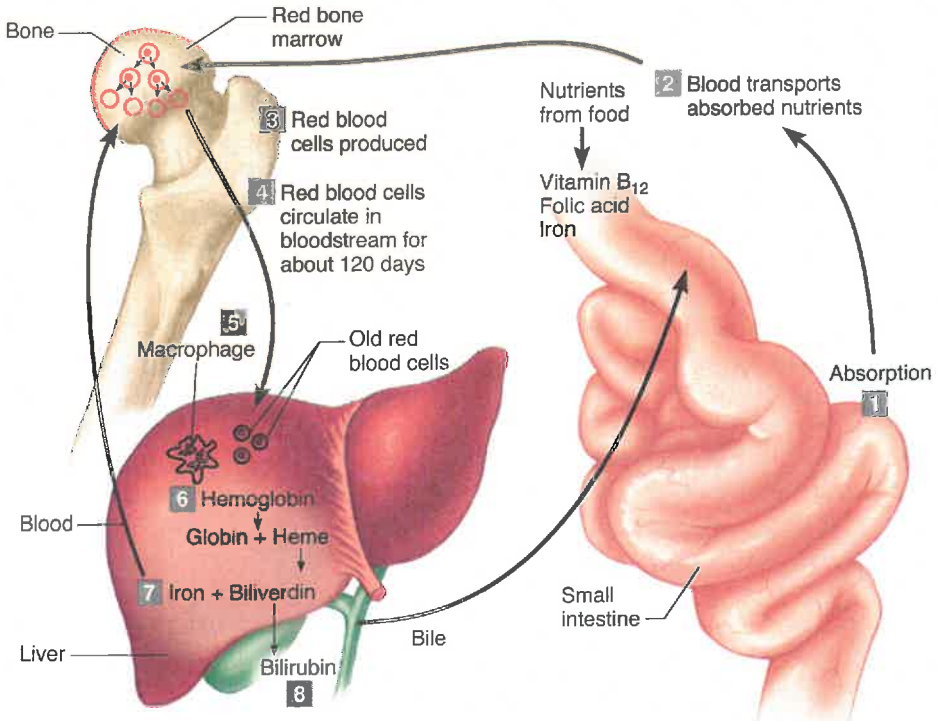


Figure 12.6 AP|R

Life cycle of a red blood cell. **(1)** The small intestine absorbs essential nutrients. **(2)** Blood transports nutrients to red bone marrow. **(3)** In the marrow, red blood cells arise from the division of less specialized progenitor cells. **(4)** Mature red blood cells are released into the bloodstream, where they circulate for about 120 days. **(5)** Macrophages destroy damaged red blood cells in the spleen and liver. **(6)** Hemoglobin liberated from red blood cells is broken down into heme and globin. **(7)** Iron from heme returns to red bone marrow and is reused. **(8)** Biliverdin and bilirubin are excreted in bile.

neutrophils, eosinophils, and basophils. Granulocytes develop in red bone marrow as do red blood cells, but have short life spans, averaging about 12 hours.

Neutrophils (nu'tro-filz) have fine cytoplasmic granules that appear light purple in neutral stain. The nucleus of an older neutrophil is lobed and consists of two to five sections (segments, so these cells are sometimes called *segs*) connected by thin strands of chromatin (fig. 12.7). Younger neutrophils are also called *bands* because their nuclei are C-shaped. Neutrophils account for 54–62% of the leukocytes in a typical blood sample from an adult.

Eosinophils (e''o-sin'o-filz) contain coarse, uniformly sized cytoplasmic granules that appear deep red in acid stain (fig. 12.8). The nucleus usually has only two lobes (termed bilobed). Eosinophils make up 1–3% of the total number of circulating leukocytes.

Basophils (ba'so-filz) are similar to eosinophils in size and in the shape of their nuclei, but they have fewer, more irregularly shaped cytoplasmic granules that become deep blue in basic stain (fig. 12.9). Basophils usually account for less than 1% of the circulating leukocytes.

The leukocytes of the agranulocyte group include monocytes and lymphocytes. Monocytes generally arise from red bone marrow. Lymphocytes are formed in the organs of the lymphatic system, as well as in the red bone marrow (see chapter 14, p. 382).

Monocytes (mon'o-sītz), the largest blood cells, are two to three times greater in diameter than red blood cells (fig. 12.10). Their nuclei vary in shape and are round, kidney-shaped, oval, or lobed. They usually make up 3–9% of the leukocytes in a blood sample and live for several weeks or even months.

Lymphocytes (lim'fo-sītz) are usually only slightly larger than red blood cells. A typical lymphocyte has a large, round nucleus surrounded by a thin rim of cytoplasm (fig. 12.11). These cells account for 25–33% of circulating leukocytes. Lymphocytes may live for years.

Practice

13. Which hormones are necessary for differentiation of white blood cells from hematopoietic stem cells in the red bone marrow?
14. Distinguish between granulocytes and agranulocytes.
15. List the five types of white blood cells, and explain how they differ from one another.

Functions of White Blood Cells

White blood cells protect against infection in various ways. Some leukocytes phagocytize bacterial cells in the body, and others produce proteins (*antibodies*) that destroy or disable foreign particles.

Leukocytes can squeeze between the cells that form blood vessel walls. This movement, called *diapedesis,* allows the white blood cells to leave the circulation (fig. 12.12). Once outside the blood, they move through interstitial spaces using a form of self-propulsion called *amoeboid motion.*

The most mobile and active phagocytic leukocytes are neutrophils and monocytes. Monocytes leave the bloodstream and become *macrophages* that phagocytize bacteria, dead cells, and other debris in the tissues. Neutrophils cannot ingest particles much larger than bacterial cells, but monocytes can engulf large objects. Both of these phagocytes contain many *lysosomes,* which are organelles filled with digestive enzymes that break down organic molecules in captured bacteria, nutrients, and worn-out organelles. Neutrophils and monocytes may become so engorged with digestive products and bacterial toxins that they die.

Eosinophils are only weakly phagocytic, but they are attracted to and can kill certain parasites. Eosinophils also help control inflammation and allergic reactions by removing biochemicals associated with these reactions.

Basophils migrate to damaged tissues where they release *heparin,* which inhibits blood clotting, and *histamine,* which promotes inflammation, thus increasing blood flow to injured tissues. Basophils also play major roles in certain allergic reactions.

Lymphocytes are important in *immunity.* Some, for example, produce antibodies that attack specific foreign substances that enter the body. Chapter 14 (pp. 386–392) discusses immunity.

Practice

16. How do white blood cells fight infection?
17. How do white blood cells reach microorganisms that are outside blood vessels?
18. Which white blood cells are the most active phagocytes?

White Blood Cell Counts

The number of white blood cells in a microliter of human blood, called the *white blood cell count* (*WBCC* or *WCC*), normally is 4,000–11,000 cells. White blood cell counts are of clinical interest because their number may change in response to abnormal conditions. A total number of white blood cells exceeding 11,000 per microliter of blood constitutes **leukocytosis,** indicating acute infection, such as appendicitis. The white blood

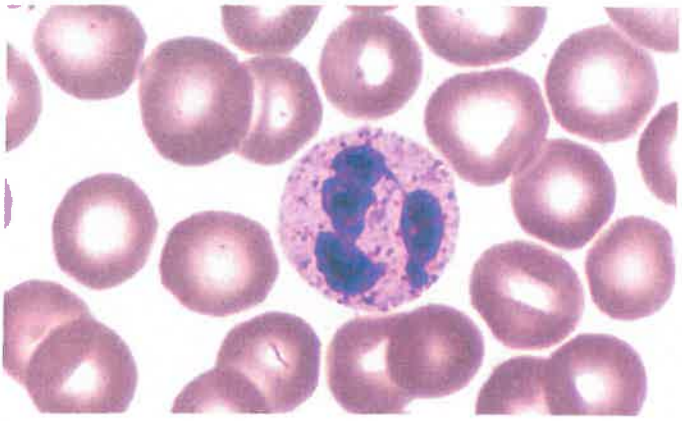


Figure 12.7 AP|R
A neutrophil has a lobed nucleus with two to five segments (2,000×).

