chapter 12

Blood

BLOOD SUBSTITUTES. Finding a substitute for human blood is a tall order, especially trying to mimic the major functions of this connective tissue. Blood carries oxygen (red blood cells), provides protection against infection (white blood cells), promotes clotting (platelets), and carries other vital substances. Efforts to replace blood in the past have sought to fill in the missing fluid volume or to reproduce blood's oxygen-carrying role. The search for blood substitutes intensified after each of the two world wars, because injured soldiers had desperately needed transfusions, and again when the AIDS pandemic made transfusions dangerous unless blood is properly screened.

A red blood cell substitute must meet several requirements: It must carry oxygen and give it up to tissues, be nontoxic, be storeable, function until the body can take over, and not provoke an immune response. The nine red blood cell substitutes currently in clinical trials are of two basic types. Perfluorocarbons are synthetic chemicals that carry dissolved oxygen. These were actually developed in the 1960s, and a famous photo shows a mouse apparently drowning in a beaker of the chemical—but still breathing even though submerged.

The second type of red blood cell substitute dismantles red blood cells and isolates the oxygen-carrying hemoglobin molecules, which are then linked in various ways. The starting material is usually cow's blood or old stored human blood. Red blood cell substitutes used in times past include wine, ale, milk, plant resins, urine, and opium!

Photo:
At this biotechnology company, hemoglobin is purified in efforts to develop a red blood cell substitute.

Chapter Objectives

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. 307)

12.2 Blood and Blood Cells

2. Distinguish among the formed elements of the blood. (p. 307)
3. Explain the control of red blood cell production. (p. 308)
4. Distinguish among the five types of white blood cells, and give the function(s) of each type. (p. 311)

12.3 Blood Plasma

5. List the major components of blood plasma, and describe the functions of each. (p. 314)

12.4 Hemostasis

6. Define *hemostasis,* and explain the mechanisms that help achieve it. (p. 317)
7. Review the major steps in blood coagulation. (p. 318)

12.5 Blood Groups and Transfusions

8. Explain blood typing and how it is used to avoid adverse reactions following blood transfusions. (p. 320)
9. Describe how blood reactions may occur between fetal and maternal tissues. (p. 323)

Aids to Understanding Words

agglutin- [to glue together] *agglutin*ation: Clumping together of red blood cells.
bil- [bile] *bil*irubin: Pigment excreted in the bile.
embol- [stopper] *embol*ism: Obstruction of a blood vessel.
erythr- [red] *erythr*ocyte: Red blood cell.
hem- [blood] *hem*oglobin: Red pigment responsible for the color of blood.
leuko- [white] *leuko*cyte: White blood cell.
-osis [abnormal condition] leukocyt*osis*: Condition in which white blood cells are overproduced.
-poie [make, produce] erythro*poie*tin: Hormone that stimulates the production of red blood cells.
-sta [halt] hemo*sta*sis: Arrest of bleeding from damaged blood vessels.
thromb- [clot] *thromb*ocyte: Blood platelet involved in the formation of a blood clot.

Key Terms

albumin (al-bu´min)
antibody (an´ti-bod´´e)
antigen (an´ti-jen)
basophil (ba´so-fil)
coagulation (ko-ag´´u-la´shun)
eosinophil (e´´o-sin´o-fil)
erythrocyte (ĕ-rith´ro-sīt)
erythropoietin (ĕ-rith´´ro-poi´ĕ-tin)
fibrinogen (fi-brin´o-jen)
globulin (glob´u-lin)
hemostasis (he´´mo-sta´sis)
leukocyte (lu´ko-sīt)
lymphocyte (lim´fo-sīt)
monocyte (mon´o-sīt)
neutrophil (nu´tro-fil)
plasma (plaz´mah)
platelet (plāt´let)

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 material. Blood is vital in transporting substances between body cells and the external environment, thereby promoting homeostasis.

12.2 Blood and Blood Cells

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 and white blood cells. Blood also contains cellular fragments called blood platelets (fig. 12.1). The cells and platelets are termed "formed elements" of the blood, in contrast to the liquid portion.

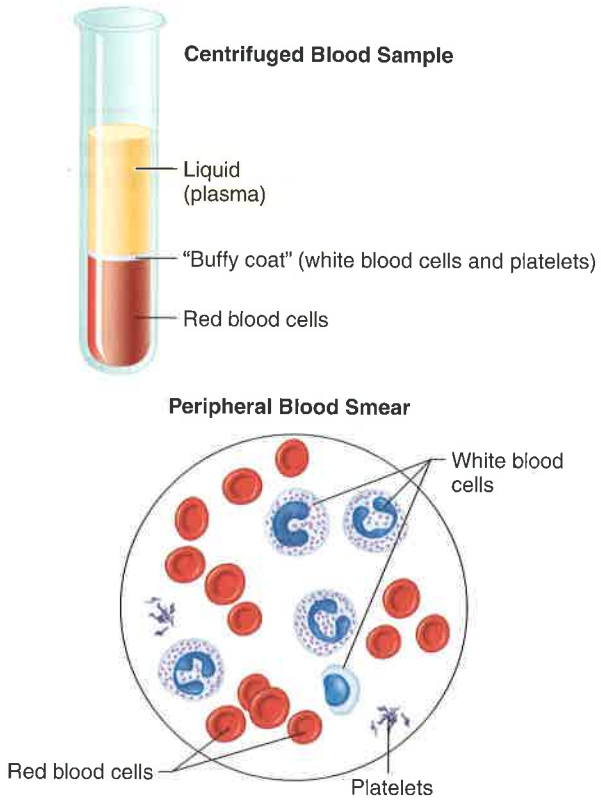


Figure 12.1
Blood consists of a liquid portion called plasma and a solid portion that includes red blood cells, white blood cells, and platelets. (Note: When blood components are separated, the white blood cells and platelets form a thin layer, called the "buffy coat," between the plasma and the red blood cells.)

Blood Volume and Composition

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

Men have more blood than women. Men have 1.500 gallons, compared to 0.875 gallons for women.

A blood sample is usually about 45% cells by volume. This percentage is called the **hematocrit (HCT).** Most blood cells are red cells, with much smaller numbers of white cells and blood platelets. The remaining 55% of a blood sample is a clear, straw-colored liquid called **plasma** (plaz´mah) (fig. 12.1). Plasma is a complex mixture of water, amino acids, proteins, carbohydrates, lipids, vitamins, hormones, electrolytes, and cellular wastes.

CHECK YOUR RECALL

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

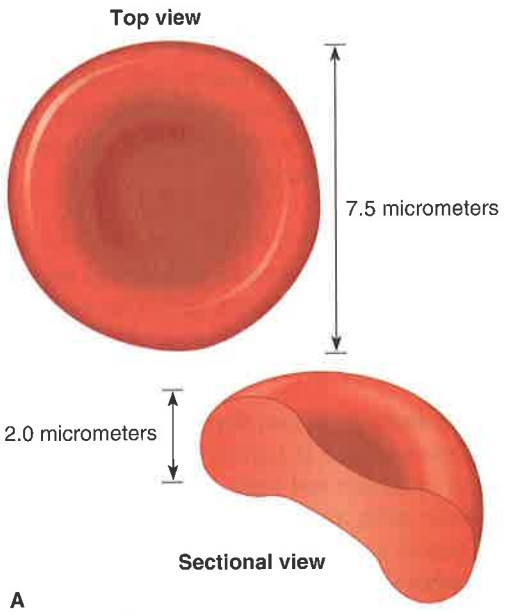
Red Blood Cells

Red blood cells, or **erythrocytes** (ĕ-rith´ro-sīts), are biconcave discs. This shape is an adaptation for transporting gases; it increases the surface area through which gases can diffuse (fig. 12.2). The red blood cell's shape also places the cell membrane closer to oxygen-carrying *hemoglobin* within the cell.

Each red blood cell is about one-third hemoglobin by volume. This protein is responsible for the color of the blood. When hemoglobin combines with oxygen, the resulting *oxyhemoglobin* is bright red, and when oxygen is released, the resulting *deoxyhemoglobin* is darker.

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

A person experiencing prolonged oxygen deficiency (hypoxia) may become *cyanotic.* The skin and mucous membranes appear bluish due to an abnormally high blood concentration of deoxyhemoglobin. Exposure to low temperature may also result in cyanosis. Such exposure constricts superficial blood vessels, which slows blood flow and removes more oxygen than usual from blood flowing through the vessels.



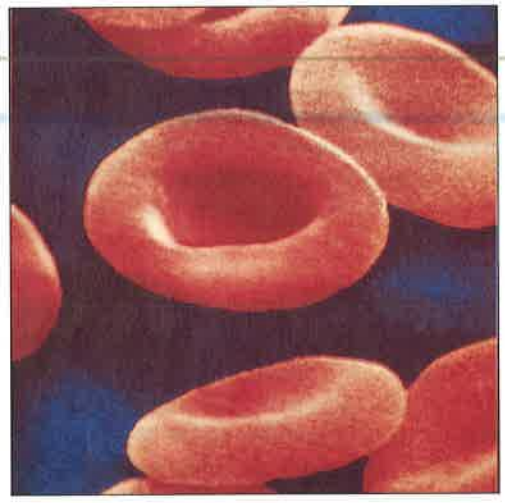


Figure 12.2
Red blood cells. (*A*) The biconcave shape of a red blood cell makes possible its function. (*B*) Scanning electron micrograph of human red blood cells (falsely colored) (5,000×).

Red Blood Cell Counts

The number of red blood cells in a cubic millimeter (mm^3) of blood is called the *red blood cell count* (*RBCC* or *RCC*). The typical range for adult males is 4,600,000–6,200,000 cells per mm^3, and that for adult females is 4,200,000–5,400,000 cells per mm^3.

Since 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.

CHECK YOUR RECALL

1. Describe a red blood cell.
2. What is the function of hemoglobin?
3. How does a red blood cell change as it matures?
4. 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. 133) that red blood cell formation (hemopoiesis) initially occurs in the yolk sac, liver, and spleen. After an infant is born, these cells are produced almost exclusively in tissue lining the spaces in bones, the red bone marrow.

The average life span of a red blood cell is 120 days. Many of these cells are removed from the circulation each day, 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.

A *negative feedback mechanism* utilizing the hormone **erythropoietin** (ĕ-rith´´ro-poi´ĕ-tin) controls the rate of red blood cell formation. The kidneys, and to a lesser extent the liver, release erythropoietin in response to prolonged oxygen deficiency (fig. 12.3). At high altitudes, for example, where the percentage of oxygen in the air is reduced, the amount of oxygen delivered 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 these tissues with their oxygen requirements. When the oxygen level in the air returns to normal, erythropoietin release decreases, and the rate of red blood cell production returns to normal as well. Figure 12.4 illustrates the stages in the development and differentiation of red blood cells from *hemocytoblasts* (stem cells).

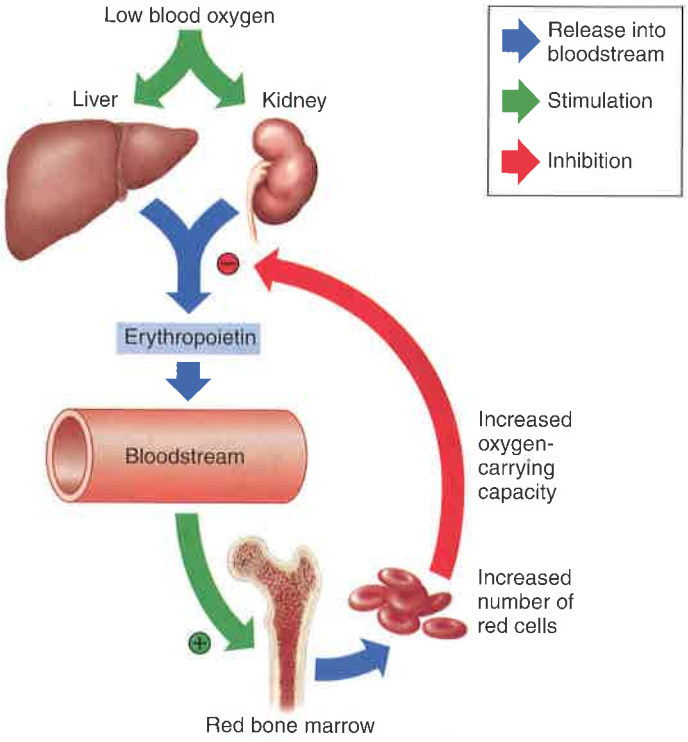


Figure 12.3
Low blood oxygen causes the kidneys and liver to release erythropoietin, which stimulates the production of red blood cells that carry oxygen to tissues.

CHECK YOUR RECALL

1. Where are red blood cells produced?
2. How is red blood cell production controlled?
3. Which vitamins are necessary for red blood cell production?
4. Why is iron required for the development of red blood cells?

In *sickle cell disease,* a single DNA base change causes an incorrect amino acid to be incorporated into globin, causing hemoglobin to crystallize in a low-oxygen environment. This bends the red blood cells containing the hemoglobin into a sickle shape, which blocks circulation in small blood vessels, causing excruciating joint pain and damaging many organs. As the spleen works harder to recycle the abnormally short-lived red blood cells, infection becomes likely.

Most children with sickle cell disease are diagnosed at birth and receive antibiotics daily for years to prevent infection. Hospitalization for blood transfusions may be necessary if the person experiences painful sickling "crises" of blocked circulation.

A bone marrow transplant can completely cure sickle cell disease but has a 15% risk of causing death. A new treatment is an old drug, used to treat cancer, called hydroxyurea. It activates a slightly different form of hemoglobin in the fetus. Because of the presence of the functional fetal hemoglobin, the sickle hemoglobin cannot crystallize as quickly as it otherwise would. Sickling becomes delayed, which enables red blood cells carrying sickled hemoglobin to more quickly reach the lungs—where fresh oxygen restores the cells' normal shapes.

Dietary Factors Affecting Red Blood Cell Production

B-complex vitamins—*vitamin B_{12}* and *folic acid*—significantly influence red blood cell production. These vitamins are necessary for DNA synthesis, so all cells with nuclei require them to grow and divide. Since cell division occurs frequently in the blood-cell-forming (hemopoietic) tissue, this tissue is especially vulnerable to 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 during decomposition of hemoglobin from damaged red blood cells. Therefore, the diet need only supply small quantities of iron.

Too few red blood cells or too little hemoglobin causes *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.

Destruction of Red Blood Cells

Red blood cells are quite elastic and flexible, and they readily bend as they pass through small blood vessels. With age, however, these cells become more fragile, and they are frequently damaged simply by passing through capillaries, particularly those in active muscles. **Macrophages** phagocytize and destroy damaged red blood cells, primarily in the liver and spleen (see chapter 5, p. 99).

Hemoglobin molecules liberated from the red blood cells are broken down into subunits of *heme,* an iron-containing portion, and *globin,* a protein. The heme further decomposes into iron and a greenish pigment called **biliverdin.** The blood may transport the iron, combined with a protein, to the hemopoietic tissue in red bone marrow to be reused in synthesizing new hemoglobin. Otherwise, the liver stores iron 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. 409). Figure 12.5 summarizes the life cycle of a red blood cell.