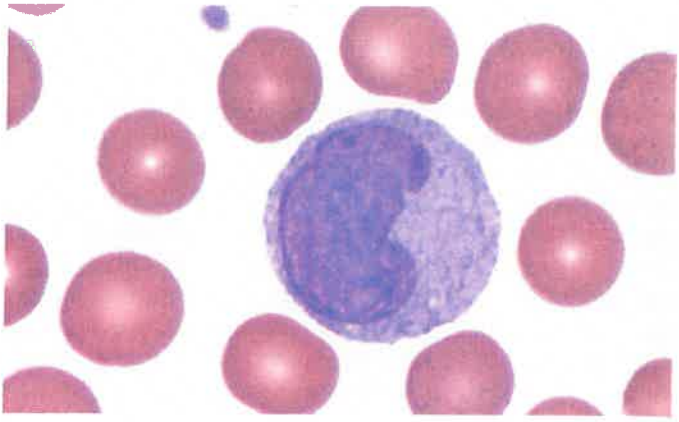


Figure 12.10 AP|R
A monocyte is the largest of the blood cells (2,000×).

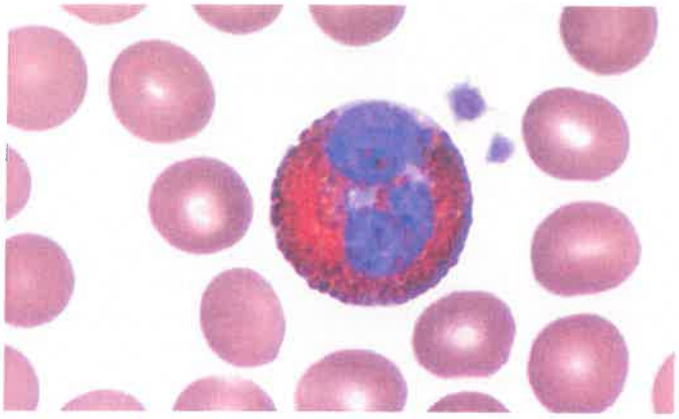


Figure 12.8 AP|R
An eosinophil has red-staining cytoplasmic granules (2,000×).

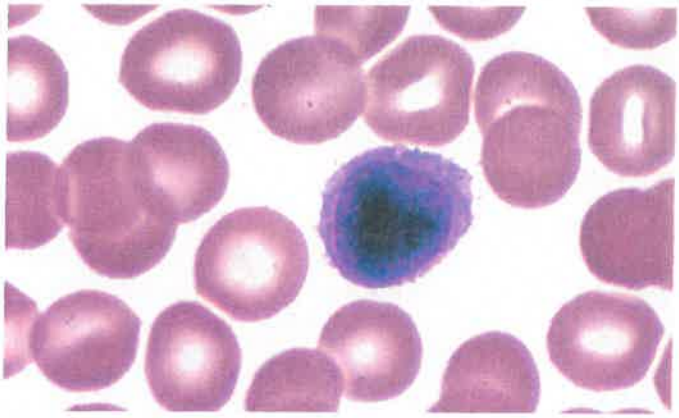


Figure 12.11 AP|R
A lymphocyte, the smallest of the white blood cells, has a large, round nucleus (2,000×).

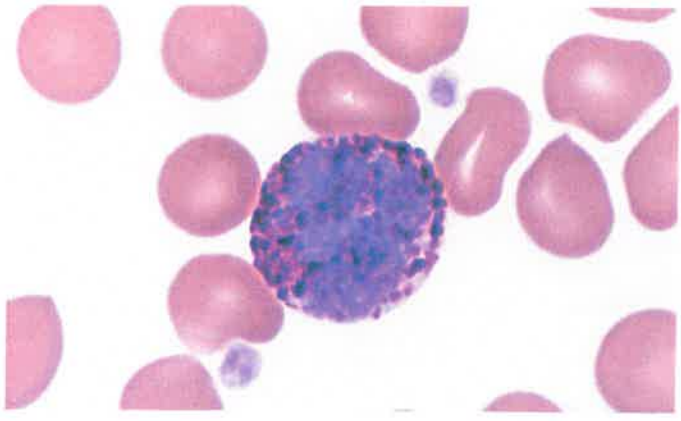


Figure 12.9 AP|R
A basophil has cytoplasmic granules that stain deep blue (2,000×).

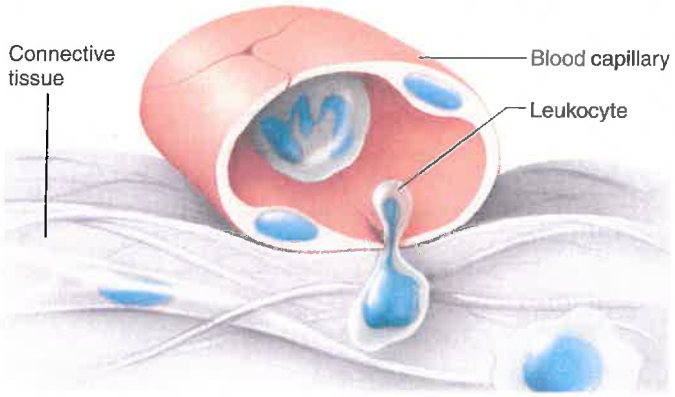


Figure 12.12
In a type of movement called diapedesis, leukocytes squeeze between the endothelial cells of a capillary wall and enter the tissue space outside the blood vessel.

Q: *What is a monocyte called once it has left the bloodstream and entered the tissues?*

Answer can be found in Appendix E on page 568.

cell count is greatly elevated in leukemia, as Clinical Application 12.1 describes.

A total white blood cell count below 4,000 per microliter of blood is called **leukopenia.** Such a deficiency may accompany typhoid fever, influenza, measles, mumps, chickenpox, AIDS, or poliomyelitis.

A *differential white blood cell count* (*DIFF*) lists percentages of the types of leukocytes in a blood sample. This test is useful because the relative proportions of white blood cells may change in particular diseases. For instance, the number of neutrophils usually increases during bacterial infections, and the number of eosinophils may increase during certain parasitic infections and allergic reactions. In AIDS, the numbers of a certain type of lymphocyte drop sharply.

Practice

19. What is the normal human white blood cell count?
20. Distinguish between leukocytosis and leukopenia.
21. What is a differential white blood cell count?

Blood Platelets AP|R

Platelets (plāt'letz), or **thrombocytes** (throm'bo-sītz), are not complete cells. They arise from very large cells in red bone marrow, called **megakaryocytes** (meg"ah-kar'e-o-sītz), that fragment like a shattered plate, releasing small sections of cytoplasm—platelets—into the circulation. The larger fragments of the megakaryocytes shrink and become platelets as they pass through blood vessels in the lungs. Megakaryocytes, and therefore platelets, develop from hematopoietic stem cells (see fig. 12.4) in response to the hormone **thrombopoietin** (throm"bo-poi'ĕ-tin).

Each platelet lacks a nucleus and is less than half the size of a red blood cell. It is capable of amoeboid movement and may live for about ten days. In normal blood, the *platelet count* varies from 130,000 to 360,000 per microliter. Platelets help close breaks in damaged blood vessels, as section 12.4 explains on page 331. Table 12.1 summarizes the characteristics of blood cells and platelets.

Practice

22. What is the normal blood platelet count?
23. What is the function of blood platelets?

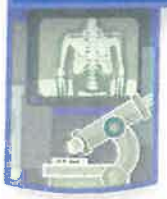
12.3 BLOOD PLASMA

Plasma is the clear, straw-colored, liquid portion of the blood in which the cells and platelets are suspended. It is approximately 92% water and contains a complex

Table 12.1 Cellular Components of Blood

Component	Description	Number Present	Function
Red blood cell (erythrocyte)	Biconcave disc without a nucleus; about one-third hemoglobin	4,200,000–6,200,000 per microliter	Transports oxygen and carbon dioxide
White blood cell (leukocyte)		4,000–11,000 per microliter	Destroys pathogenic microorganisms and parasites and removes worn cells
Granulocytes	About twice the size of red blood cells; cytoplasmic granules are present		
1. Neutrophil	Nucleus with two to five lobes; cytoplasmic granules stain light purple in neutral stain	54–62% of white blood cells present	Phagocytizes small particles
2. Eosinophil	Bilobed nucleus, cytoplasmic granules stain red in acid stain	1–3% of white blood cells present	Kills parasites and moderates allergic reactions
3. Basophil	Bilobed nucleus, cytoplasmic granules stain blue in basic stain	Less than 1% of white blood cells present	Releases heparin and histamine
Agranulocytes	Cytoplasmic granules are absent		
1. Monocyte	Two to three times larger than a red blood cell; nuclear shape varies from spherical to lobed	3–9% of white blood cells present	Phagocytizes large particles
2. Lymphocyte	Only slightly larger than a red blood cell; its nucleus nearly fills cell	25–33% of white blood cells present	Provides immunity
Platelet (thrombocyte)	Cytoplasmic fragment	130,000–360,000 per microliter	Helps control blood loss from broken vessels

Clinical Application 12.1



Leukemia

When the twenty-three-year-old had a routine physical examination, she expected reassurance that her healthy lifestyle had indeed been keeping her healthy. After all, she felt great. What she got, a few days later, was a shock. Instead of having 4,000 to 11,000 white blood cells per microliter of blood, she had more than ten times that number—and many of the cells were cancerous. She had chronic myeloid leukemia (CML). Her red bone marrow was flooding her circulation with too many granulocytes, most of them poorly differentiated (figure 12A).