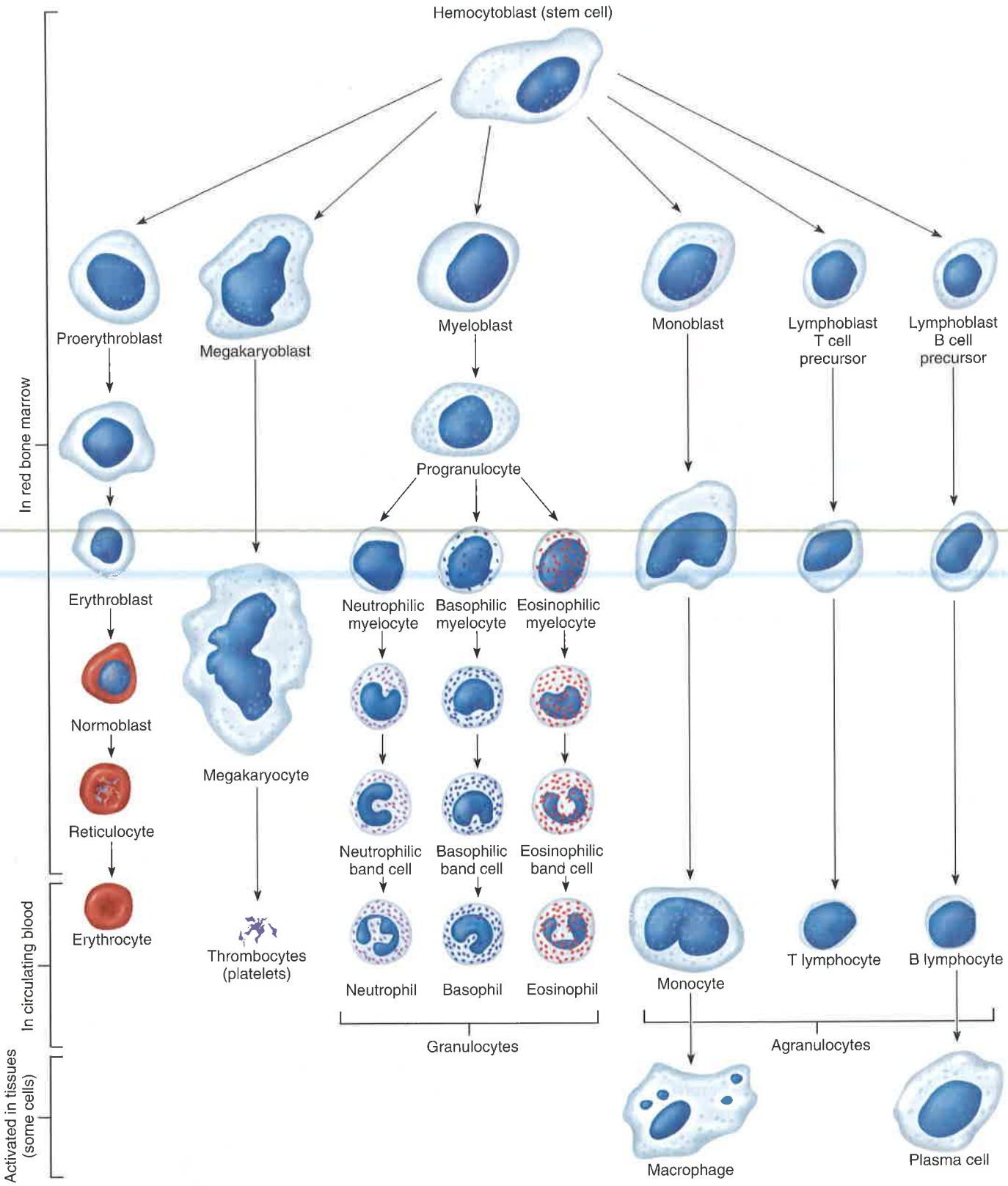


Figure 12.4
Origin and development of blood cells from hemocytoblasts (stem cells) in bone marrow.

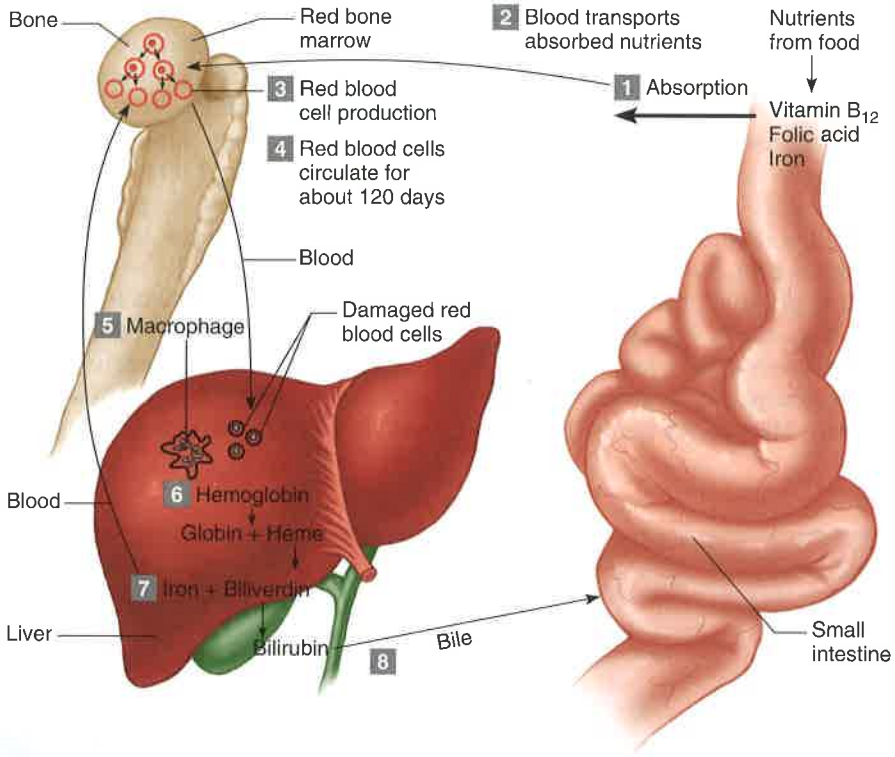


Figure 12.5
Life cycle of a red blood cell. (*1*) The small intestine absorbs essential nutrients. (*2*) Blood transports nutrients to red bone marrow. (*3*) In the marrow, red blood cells arise from the division of less specialized cells. (*4*) Mature red blood cells are released into the bloodstream, 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.

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

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.

CHECK YOUR RECALL

1. What happens to damaged red blood cells?
2. What are the products of hemoglobin breakdown?

White Blood Cells

White blood cells, or **leukocytes** (lu´ko-sītz), protect against disease. Leukocytes develop from *hemocytoblasts* (see fig. 12.4) in response to hormones also. 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 later in this chapter.

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. 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 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 stain light purple in neutral stain. The nucleus of a neutrophil is lobed and consists of two to five sections connected by thin strands of chromatin

(fig. 12.6). 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 stain deep red in acid stain (fig. 12.7). The nucleus usually has only two lobes (termed bilobed). These cells 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 stain deep blue in basic stain (fig. 12.8). 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. 371).

Monocytes (mon´o-sītz), the largest blood cells, are two to three times greater in diameter than red blood cells (fig. 12.9). 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 contains a large, round nucleus surrounded by a thin rim of cytoplasm (fig. 12.10). These cells account for 25–33% of circulating leukocytes. They may live for years.

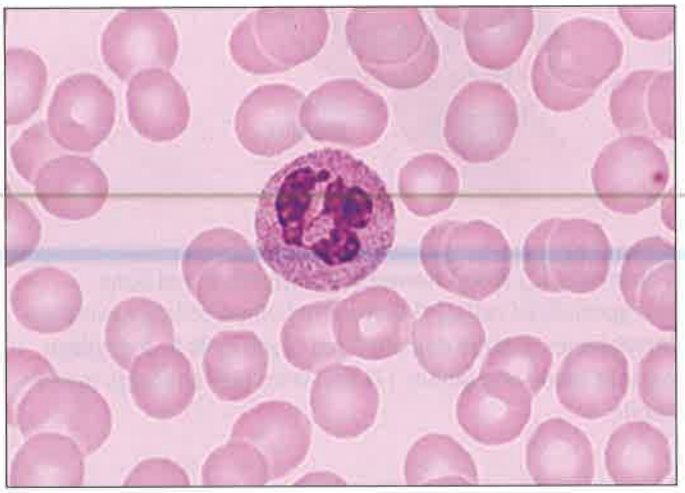


Figure 12.6
The neutrophil has a lobed nucleus with two to five components (1,060×).