Another type of leukemia is lymphoid, in which the cancer cells are lymphocytes, produced in lymph nodes. Both myeloid and lymphoid leukemia can cause fatigue, headaches, nosebleeds and other bleeding, frequent respiratory infections, fever, bone pain, bruising, and other signs of slow blood clotting. The symptoms arise from the disrupted proportions of the blood's formed elements and their malfunction.

Immature white blood cells increase the risk of infection. Leukemic cells crowd out red blood cells and their precursors in the red marrow, causing anemia and resulting fatigue. Platelet deficiency (thrombocytopenia) slows clotting time, causing bruises and bleeding. Finally, spread of the cancer cells outside the marrow painfully weakens the surrounding bone. Eventually, without treatment, cancer cells spread outside the cardiovascular system, causing other tissues that would normally not produce white blood cells to do so.

Leukemia is also classified as acute or chronic. An acute condition appears suddenly, symptoms progress rapidly, and without treatment, death occurs in a few months. Chronic forms begin more slowly and may remain undetected for months or even years or, in rare cases, decades. Without treatment, life expectancy after symptoms develop is about three years.

Traditional cancer treatments destroy any cell that divides rapidly. A newer drug, Gleevec, targets only the cancer cells by nestling into ATP-binding sites on a type of enzyme called a tyrosine kinase, which blocks the message to divide. People with leukemia have other options. Bone marrow and stem cell transplants can cure the condition.

Another way that leukemia treatment is improving is refining diagnosis, based on identifying the proteins that leukemia cells produce. This information is used to predict which drugs are most likely to be effective, and which will cause intolerable side effects or not work in particular individuals. For example, some people with acute lymphoblastic leukemia (ALL), diagnosed on the basis of the appearance of the cancer cells in a blood smear, do not respond to standard chemotherapy. However, DNA microarray (also called DNA chip) technology revealed that the cells of patients who do not improve produce different proteins than the cancer cells of patients who do respond to the drugs used to treat ALL—the nonresponders have a different form of leukemia, called mixed-lineage leukemia. These patients respond to different drugs.

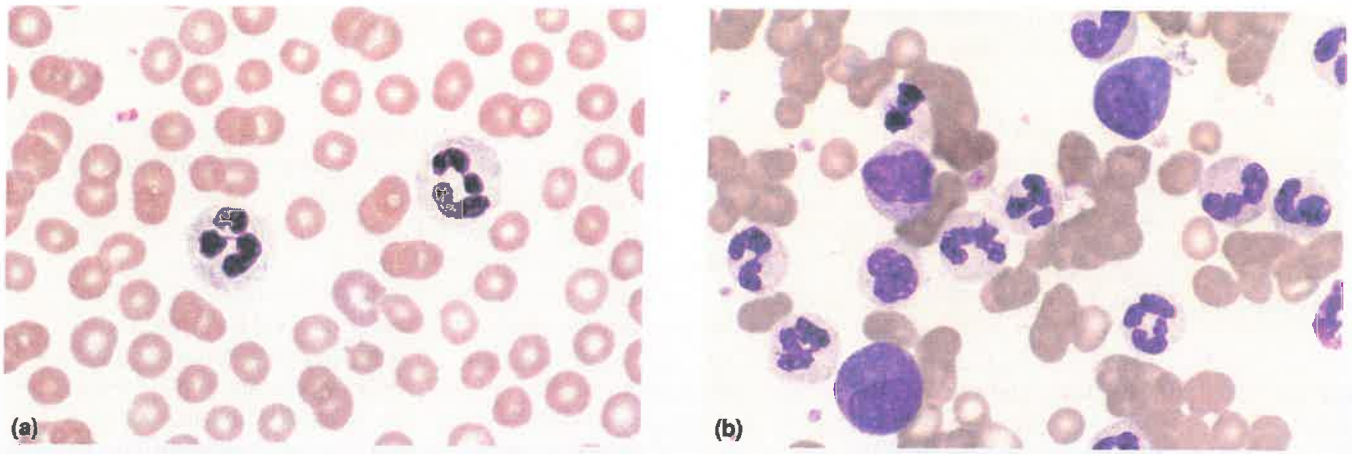


Figure 12A

Leukemia and blood cells. (a) Normal blood cells (700×). (b) Blood cells from a person with granulocytic leukemia, a type of myeloid leukemia (700×). Note the increased number of leukocytes.

mixture of organic and inorganic biochemicals. The functions of plasma constituents include transporting nutrients, gases, and vitamins; helping regulate fluid and electrolyte balance; and maintaining a favorable pH.

Plasma Proteins

Plasma proteins (plaz'mah pro'tēnz) are the most abundant of the dissolved substances (solutes) in plasma. These proteins remain in the blood and interstitial fluids, and ordinarily are not used as energy sources. The three main types of plasma proteins—albumins, globulins, and fibrinogen—differ in composition and function.

Albumins (al-bu'minz) are the smallest of the plasma proteins, yet account for about 60% of these proteins by weight. They are synthesized in the liver, and because they are so plentiful, albumins are an important determinant of the *osmotic pressure* of the plasma.

Recall from chapter 3 (p. 63) that the presence of an impermeant solute on one side of a selectively permeable membrane creates an osmotic pressure and that water always moves toward a greater osmotic pressure. Plasma proteins are too large to pass through the capillary walls, they are impermeant, and they create an osmotic pressure that holds water in the capillaries, despite blood pressure forcing water out of capillaries by filtration (see chapter 3, p. 64). The term *colloid osmotic pressure* is used to describe this osmotic effect due to the plasma proteins.

By maintaining the colloid osmotic pressure of plasma, albumins and other plasma proteins help regulate water movement between the blood and the tissues. In doing so, they help control blood volume, which, in turn, directly affects blood pressure (see chapter 13, p. 360).

If the concentration of plasma proteins falls, tissues swell, a condition called *edema*. This may result from starvation or a protein-deficient diet or from an impaired liver that cannot synthesize plasma proteins. As the concentration of plasma proteins drops, so does the colloid osmotic pressure, allowing fluid to accumulate in the interstitial spaces.

Globulins (glob'u-linz), which make up about 36% of the plasma proteins, can be further subdivided into *alpha, beta,* and *gamma globulins*. The liver synthesizes alpha and beta globulins, which have a variety of functions, including transport of lipids and fat-soluble vitamins. Lymphatic tissues produce the gamma globulins, which are a type of antibody (see chapter 14, p. 391).

Fibrinogen (fi-brin'o-jen), which constitutes about 4% of the plasma proteins, functions in blood coagulation, as discussed in section 12.4 on page 331. Synthesized in the liver, fibrinogen is the largest of the plasma proteins. Table 12.2 summarizes the characteristics of the plasma proteins.

Table 12.2 Plasma Proteins

Protein	Percentage of Total	Origin	Function
Albumin	60%	Liver	Helps maintain colloid osmotic pressure
Globulin	36%		
Alpha globulins		Liver	Transport lipids and fat-soluble vitamins
Beta globulins		Liver	Transport lipids and fat-soluble vitamins
Gamma globulins		Lymphatic tissues	Constitute a type of antibody
Fibrinogen	4%	Liver	Plays a key role in blood coagulation

Practice

24. List three types of plasma proteins.
25. How do albumins help maintain water balance between the blood and the tissues?
26. What are the functions of the globulins?
27. What is the role of fibrinogen?

Gases and Nutrients

The most important *blood gases* are oxygen and carbon dioxide. Plasma also contains a considerable amount of dissolved nitrogen, which ordinarily has no physiological function. Chapter 16 (pp. 459–461) discusses the blood gases and their transport.

The *plasma nutrients* include amino acids, simple sugars, nucleotides, and lipids absorbed from the digestive tract. For example, plasma transports glucose from the small intestine to the liver, where it may be stored as glycogen or converted to fat. If blood glucose concentration drops below the normal range, glycogen may be broken down into glucose, as described in chapter 11 (p. 308). Plasma also carries recently absorbed amino acids to the liver, where they can be used to manufacture proteins, or deaminated and used as an energy source (see chapter 15, p. 431).

Plasma lipids include fats (triglycerides), phospholipids, and cholesterol. Because lipids are not water-soluble and plasma is almost 92% water, these lipids are

carried in the plasma by joining with proteins, forming lipoprotein complexes.