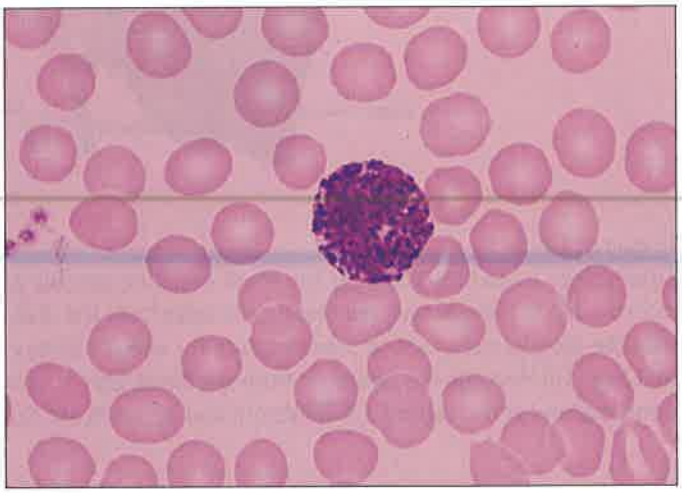


Figure 12.8
The basophil has cytoplasmic granules that stain deep blue (1,060×).

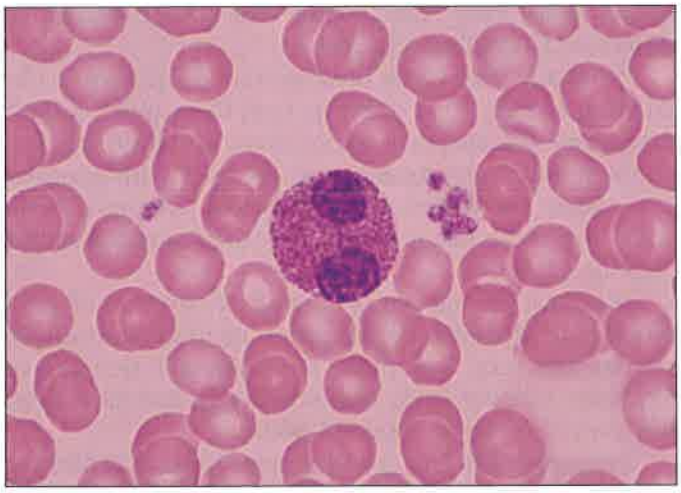


Figure 12.7
The eosinophil has red-staining cytoplasmic granules (1,060×).

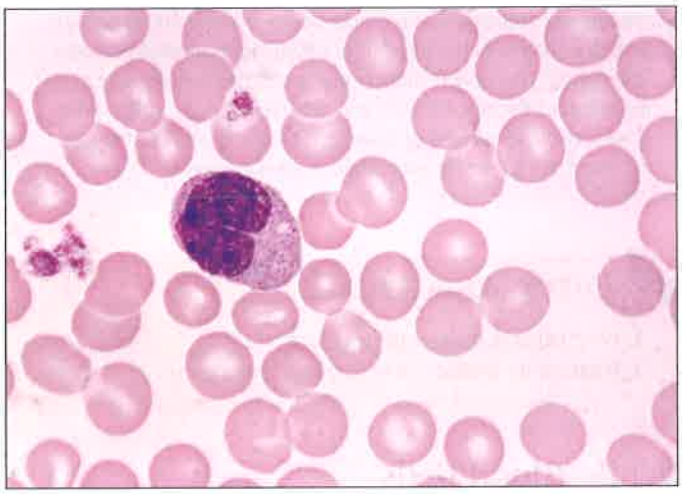


Figure 12.9
A monocyte may leave the bloodstream and become a macrophage (1,060×).

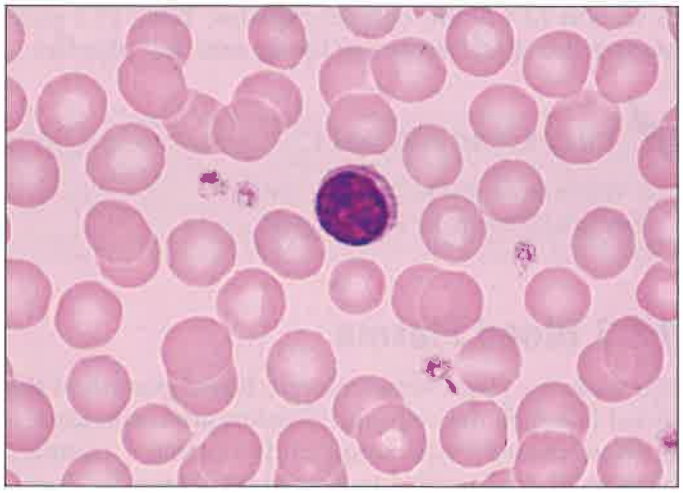


Figure 12.10
The lymphocyte contains a large, round nucleus (1,060×).

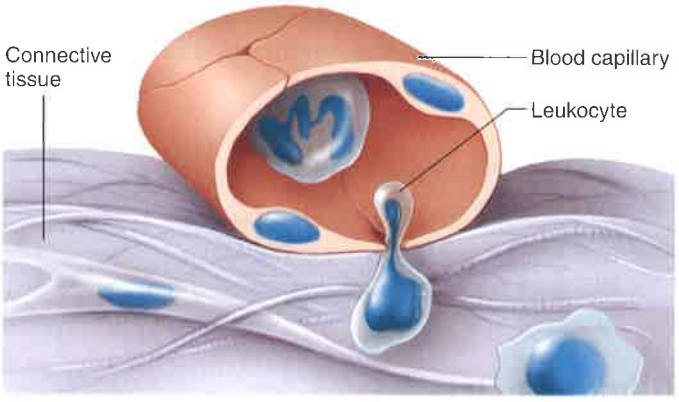


Figure 12.11
In a type of movement called diapedesis, leukocytes squeeze between the cells of a capillary wall and enter the tissue space outside the blood vessel.

CHECK YOUR RECALL

1. Which hormones are necessary for development of white blood cells from hemocytoblasts in the red bone marrow?
2. Distinguish between granulocytes and agranulocytes.
3. 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. 12.11). 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. 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. Neutrophils and monocytes often become so engorged with digestive products and bacterial toxins that they also 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.

Some of the cytoplasmic granules of basophils contain a blood-clot-inhibiting substance called *heparin,* and other granules contain *histamine.* Basophils release heparin which helps prevent intravascular blood clot formation, and they release histamines which increase 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 discusses immunity.

CHECK YOUR RECALL

1. What are the primary functions of white blood cells?
2. Which white blood cells are the most active phagocytes?
3. What are the functions of eosinophils and basophils?

White Blood Cell Counts

The number of white blood cells in a cubic millimeter of human blood, called the *white blood cell count (WBCC),* normally includes 5,000–10,000 cells. Because this number may change in response to abnormal conditions, white blood cell counts are of clinical interest. For example, a rise in the number of circulating white blood cells may indicate infection. A total number of white blood cells exceeding 10,000 per mm^3 of blood constitutes **leukocytosis,** indicating acute infection, such as appendicitis.