Nonprotein Nitrogenous Substances

Molecules that contain nitrogen atoms but are not proteins form a group called **nonprotein nitrogenous substances.** In plasma, this group includes amino acids, urea, uric acid, creatine (kre'ah-tin) and creatinine (kre-at'i-nin). Amino acids come from protein digestion and amino acid absorption. Urea and uric acid are products of protein and nucleic acid catabolism, respectively. Creatinine results from the metabolism of creatine. As discussed in chapter 8 (p. 185), creatine is present in *creatine phosphate* in muscle tissue as well as in the blood, where it stores energy in phosphate bonds.

Plasma Electrolytes

Blood plasma contains a variety of *electrolytes* that are absorbed from the intestine or released as by-products of cellular metabolism. They include sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, and sulfate ions. Sodium and chloride ions are the most abundant. Bicarbonate ions are important in maintaining the osmotic pressure and pH of plasma, and like other plasma constituents, they are regulated so that their blood concentrations remain relatively stable. Chapter 18 discusses these electrolytes in connection with water and electrolyte balance.

Practice

28. Which gases are in plasma?
29. Which nutrients are in plasma?
30. What is a nonprotein nitrogenous substance?
31. What are the sources of plasma electrolytes?

12.4 HEMOSTASIS

Hemostasis (he"mo-sta'sis) is the stoppage of bleeding, which is vitally important when blood vessels are damaged. Following an injury to the blood vessels, several actions may help to limit or prevent blood loss, including blood vessel spasm, platelet plug formation, and blood coagulation.

Blood Vessel Spasm

Cutting or breaking a small blood vessel stimulates the smooth muscles in its walls to contract, a phenomenon called **vasospasm,** and blood loss lessens almost immediately. Vasospasm may completely close the ends of a severed vessel.

Vasospasm may last only a few minutes, but the effect of the direct stimulation usually continues for about 30 minutes. By then, a *platelet plug* has formed, and blood is coagulating. Also, platelets release **serotonin,** which contracts smooth muscles in the blood vessel walls. This vasoconstriction further helps reduce blood loss.

Platelet Plug Formation

Platelets adhere to any rough surface, particularly to the collagen in connective tissue. When a blood vessel breaks, platelets adhere to the collagen underlying the endothelial lining of blood vessels. Platelets also adhere to each other, forming a platelet plug in the vascular break. A plug may control blood loss from a small break, but a larger break may require a blood clot to halt bleeding. Figure 12.13 shows the steps in platelet plug formation.

Practice

32. What is hemostasis?
33. How does a blood vessel spasm help control bleeding?
34. Describe the formation of a platelet plug.

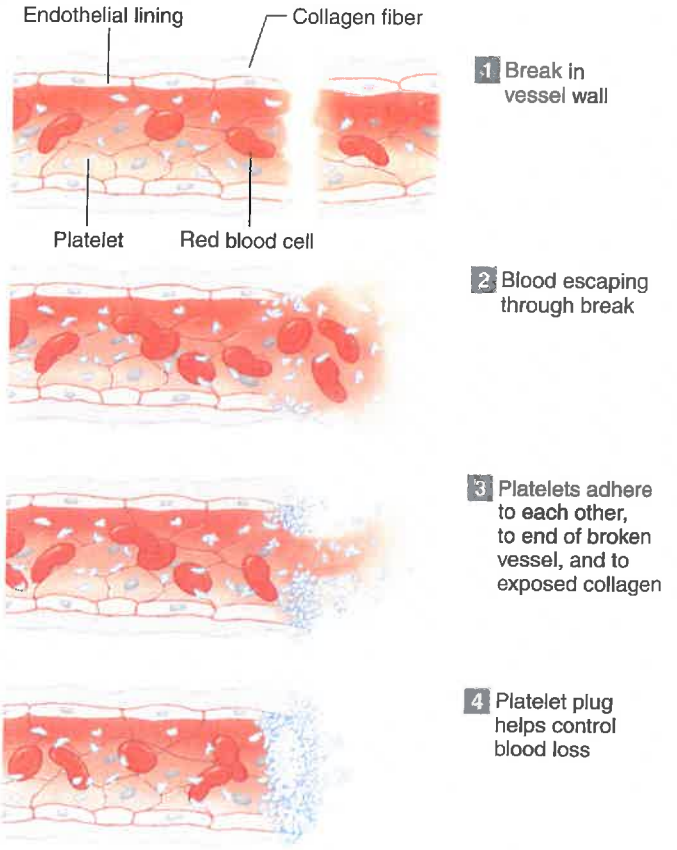


Figure 12.13
Steps in platelet plug formation.

Blood Coagulation

Coagulation (ko-ag″u-la′shun), the most effective hemostatic mechanism, is the formation of a *blood clot.* Blood coagulation is complex and utilizes many biochemicals called *clotting factors.* Some of these factors promote coagulation, and others inhibit it. Whether or not blood coagulates depends on the balance between these two groups of factors. Normally, anticoagulants prevail, and the blood does not clot. However, as a result of injury (trauma), biochemicals that favor coagulation may increase in concentration, and the blood may coagulate.

The major event in blood clot formation is the conversion of the soluble plasma protein fibrinogen into insoluble threads of the protein **fibrin.** Formation of fibrin takes several steps. First, damaged tissues release *tissue thromboplastin,* initiating a series of reactions that results in the production of *prothrombin activator.* This series of changes requires calcium ions as well as certain proteins and phospholipids. As its name suggests, prothrombin activator acts on prothrombin (see figure 12.16).

Prothrombin is an alpha globulin that the liver continually produces and is thus a normal constituent of plasma. Prothrombin activator converts prothrombin into **thrombin,** which in turn catalyzes a reaction that joins fragments of fibrinogen into long threads of fibrin.

Once fibrin threads form, they stick to the exposed surfaces of damaged blood vessels, creating a meshwork that entraps blood cells and platelets (fig. 12.14). The resulting mass is a blood clot, which may block a vascular break and prevent further blood loss. The clear, yellow liquid that remains after the clot forms is called **serum.** Serum is plasma minus clotting factors.

The amount of prothrombin activator in the blood is directly proportional to the degree of tissue damage. Once a blood clot begins to form, it promotes additional clotting because thrombin also acts directly on blood clotting factors other than fibrinogen, causing prothrombin to form more thrombin. This is an example of a *positive feedback system,* in which the original action stimulates more of the action. Such a positive feedback mechanism produces unstable conditions and can operate for only a short time without disrupting the stable internal environment (see chapter 1, p. 7).

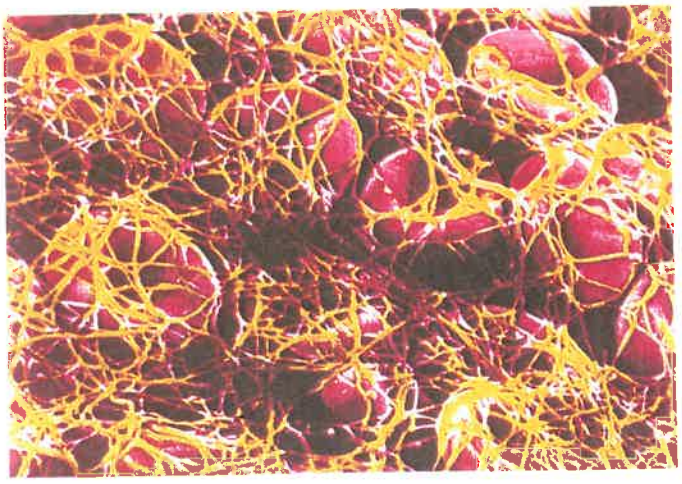


Figure 12.14
Falsely-colored scanning electron micrograph of fibrin threads forming a blood clot (2,800×).

Laboratory tests commonly used to evaluate the blood coagulation mechanisms include *prothrombin time (PT)* and *partial thromboplastin time (PTT).* These tests measure the time it takes for fibrin threads to form in a sample of plasma.

Normally, blood flow prevents formation of a massive clot by rapidly carrying excess thrombin away, keeping its concentration too low in any one place to promote further clotting. Consequently, blood usually coagulates in blood that is standing still (or moving slowly). Clotting ceases where a clot contacts circulating blood.

Fibroblasts (see chapter 5, p. 102) invade blood clots that form in ruptured vessels, producing fibrous connective tissue throughout, which helps strengthen and seal vascular breaks. Many clots, including those that form in tissues as a result of blood leakage (hematomas), disappear in time. This dissolution requires conversion of a plasma protein, *plasminogen,* to *plasmin,* a protein-splitting enzyme that can digest fibrin threads and other proteins associated with blood clots. Plasmin formation may dissolve a whole clot; however, clots that fill large blood vessels are seldom removed naturally.

A blood clot abnormally forming in a vessel is a **thrombus** (throm′bus). A clot that dislodges, or a fragment of a clot that breaks loose and is carried away by the blood flow, is called an **embolus** (em′bo-lus). Generally, emboli continue to move until they reach narrow places in vessels where they may lodge and block blood flow.

A blood clot forming in a vessel that supplies a vital organ, such as the heart (coronary thrombosis) or the brain (cerebral thrombosis), kills tissues the vessel serves (*infarction*) and may be fatal. A blood clot that travels and then blocks a vessel that supplies a vital organ, such as the lungs (pulmonary embolism), affects the portion of the organ the blocked blood vessel supplies. Genetics Connection 12.1 discusses several blood clotting disorders.

Drugs based on "clot-busting" biochemicals can be lifesavers. *Tissue plasminogen activator* (tPA) may restore blocked coronary or cerebral circulation if given within three hours of a heart attack or stroke. A drug derived from bacteria called *streptokinase* may also be successful, for a fraction of the cost. Another plasminogen activator used as a drug is *urokinase,* an enzyme produced in certain kidney cells. Heparin and coumadin are drugs that interfere with clot formation, but do not dissolve clots.

Genetics Connection 12.1

Coagulation Disorders

Genetic mutations cause several types of clotting disorders. Environmental factors can affect the severity of these conditions.

Hemophilia

Abnormalities of different clotting factors cause different forms of the bleeding disorder hemophilia. Symptoms include severe hemorrhage following minor injuries, frequent nosebleeds, large intramuscular hematomas, and blood in the urine. In the most common form, hemophilia A, factor VIII is deficient or absent. The gene for this clotting factor is on the X chromosome, so that primarily males are affected, because they do not have a second X chromosome to block the mutation's expression. One in 10,000 males has hemophilia A. Treatment is replacing factor VIII.

Hemophilia A has left its mark on history. A second-century B.C. Jewish document, the Talmud, states, "If she circumcised her first child and he died, and a second one also died, she must not circumcise her third child." Hemophilia A affected the royal families of England, Russia, Germany, and Spain. In 1985 hemophilia made history again when many patients who had received factor VIII pooled from donors contracted HIV infection. Today, the clotting factor is manufactured using recombinant DNA technology, so it is free of viruses.

von Willebrand Disease

The tendency to bleed and bruise easily may be a sign of von Willebrand disease, which is the most common hereditary coagulation disorder. One in 100 people inherits a mutation in any of four genes that encode the von Willebrand clotting factor, but only 1 in 10,000 individuals actually develops symptoms. It is equally likely to affect males as females.

Von Willebrand factor is a plasma protein secreted by the endothelial cells lining blood vessels. It enables platelets to adhere to damaged blood vessel walls, which is a key step preceding actual clotting. In von Willebrand disease, the mucous membranes of the gastrointestinal and urinary tracts can spontaneously bleed. Some people do not discover that they have von Willebrand disease until they bleed excessively following an injury. Usually no treatment is required. However, women who bleed very heavily during their menstrual periods may be advised to take oral contraceptives to diminish the flow, and a combination of factor VIII and von Willebrand factor can be taken before planned surgery to reduce the risk of uncontrolled bleeding.

Factor V Leiden

An inherited susceptibility plus other risk factors can cause dangerous clotting. This is the case for factor V Leiden, which is a mutation in the gene that encodes clotting factor V. This factor normally interacts with factor X to inactivate thrombin, which converts fibrinogen to fibrin to form a clot. A person with factor V Leiden has just one altered DNA base, which changes one amino acid in the clotting factor.

A forty-two-year-old woman who unknowingly had factor V Leiden went to an emergency department when she experienced shortness of breath, light-headedness, and difficulty walking. Her left leg was painful and had turned bluish-purple. An ultrasound scan revealed a clot in a leg vein extending from her hip to the calf. A careful clinical workup revealed several risk factors at play in the formation of the woman's dangerous blood clot:

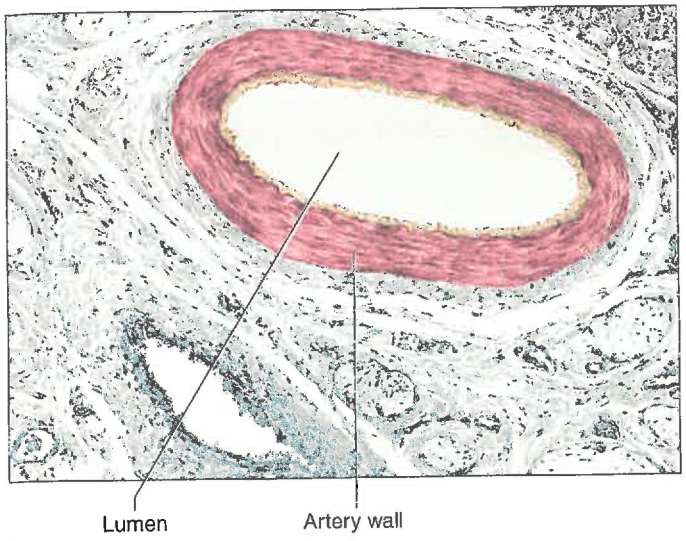
- Factor V Leiden (inherited tendency to form clots)
- A very long car ride (stagnation of blood due to immobility)
- Oral contraceptives (increased risk of clotting)
- Following the grapefruit diet for the preceding three days (grapefruit inactivates the enzyme that breaks down the oral contraceptive)

Infusion of a "clot-buster" drug directly into the vein opened it up, and the woman recovered.

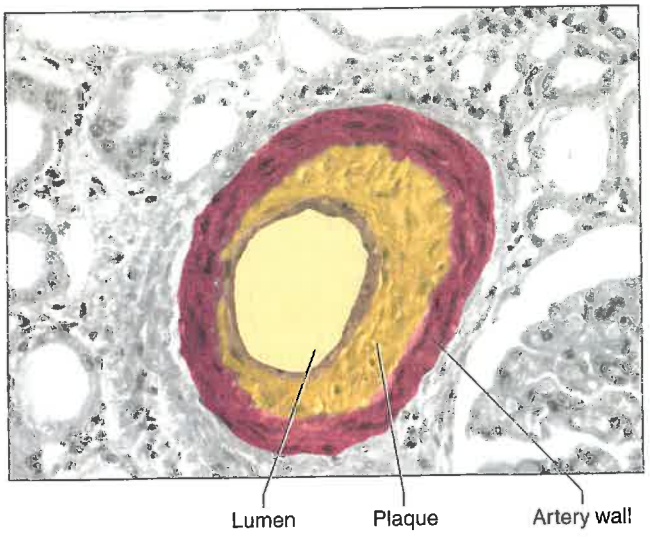
Abnormal clot formations are often associated with conditions that change the endothelial linings of vessels. For example, in *atherosclerosis* (ath″er-o″skle-ro′sis), accumulations of fatty deposits change arterial linings, sometimes initiating inappropriate clotting (fig. 12.15). Figure 12.16 summarizes the three primary hemostatic mechanisms: blood vessel spasm, platelet plug formation, and blood coagulation.

Practice

35. Review the major steps in blood clot formation.
36. What prevents the formation of massive clots throughout the cardiovascular system?
37. Distinguish between a thrombus and an embolus.



(a)



(b)

Figure 12.15

Artery cross sections, falsely-colored light micrographs. **(a)** Normal artery (50×), and **(b)** the inner wall of an artery changed as a result of atherosclerosis (100×). Not only is blood flow impeded, but the uneven inner surface can snag platelets, triggering coagulation.

12.5 BLOOD GROUPS AND TRANSFUSIONS

Early attempts to transfer blood from one person to another produced varied results. Sometimes, the recipient improved. Other times, the recipient suffered a blood transfusion reaction in which the red blood cells clumped, obstructing vessels and producing great pain and organ damage.

Eventually, scientists determined that blood is of differing types and that only certain combinations of blood types are compatible. These discoveries led to the development of procedures for typing blood. Today, safe transfusions of whole blood depend on properly matching the blood types of donors and recipients.