A total white blood cell count below 5,000 per mm^3 of blood is called **leukopenia.** Such a deficiency may accompany typhoid fever, influenza, measles, mumps, chicken pox, 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. The number of neutrophils, for instance, usually increases during bacterial infections, and the number of eosinophils

may increase during certain parasitic infections and allergic reactions. In AIDS, the number of a certain type of lymphocyte drops sharply.

CHECK YOUR RECALL

1. What is the normal human white blood cell count?
2. Distinguish between leukocytosis and leukopenia.
3. What is a differential white blood cell count?

Blood Platelets

Platelets (plāt´letz), or **thrombocytes,** are not complete cells. They arise from very large cells in red bone marrow, called **megakaryocytes,** that fragment like a shattered plate, releasing small sections of cytoplasm—the 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 *hemocytoblasts* (see fig. 12.4) in response to the hormone **thrombopoietin.**

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 circulate for about ten days. In normal blood, the *platelet count* varies from 130,000 to 360,000 per mm^3. Platelets help close breaks in damaged blood vessels and initiate formation of blood clots, as section 12.4 of this chapter explains. Table 12.1 summarizes the characteristics of blood cells and platelets.

CHECK YOUR RECALL

1. What is the normal blood platelet count?
2. 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 mixture of organic and inorganic biochemicals. 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 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 plasma protein groups—albumins, globulins, and fibrinogen—differ in chemical composition and physiological function.

Albumins (al-bu´minz) are the smallest of the plasma proteins, yet account for about 60% of these pro-

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 mm^3	Transports oxygen and carbon dioxide
White blood cell (leukocyte)		5,000–10,000 per mm^3	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 helps control inflammation and 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 mm^3	Helps control blood loss from broken vessels

Topic of Interest LEUKEMIA

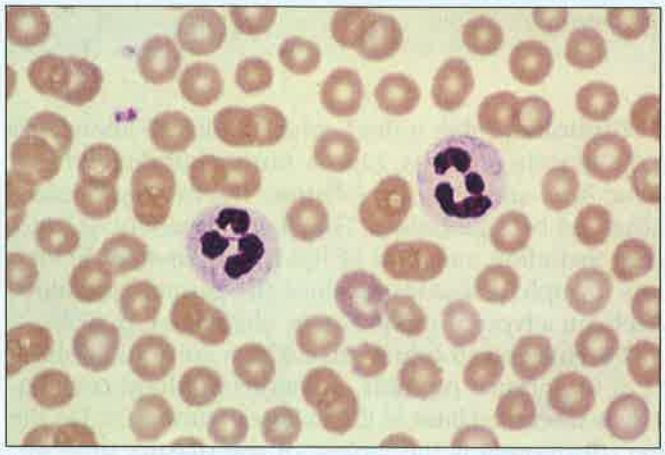
The young woman at first noticed fatigue and headaches, which she attributed to studying for final exams. She had frequent colds and bouts of fever, chills, and sweats that she thought were just minor infections. When she developed several bruises and bone pain and noticed that her blood did not clot very quickly after cuts and scrapes, she consulted her physician, who examined her and took a blood sample. One glance at a blood smear under a microscope alarmed the doctor—there were far too few red blood cells and platelets and too many white blood cells. She sent the sample to a laboratory to diagnose the type of *leukemia,* or cancer of the white blood cells, that was causing her patient's symptoms.

The young woman had *myeloid leukemia.* Her red bone marrow was producing too many granulocytes, but they were immature cells, unable to fight infection (fig. 12A). This explained the frequent illnesses. The leukemic cells were crowding out red blood cells and their precursors in the red marrow, causing anemia and resulting fatigue. Platelet deficiency (thrombocytopenia) led to an increased tendency to bleed. Finally, spread of the cancer cells outside the marrow painfully weakened the surrounding bone. Eventually, if the patient was not treated, the cancer cells would spread outside the cardiovascular system, causing other tissues that would normally not produce white blood cells to do so.

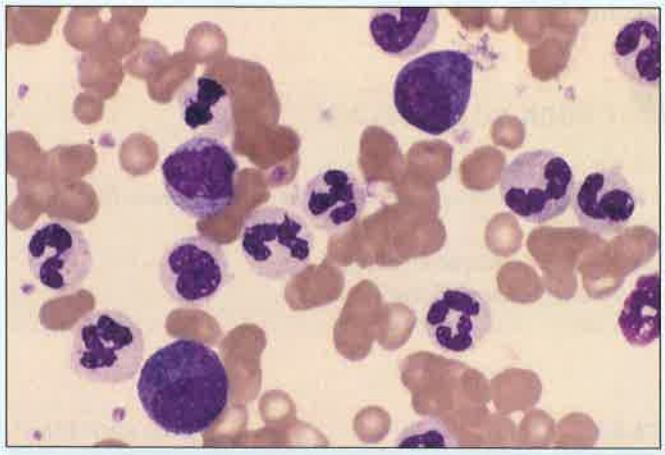
A second type of leukemia, distinguished by the source of the cancer cells, is *lymphoid leukemia.* These cancer cells are lymphocytes, produced in lymph nodes. Many of the symptoms are similar to those of myeloid leukemia. Sometimes a person has no leukemia symptoms at all, and a routine blood test detects the condition.

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. With treatment, 50–80% of patients enter remission, a period of stability that may become a cure. Chemotherapy may be necessary for a year or two to increase the chances of long remission.

Leukemia treatment includes correcting the symptoms with blood transfusions, treating infections, and using drugs that kill cancer cells. Several drugs in use for many years have led to spectacular increases in cure rates, particularly for acute lymphoid leukemia in children. A new drug called Gleevec has had spectacular success in treating a type of chronic leukemia. If other treatments fail, a bone marrow transplant can cure leukemia, but the procedure is very risky. Stem cell transplants, using cells from donated umbilical cord blood, can also cure leukemia. Therefore, people with leukemia often have many treatment options.



A



B

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.

teins 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. 60) that the presence of solute that cannot cross a selectively permeable membrane creates an osmotic pressure and that water always diffuses toward a greater osmotic pressure. Because plasma proteins are too large to pass through the capillary walls, they create an osmotic pressure that tends to hold water in the capillaries, despite the fact that blood pressure tends to force water out of capillaries by filtration (see chapter 3, p. 61). The term *colloid osmotic pressure* is often 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 is directly related to blood pressure (see chapter 13, p. 348).

If the concentration of plasma proteins falls, tissues swell—a condition called *edema*. This may result from starvation or a protein-deficient diet, either of which requires the body to use protein for energy, or from an impaired liver that cannot synthesize plasma proteins. As the concentration of plasma proteins drops, so does colloid osmotic pressure, sending fluids into intercellular 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. They 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. 378).

Fibrinogen (fi-brin´o-jen), which constitutes about 4% of the plasma proteins, functions in blood coagulation, as discussed later in the chapter. Synthesized in the liver, fibrinogen is the largest of the plasma proteins. Table 12.2 summarizes the characteristics of the plasma proteins.

CHECK YOUR RECALL

1. List three types of plasma proteins.
2. How do albumins help maintain water balance between blood and tissues?
3. What are the functions of the globulins?
4. What is the role of fibrinogen?

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	Blood coagulation

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 (p. 451) 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 glucose can 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 chapter 11 (p. 296) describes. 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. 422).

Plasma lipids include fats (triglycerides), phospholipids, and cholesterol. Because lipids are not water soluble and plasma is almost 92% water, these lipids combine with proteins in **lipoprotein** complexes. Lipoprotein molecules are relatively large and consist of a surface layer of phospholipid, cholesterol, and protein surrounding a triglyceride core. The protein constituents of lipoproteins in the outer layer, called *apoproteins,* can combine with receptors on the membranes of specific target cells. Lipoprotein molecules vary in the proportions of lipids they contain.

Because lipids are less dense than proteins, as the proportion of lipids in a lipoprotein increases, the density of the particle decreases. Conversely, as the proportion of lipids decreases, the density increases. Lipoproteins are classified on the basis of their densities, which reflect their composition. *Chylomicrons* mainly consist of triglycerides absorbed from the small intestine (see chapter 15, p. 414). *Very low-density lipoproteins (VLDL)* have a relatively high concentration of triglycerides. *Low-density lipoproteins (LDL)* have a relatively high concentration of cholesterol and are the major cholesterol-carrying lipoproteins. *High-density lipoproteins (HDL)* have a relatively high concentration of protein and a lower concentration of lipids. Chylomicrons transport dietary fats to muscle and adipose cells. Table 12.3 summarizes the characteristics and functions of lipoproteins.

Nonprotein Nitrogenous Substances

Molecules that contain nitrogen atoms but are not proteins comprise a group called **nonprotein nitrogenous substances.** In plasma, this group includes amino acids, urea, and uric acid. Amino acids come from protein digestion and amino acid absorption. Urea and uric acid are products of protein and nucleic acid catabolism, respectively, and are excreted in the urine.

TABLE 12.3 PLASMA LIPOPROTEINS

LIPOPROTEIN	CHARACTERISTICS	FUNCTIONS
Chylomicron	High concentration of triglycerides	Transports dietary fats to muscle and adipose cells
Very low-density lipoprotein (VLDL)	Relatively high concentration of triglycerides; produced in the liver	Transports triglycerides from the liver to adipose cells
Low-density lipoprotein (LDL)	Relatively high concentration of cholesterol; formed from remnants of VLDL molecules that have given up their triglycerides	Delivers cholesterol to various cells, including liver cells
High-density lipoprotein (HDL)	Relatively high concentration of protein and low concentration of lipids	Transports to the liver remnants of chylomicrons that have given up their triglycerides

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. Of these, 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 (p. 482) discusses these electrolytes in connection with water and electrolyte balance.

CHECK YOUR RECALL

1. Which gases are in plasma?
2. Which nutrients are in plasma?
3. What is a nonprotein nitrogenous substance?
4. 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 limit or prevent blood loss, including blood vessel spasm, platelet plug formation, and blood coagulation.

Blood Vessel Spasm

Cutting or breaking a smaller blood vessel stimulates the smooth muscles in its walls to contract, and blood loss lessens almost immediately. In fact, the ends of a severed vessel may close completely by such a **vasospasm.**

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 and to the collagen in connective tissue. Consequently, 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 12.12 shows the steps in platelet plug formation.

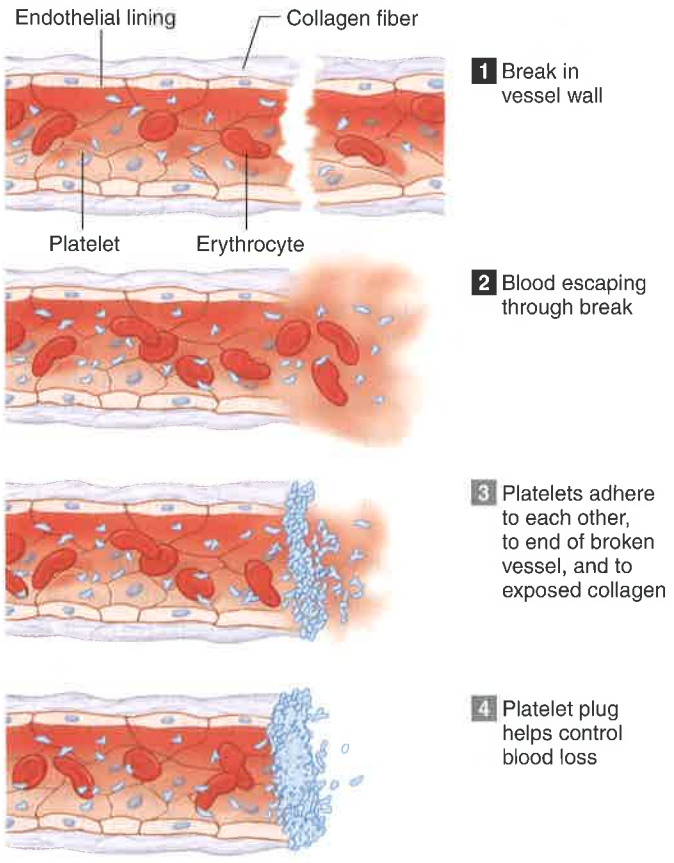


Figure 12.12
Steps in platelet plug formation.

CHECK YOUR RECALL

1. What is hemostasis?
2. How does a blood vessel spasm help control bleeding?
3. Describe the formation of a platelet plug.

Blood Coagulation

Coagulation (ko-ag´´u-la´shun), the most effective hemostatic mechanism, causes 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.** Damaged tissues release *tissue thromboplastin,* initiating a series of reactions that results in the production of *prothrombin activator.* This series of changes depends on the presence of calcium ions as well as certain proteins and phospholipids for completion.

Prothrombin is an alpha globulin that the liver continually produces and is thus a normal constituent of plasma. In the presence of calcium ions, prothrombin activator converts prothrombin into **thrombin.** Thrombin, in turn, catalyzes a reaction that fragments fibrinogen. The fibrinogen pieces join, forming long threads of fibrin. Certain other proteins also enhance fibrin formation.

Once fibrin threads form, they stick to the exposed surfaces of damaged blood vessels, creating a meshwork that entraps blood cells and platelets (fig. 12.13). 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 the same as plasma, minus clotting factors.

The amount of prothrombin activator that appears in the blood is directly proportional to the degree of tissue damage. Once a blood clot begins to form, it promotes more 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 same type of action. Such a positive feedback mechanism produces unstable conditions and can operate for only a short time in a living system because life depends on the maintenance of a stable internal environment (see chapter 1, p. 5).

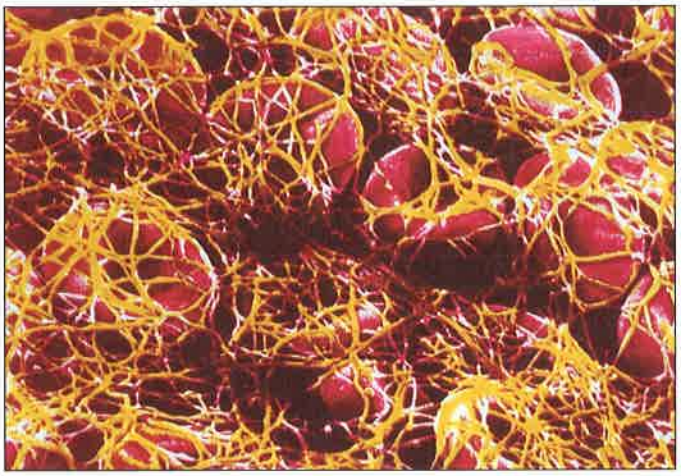


Figure 12.13
A scanning electron micrograph of fibrin threads (2,700×).

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

Normally, blood flow throughout the body prevents the formation of a massive clot within the cardiovascular system by rapidly carrying excess thrombin away and keeping its concentration too low to enhance further clotting. Consequently, blood coagulation is usually limited to blood that is standing still (or moving relatively slowly), and clotting ceases where a clot contacts circulating blood.

Fibroblasts (see chapter 5, p. 99) invade blood clots that form in ruptured vessels, producing connective tissue with numerous fibers throughout the clots, 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 depends on activation of a plasma protein that can digest fibrin threads and other proteins associated with clots. Clots that fill large blood vessels, however, are seldom removed naturally.

A blood clot abnormally forming in a vessel is a **thrombus** (throm´bus). If the clot dislodges or if a fragment of it breaks loose and is carried away by the blood flow, it 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.

Abnormal clot formations are often associated with conditions that change the endothelial linings of vessels. For example, in *atherosclerosis,* accumulations of fatty deposits change the arterial linings, sometimes initiating inappropriate clotting (fig. 12.14). Figure 12.15 summarizes the three primary hemostatic mechanisms.