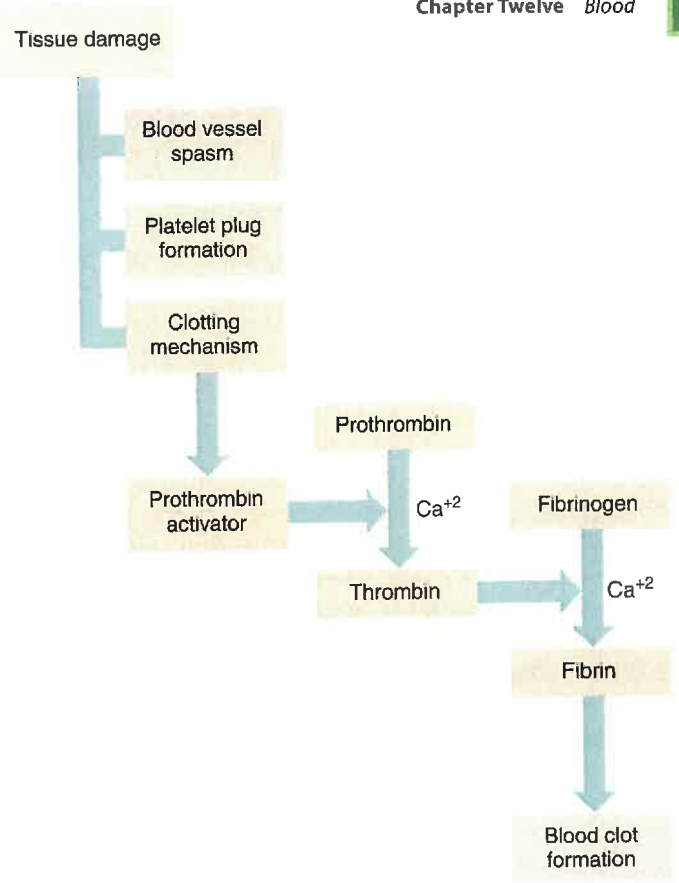


Figure 12.16

The three mechanisms of hemostasis: blood vessel spasm, platelet plug formation, and blood coagulation.

Q: *What is the major event in blood clot formation?*

Answer can be found in Appendix E on page 568.

Antigens and Antibodies

Agglutination is the clumping of red blood cells following a transfusion reaction. Red blood cell surface molecules called **antigens** (an′tĭ-jenz), also called *agglutinogens,* react with protein **antibodies** (an′tĭ-bod″ēz), also called *agglutinins,* carried in plasma.

Only a few of the many different antigens on red blood cell membranes can produce serious transfusion reactions. These include the antigens of the ABO group and those of the Rh group. Avoiding the mixture of certain kinds of antigens and antibodies prevents adverse transfusion reactions.

A mismatched blood transfusion quickly produces telltale signs of agglutination—anxiety, breathing difficulty, facial flushing, headache, and severe pain in the neck, chest, and lumbar area. Red blood cells burst, releasing free hemoglobin. Macrophages phagocytize the hemoglobin, converting it to bilirubin, which may sufficiently accumulate to cause the yellow skin of jaundice. Free hemoglobin in the kidneys may ultimately cause them to fail.

ABO Blood Group

The *ABO blood group* is based on the presence (or absence) of two major protein antigens on red blood cell membranes—antigen A and antigen B. A person's erythrocytes have on their surfaces one of four antigen combinations: only A, only B, both A and B, or neither A nor B. The resulting ABO blood type, because it reflects a protein combination, is inherited.

A person with only antigen A has *type A blood*. A person with only antigen B has *type B blood*. An individual with both antigen A and B has *type AB blood*. A person with neither antigen A nor B has *type O blood*. Thus, all people have one of four possible ABO blood types—A, B, AB, or O.

In the United States, the most common ABO blood types are O (47%) and A (41%). Rarer are type B (9%) and type AB (3%). These percentages vary in subpopulations and over time, reflect changes in the genetic structure of populations.

Certain antibodies that affect the ABO blood group are synthesized in the plasma about two to eight months following birth. Specifically, whenever antigen A is absent in red blood cells, an antibody called *anti-A* is produced, and whenever antigen B is absent, an antibody called *anti-B* is produced. Therefore, persons with type A blood have anti-B antibody in their plasma; those with type B blood have anti-A antibody; those with type AB blood have neither antibody; and those with type O blood have both anti-A and anti-B antibodies (fig. 12.17 and table 12.3). The antibodies anti-A and anti-B are large and do not cross the placenta. Thus, a pregnant woman and her fetus may be of different ABO blood types, and agglutination in the fetus will not occur.

Table 12.3 Antigens and Antibodies of the ABO Blood Group

Blood Type	Antigen	Antibody
A	A	Anti-B
B	B	Anti-A
AB	A and B	Neither anti-A nor anti-B
O	Neither A nor B	Both anti-A and anti-B

An antibody of one type will react with an antigen of the same type and clump red blood cells (fig. 12.18); therefore, such combinations must be avoided. The major concern in blood transfusion procedures is that the cells in the donated blood not clump due to antibodies in the recipient's plasma. For this reason, a person with type A (anti-B) blood must not receive blood of type B or AB, either of which would clump in the presence of anti-B in the recipient's type A blood. Likewise, a person with type B (anti-A) blood must not receive type A or AB blood, and a person with type O (anti-A and anti-B) blood must not receive type A, B, or AB blood.

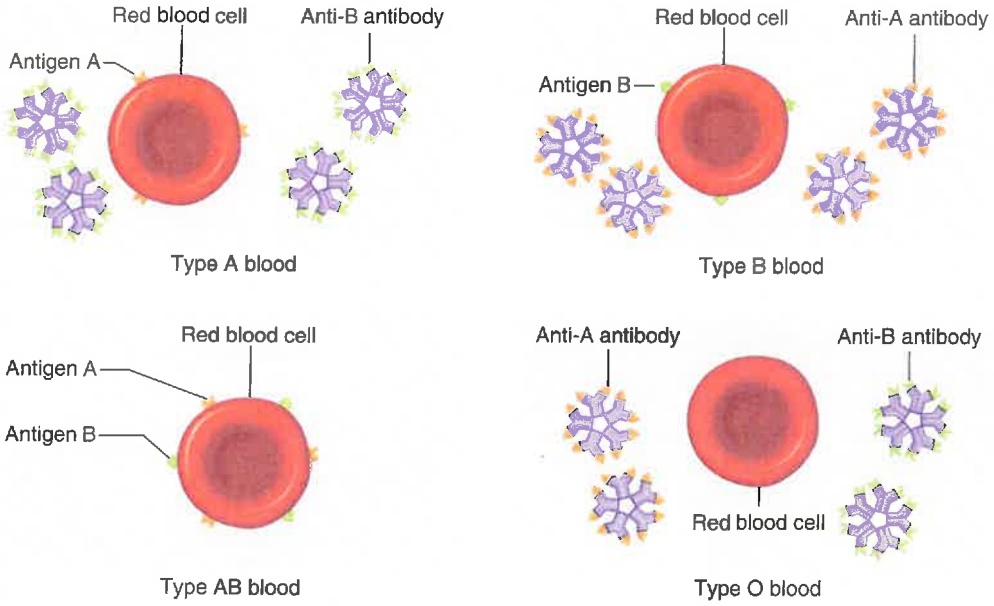
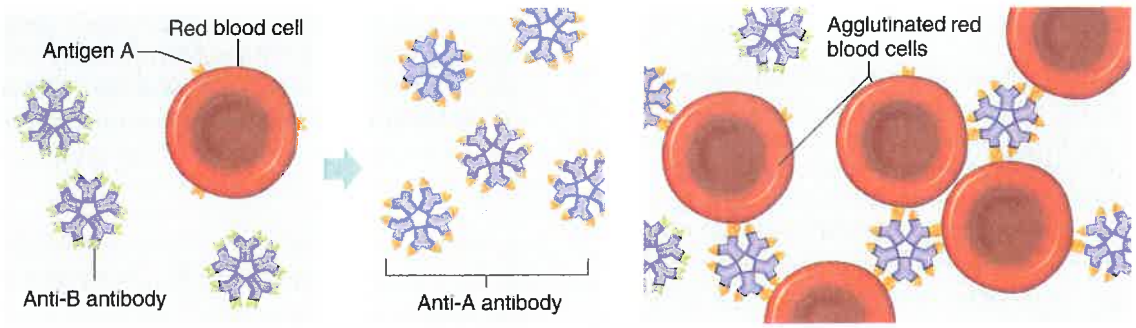
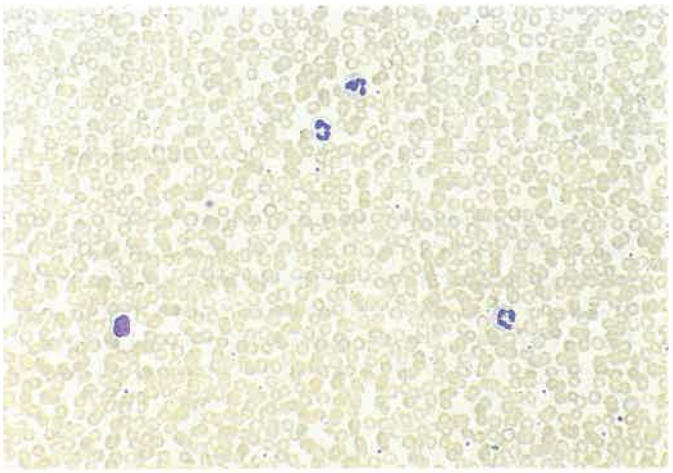


Figure 12.17
Different combinations of antigens and antibodies distinguish blood types. (Cells and antibodies not drawn to scale.)