Genetics Connection COAGULATION DISORDERS

Hemophilia

In 1962, five-year-old Bob Massie developed uncontrollable bleeding in his left knee, a symptom of his *hemophilia A,* an inherited clotting disorder. It took thirty transfusions of plasma over the next three months to stop the bleeding. Because the knee joint had swelled and locked into place during that time, Bob was unable to walk for the next seven years. Today, Bob still suffers from painful joint bleeds, but he injects himself with factor VIII, the coagulation protein his body cannot make. Factor VIII controls his bleeding.

Hemophilia has left its mark on history. One of the earliest descriptions is in the Talmud, a second century B.C. Jewish document, which reads, "If she circumcised her first child and he died, and a second one also died, she must not circumcise her third child." England's Queen Victoria (1819–1901) passed the hemophilia gene to several of her children, eventually spreading the condition to the royal families of Russia, Germany, and Spain. Hemophilia achieved notoriety when factor VIII pooled from blood donations was discovered to transmit HIV in 1985. Ninety percent of people with severe hemophilia who used such pooled factor VIII in the few years prior to that time have developed AIDS.

Abnormalities of different clotting factors cause different forms of hemophilia, but hemophilia A is the most common. Symptoms of the hemophilias include severe hemorrhage following minor injuries, frequent nosebleeds, large intramuscular hematomas, and blood in the urine.

von Willebrand Disease

The tendency to bleed and bruise easily is a sign of *von Willebrand disease,* another inherited clotting disorder that is usually far less severe than hemophilia. Affected persons lack a plasma protein, von Willebrand factor, that is secreted by endothelial cells lining blood vessels and enables platelets to adhere to damaged blood vessel walls, a key step preceding actual clotting. Sometimes, the condition can cause spontaneous bleeding from the mucous membranes of the gastrointestinal and urinary tracts.

Figure 12.14
Artery cross sections. (*A*) Light micrograph of a normal artery (90×). (*B*) The inner wall of this artery changed as a result of atherosclerosis (55×).

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. Tissue plasminogen activators (tPA) break up abnormal blood clots and are used to treat heart attacks and strokes.

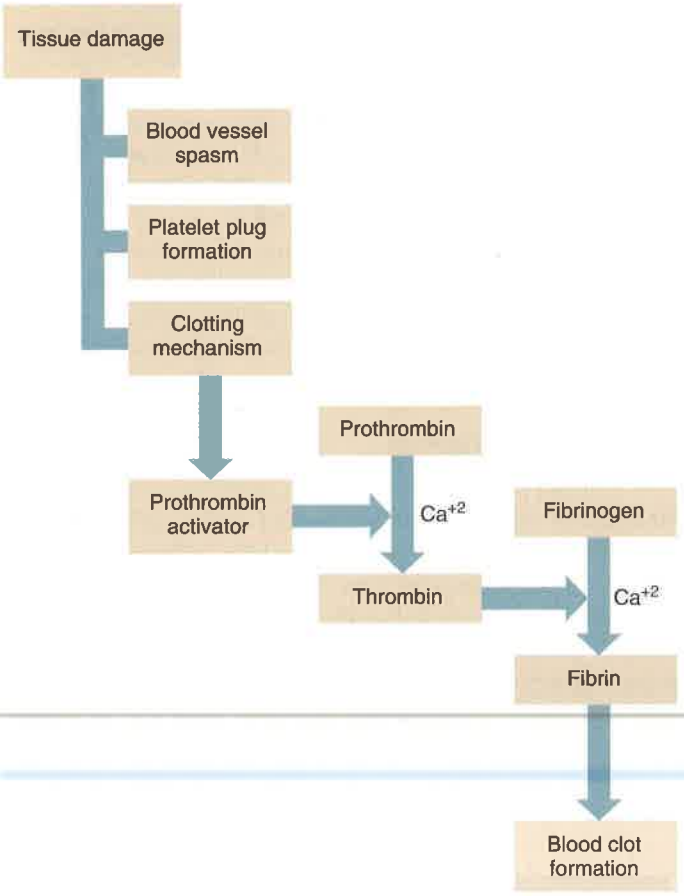


Figure 12.15
Blood vessel spasm, platelet plug formation, and blood coagulation provide hemostasis following tissue damage.

CHECK YOUR RECALL

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

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 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.

Antigens and Antibodies

Agglutination is the clumping of red blood cells following a transfusion reaction. This phenomenon is due to a reaction between red blood cell surface molecules called **antigens** (an´ti-jenz), formerly called *agglutinogens,* and protein **antibodies** (an´ti-bod´´ēz), formerly called *agglutinins,* carried in plasma.

Only a few of the many 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 tranfusion 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 antigens on red blood cell membranes—antigen A and antigen B. A person's erythrocytes have on their surfaces one of four antigen combinations as a result of inheritance: only A, only B, both A and B, or neither A nor B.

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 humans have one of four possible ABO blood types—A, B, AB, or O.

In the U.S., the most common ABO blood types are O (47%) and A (41%). Rarer are type B (9%) and type AB (3%).

Certain antibodies 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 antibody anti-B in their plasma; those with type B blood have antibody anti-A; those with type AB blood have neither antibody; and those with type O blood have both antibody anti-A and antibody anti-B (fig. 12.16 and table

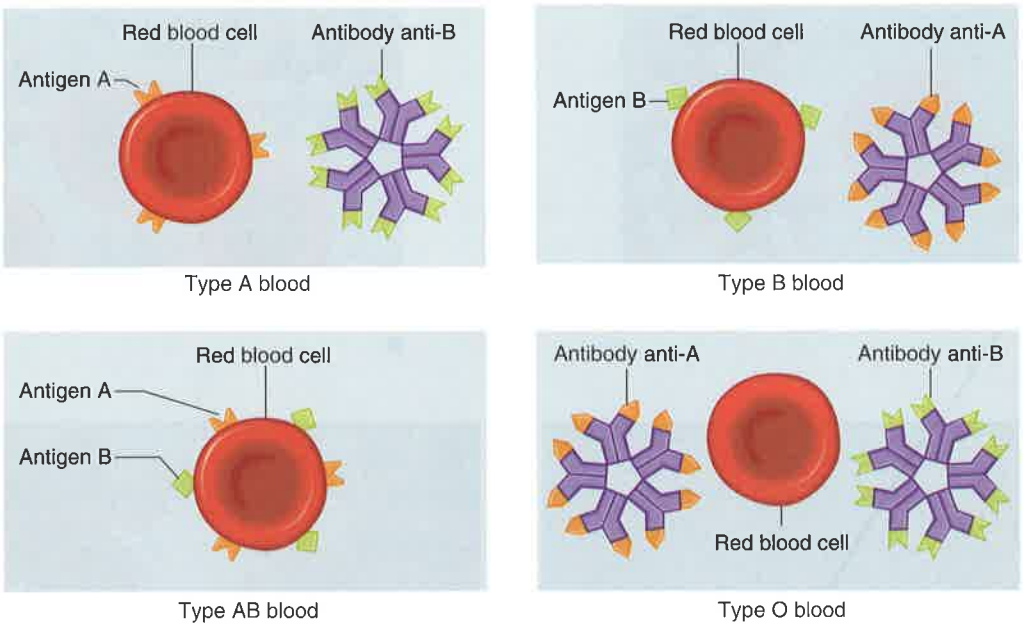


Figure 12.16
Different combinations of antigens and antibodies distinguish blood types. Cells and antibodies not drawn to scale.

TABLE 12.4 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

12.4). 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 does not occur.