(a) (b)



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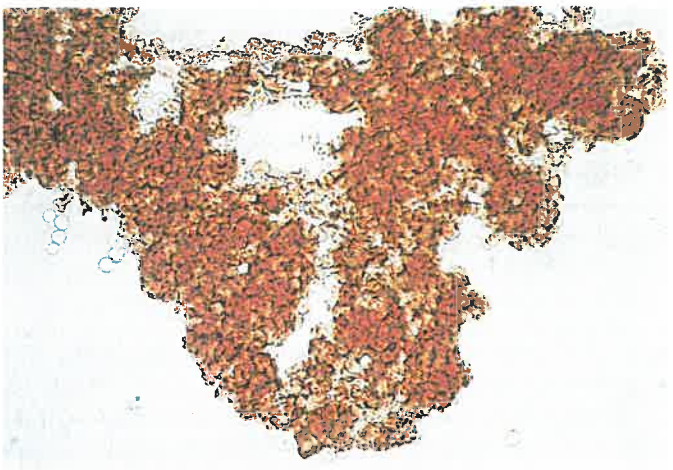

(d)

Figure 12.18

Agglutination. **(a)** If red blood cells with antigen A are added to blood containing anti-A antibody, **(b)** the antibodies react with the antigens, causing clumping (agglutination). **(c)** Nonagglutinated blood (210×). **(d)** Agglutinated blood (220×). (Cells and antibodies in **(a)** and **(b)** not drawn to scale.)

Type AB blood lacks both anti-A and anti-B antibodies, so an AB person can receive a transfusion of blood of any other type. For this reason, type AB persons are sometimes called *universal recipients*. However, type A (anti-B) blood, type B (anti-A) blood, and type O (anti-A and anti-B) blood still contain antibodies (either anti-A and/or anti-B) that could agglutinate type AB cells if transfused rapidly. Consequently, even for AB individuals, using donor blood of the same type as the recipient is best (table 12.4).

Type O blood lacks antigens A and B. Therefore, theoretically this type could be transfused into persons with blood of any other type. Individuals with type O blood are sometimes called *universal donors*. Type O blood, however, does contain both anti-A and anti-B antibodies. If type O blood is given to a person with blood type A, B, or AB, it should be transfused slowly so that the recipient's larger blood volume will dilute the donor blood, minimizing the chance of an adverse reaction.

Table 12.4 Preferred and Permissible Blood Types for Transfusions

Blood Type of Recipient	Preferred Blood Type of Donor	If Preferred Blood Type Unavailable, Permissible Blood Type of Donor
A	A	O
B	B	O
AB	AB	A, B, O
O	O	No alternate types

Blood in the umbilical cord at birth is rich in stem cells that can be used to treat a variety of disorders, including leukemias, sickle cell disease and other hemoglobin abnormalities, and certain inborn errors of metabolism. The United States and the United Kingdom have public umbilical cord blood banks that provide stem cells for free. For many illnesses it is best to receive donor stem cells, because receiving one's own could reintroduce the disease.

Practice

38. Distinguish between antigens and antibodies.
39. What is the main concern when blood is transfused from one individual to another?
40. Why is a type AB person called a universal recipient?
41. Why is a type O person called a universal donor?

Rh Blood Group

The *Rh blood group* was named after the rhesus monkey in which it was first studied. In humans, this group includes several Rh antigens (factors). The most prevalent of these is *antigen D*. If the Rh antigen is present on the red blood cell membranes, the blood is said to be *Rh-positive*. Conversely, if the red blood cells lack Rh antigen, the blood is called *Rh-negative*.

Only 15% of the U.S. population is Rh-negative.

The presence (or absence) of Rh antigen is an inherited trait, as is ABO blood type. But unlike anti-A and anti-B, antibodies that react with Rh antigen (*anti-Rh antibodies*) do not appear spontaneously. Instead, they form only in Rh-negative persons in response to the presence of red blood cells with Rh antigens.

If an Rh-negative person receives a transfusion of Rh-positive blood, the Rh antigen stimulates the recipient to begin producing anti-Rh antibodies. Generally, this initial transfusion has no serious consequences, but if the Rh-negative person—who is now sensitized to Rh-positive blood—receives another transfusion of Rh-positive blood some months later, the donated red cells are likely to agglutinate.

A related condition may occur when an Rh-negative woman is pregnant with an Rh-positive fetus for the first time. Such a pregnancy may be uneventful; however, at birth (or if a miscarriage occurs), the placental membranes that separated the maternal blood from the fetal blood during the pregnancy tear, and some of the infant's Rh-positive blood cells may enter the maternal circulation. These Rh-positive cells may then stimulate the maternal tissues to begin producing anti-Rh antibodies.

If a woman who has already developed anti-Rh antibodies becomes pregnant with a second Rh-positive fetus, these antibodies, called hemolysins, cross the placental membrane and destroy the fetal red blood cells (fig. 12.19). The fetus then develops a condition called *erythroblastosis fetalis* or hemolytic disease of the fetus and newborn.

Erythroblastosis fetalis is extremely rare today because obstetricians carefully track Rh status. An Rh-negative woman who might carry an Rh-positive fetus is given an injection of a drug called RhoGAM. This injection is actually composed of anti-Rh antibodies, which bind to and shield any Rh-positive fetal cells that might contact the woman's cells and sensitize her immune system. RhoGAM must be given within 72 hours of possible contact with Rh-positive cells—including giving birth, terminating a pregnancy, miscarrying, or undergoing amniocentesis (a prenatal test in which a needle is inserted into the uterus).

Practice

42. What is the Rh blood group?
43. What are two ways that Rh incompatibility can arise?

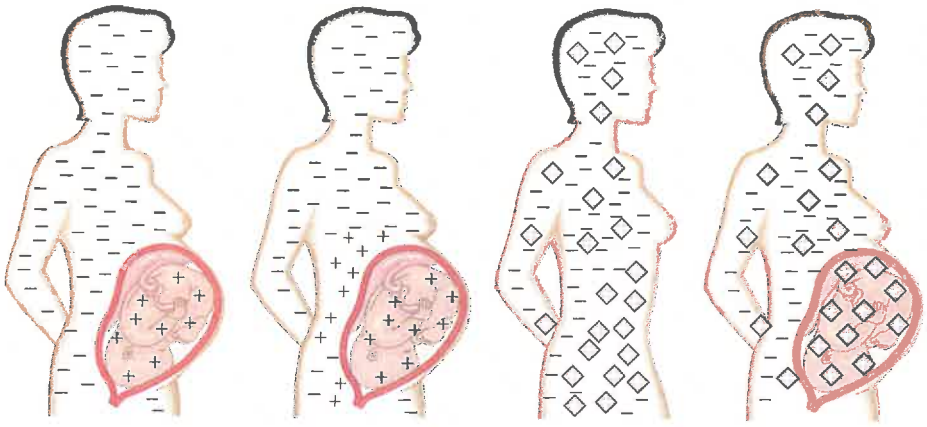

Figure 12.19
Rh incompatibility. If a man who is Rh-positive and a woman who is Rh-negative conceive a child who is Rh-positive, the woman's body may manufacture antibodies that attack future Rh-positive offspring.

Summary Outline

12.1 Introduction (p. 319)

Blood is a type of connective tissue in which cells are suspended in a liquid extracellular matrix. It transports substances between body cells and the external environment, and helps maintain a stable internal environment.

1. Blood can be separated into formed elements and liquid portions.
   a. The formed elements portion is mostly red blood cells.
   b. The liquid plasma includes water, gases, nutrients, hormones, electrolytes, and cellular wastes.
2. Blood volume varies with body size, fluid and electrolyte balance, and adipose tissue content.

12.2 Blood Cells (p. 319)

1. Red blood cells
   a. Red blood cells are biconcave discs with shapes that increase surface area.
   b. Red blood cells contain hemoglobin, which combines loosely with oxygen.
2. Red blood cell counts
   a. The red blood cell count equals the number of cells per microliter of blood.
   b. The average count ranges from approximately 4 to 6 million cells per microliter of blood.
   c. Red blood cell count determines the oxygen-carrying capacity of the blood. It is used to diagnose and evaluate the courses of certain diseases.
3. Red blood cell production and its control
   a. Red bone marrow produces red blood cells.
   b. In health, the number of red blood cells remains relatively stable.
   c. Erythropoietin controls the rate of red blood cell formation by negative feedback.
4. Dietary factors affecting red blood cell production
   a. Availability of vitamin B_{12} and folic acid influences red blood cell production.
   b. Hemoglobin synthesis requires iron.
5. Destruction of red blood cells
   a. Macrophages in the liver and spleen phagocytize damaged red blood cells.
   b. Hemoglobin molecules decompose, and nearly all of the iron they contain is recycled.
   c. Biliverdin and bilirubin are pigments, released from the heme (iron) portion, excreted in bile.
6. White blood cells
   a. White blood cells develop from hematopoietic stem cells in red bone marrow, in response to interleukins and colony-stimulating factors.
   b. Granulocytes include neutrophils, eosinophils, and basophils.
   c. Agranulocytes include monocytes and lymphocytes.
7. Functions of white blood cells
   a. Neutrophils and monocytes phagocytize foreign particles.
   b. Eosinophils kill parasites and help control inflammation and allergic reactions.
   c. Basophils release heparin, which inhibits blood clotting, and histamine, which promotes inflammation, to increase blood flow to injured tissues.
   d. Lymphocytes are important in immunity.
8. White blood cell counts
   a. Normal total white blood cell counts vary from 4,000 to 11,000 cells per microliter of blood.
   b. The number of white blood cells may change in response to abnormal conditions, such as infections, emotional disturbances, or excessive loss of body fluids.
   c. A differential white blood cell count indicates the percentages of various types of leukocytes.
9. Blood platelets
   a. Blood platelets, which develop in the red bone marrow in response to thrombopoietin, are fragments of giant cells.
   b. The normal platelet count varies from 130,000 to 360,000 platelets per microliter of blood.
   c. Platelets help close breaks in blood vessels.

12.3 Blood Plasma (p. 327)

Plasma transports gases and nutrients, helps regulate fluid and electrolyte balance, and helps maintain stable pH.

1. Plasma proteins
   a. Plasma proteins remain in blood and interstitial fluids, and are not normally used as energy sources.
   b. Three major types exist.
      (1) Albumins help maintain the colloid osmotic pressure.
      (2) Globulins transport lipids and fat-soluble vitamins and include antibodies that provide immunity.
      (3) Fibrinogen functions in blood clotting.
2. Gases and nutrients
   a. Gases in plasma include oxygen, carbon dioxide, and nitrogen.
   b. Plasma nutrients include simple sugars, amino acids, and lipids.
      (1) The liver stores glucose as glycogen and releases glucose whenever blood glucose concentration falls.
      (2) Amino acids are used to synthesize proteins and are deaminated for use as energy sources.
      (3) Lipoproteins function in the transport of lipids.
3. Nonprotein nitrogenous substances
   a. Nonprotein nitrogenous substances are composed of molecules that contain nitrogen atoms but are not proteins.
   b. They include amino acids, urea, uric acid, creatine, and creatinine.
4. Plasma electrolytes
   a. Plasma electrolytes include ions of sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, and sulfate.
   b. Bicarbonate ions are important in maintaining the osmotic pressure and pH of plasma.

12.4 Hemostasis (p. 330)

Hemostasis is the stoppage of bleeding.

1. Blood vessel spasm
   a. Smooth muscles in blood vessel walls reflexly contract following injury.
   b. Platelets release serotonin, which stimulates vasoconstriction and helps maintain vessel spasm.
2. Platelet plug formation
   a. Platelets adhere to rough surfaces and exposed collagen.
   b. Platelets adhere to each other at injury sites and form platelet plugs in broken vessels.
3. Blood coagulation
   a. Blood clotting is the most effective means of hemostasis.
   b. Clot formation depends on the balance between factors that promote clotting and those that inhibit clotting.
   c. The basic event of coagulation is the conversion of soluble fibrinogen into insoluble fibrin.
   d. Biochemicals that promote clotting include prothrombin activator, prothrombin, and calcium ions.
   e. A thrombus is an abnormal blood clot in a vessel. An embolus is a clot or fragment of a clot that moves in a vessel.

12.5 Blood Groups and Transfusions (p. 333)

Blood can be typed on the basis of cell surface antigens.

1. Antigens and antibodies
   a. Agglutination is the clumping of red blood cells following a transfusion reaction.
   b. Red blood cell membranes may contain specific antigens, and blood plasma may contain antibodies against certain of these antigens.
2. ABO blood group
   a. Blood is grouped according to the presence or absence of antigens A and B.
   b. Mixing red blood cells that contain an antigen with plasma that contains the corresponding antibody results in an agglutination reaction or adverse transfusion reaction in a patient.
3. Rh blood group
   a. Rh antigen is present on the red blood cell membranes of Rh-positive blood. Rh antigen is absent in Rh-negative blood.
   b. An Rh-negative person exposed to Rh-positive blood produces anti-Rh antibodies in response to the presence of Rh antigens.
   c. Mixing Rh-positive red blood cells with plasma that contains anti-Rh antibodies agglutinates the positive cells.
   d. Anti-Rh antibodies in maternal blood may cross the placental tissues and react with the red blood cells of an Rh-positive fetus.

Chapter Assessments

12.1 Introduction

1. Major functions of blood include: (p. 319)
   a. nutrient, hormone, and oxygen transport.
   b. helping maintain the stability of interstitial fluid.
   c. heat distribution.
   d. waste transport
   e. all of the above.

2. Formed elements in blood are _____, _____, and _____. (p. 319)

3. The liquid portion of blood is _____. (p. 319)

12.2 Blood Cells

4. Describe a red blood cell. (p. 319)

5. Contrast oxyhemoglobin and deoxyhemoglobin. (p. 319)

6. Connect the significance of red blood cell counts with the function of red blood cells. (p. 321)

7. Describe the life cycle of a red blood cell, beginning with its production and ending with its destruction. (p. 321)

8. List dietary factors affecting red blood cell production. (p. 323)

9. Name five types of leukocytes, identifying which are granulocytes and which are agranulocytes, and list the major function(s) of each type. (p. 324)

10. _____ are fragments of megakaryocytes that function in _____. (p. 327)

12.3 Blood Plasma

11. The most abundant component of plasma is: (p. 327)
   a. vitamins.
   b. oxygen.
   c. proteins.
   d. water.
   e. electrolytes.

12. Name three types of plasma proteins, and indicate the major function(s) of each type. (p. 328)

13. Name the gases and nutrients found in plasma. (p. 329)

14. Define *nonprotein nitrogenous substances,* and name those commonly present in plasma. (p. 329)

15. The most abundant plasma electrolytes are _____ and _____. (p. 330)

12.4 Hemostasis

16. _____ is the stoppage of bleeding. (p. 330)

17. Explain how blood vessel spasm is stimulated following an injury. (p. 330)

18. Platelets adhering to form a plug may control blood loss from a _____ break, but a larger break may require a _____ to halt bleeding. (p. 330)

19. Describe the major steps leading to the formation of a blood clot. (p. 331)

20. Contrast thrombus and embolus. (p. 332)

12.5 Blood Groups and Transfusions

21. An individual with B antigens and anti-A antibodies is ABO blood type _____. (p. 334)

22. Explain why the individual described in question 21 should not receive a transfusion with type AB blood. (p. 334)

23. Distinguish between Rh-positive and Rh-negative blood. (p. 335)

24. Describe *erythroblastosis fetalis,* and explain how this condition may develop. (p. 336)

Integrative Assessments/Critical Thinking

OUTCOMES 3.4, 12.2

1. If a patient with inoperable cancer is treated using a drug that reduces the rate of cell division, how might the patient's white blood cell count change? How might the patient's environment be modified to compensate for the effects of these changes?

OUTCOMES 8.3, 12.2

2. Erythropoietin is available as a drug. Why would athletes abuse it?

OUTCOME 12.2

3. How would you explain to a patient with leukemia, who has a greatly elevated white blood cell count, the importance of avoiding bacterial infections?

OUTCOMES 12.2, 12.5

4. Why can a person receive platelets donated by anyone, but must receive a particular type of whole blood?

OUTCOMES 12.3, 12.4

5. Why do patients with liver diseases commonly develop blood clotting disorders?

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