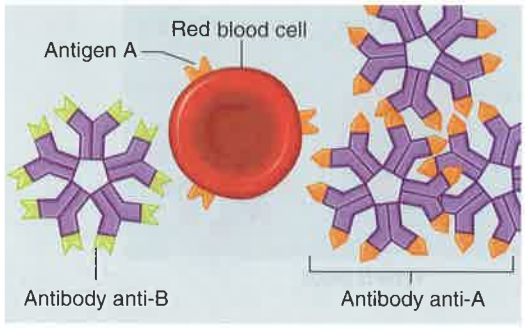
An antibody of one type will react with an antigen of the same type and clump red blood cells; therefore, such combinations must be avoided. The major concern in blood transfusion procedures is that the cells in the donated blood not clump due to antibodies in the recipient's plasma. For this reason, 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 (fig. 12.17).

Because type AB blood lacks both anti-A and anti-B antibodies, an AB person can receive a transfusion of blood of any 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 12.5).

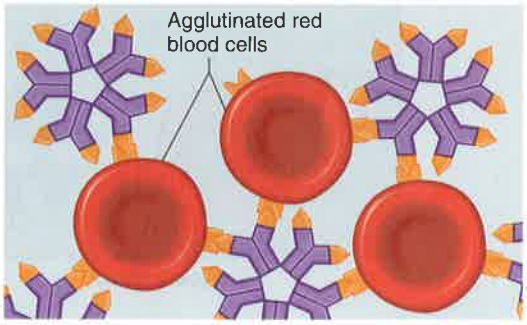
Because type O blood lacks antigens A and B, this type could theoretically be transfused into persons with blood of any other type. Therefore, persons with type O blood are sometimes called *universal donors*. Type O blood, however, does contain both anti-A and anti-B antibodies. If type O blood is given 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 it, minimizing the chance of an adverse reaction.

TABLE 12.5 PREFERRED AND PERMISSIBLE BLOOD TYPES FOR TRANSFUSIONS

BLOOD TYPE OF RECIPIENT	PREFERRED BLOOD TYPE OF DONOR	PERMISSIBLE BLOOD TYPE OF DONOR (IN EXTREME EMERGENCY)
A	A	A, O
B	B	B, O
AB	AB	AB, A, B, O
O	O	O



A



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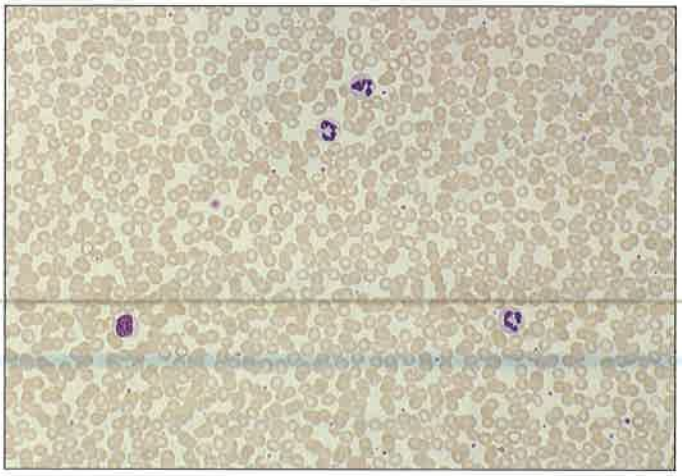

C

D

Figure 12.17
Agglutination. (*A*) If red blood cells with antigen A are added to blood containing antibody anti-A, (*B*) the antibodies react with the antigens, causing clumping (agglutination). (*C*) Nonagglutinated blood (210×). (*D*) Agglutinated blood (220×).

CHECK YOUR RECALL

1. Distinguish between antigens and antibodies.
2. What is the main concern when blood is transfused from one individual to another?
3. Why is a type AB person called a universal recipient?
4. 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 important of these is *antigen D;* however, if any of the antigen D and other Rh antigens are present on the red blood cell membranes, the blood is said to be *Rh-positive.* Conversely, if the red blood cells lack Rh antigens, the blood is called *Rh-negative.*

Only 15% of the U.S. population is Rh-negative. Therefore, AB^- blood is the rarest type, and O^+ the most common.

As in the case of antigens A and B, the presence (or absence) of Rh antigens is an inherited trait. Unlike anti-A and anti-B, antibodies for Rh (*anti-Rh*) do not appear spontaneously. Instead, they form only in Rh-negative persons in response to special stimulation.

If an Rh-negative person receives a transfusion of Rh-positive blood, the Rh antigens stimulate the recipient's antibody-producing cells 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.

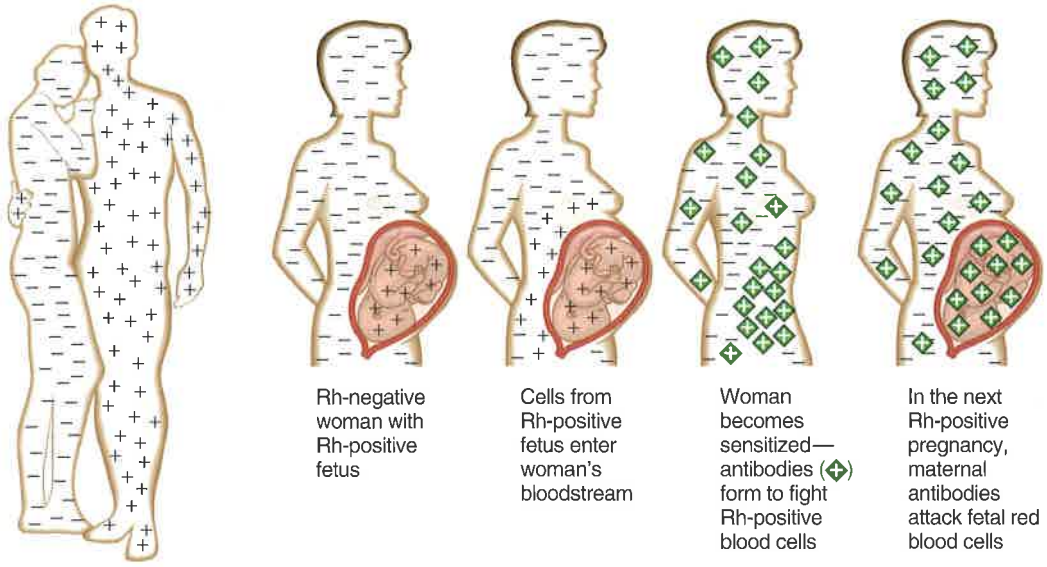

Figure 12.18
If a man who is Rh positive and a woman who is Rh negative conceive a child who is Rh positive, the woman's body may manufacture antibodies that attack future Rh-positive offspring.

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 anti-Rh antibodies, called hemolysins, cross the placental membrane and destroy the fetal red blood cells (fig. 12.18). The fetus then develops a condition called **erythroblastosis fetalis** (hemolytic disease of the newborn).

Erythroblastosis fetalis is extremely rare today because physicians 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, sensitizing 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).

CHECK YOUR RECALL

1. What is the Rh blood group?
2. What are two ways that Rh incompatibility can arise?

Clinical Terms Related to the Blood

anisocytosis (an-i´´so-si-to´sis) Abnormal variation in the size of erythrocytes.

antihemophilic plasma (an´´ti-he´´mo-fil´ik plaz´mah) Normal blood plasma that has been processed to preserve an antihemophilic factor.

citrated whole blood (sit´rāt-ed hōl blud) Normal blood to which a solution of acid citrate has been added to prevent coagulation.

dried plasma (drīd plaz´mah) Normal blood plasma that has been vacuum-dried to prevent the growth of microorganisms.

hemorrhagic telangiectasia (hem´´o-raj´ik tel-an´´je-ek-ta´ze-ah) Inherited tendency to bleed from localized lesions of the capillaries.

heparinized whole blood (hep´er-ĭ-nīzd´´ hōl blud) Normal blood to which a solution of heparin has been added to prevent coagulation.

macrocytosis (mak´´ro-si-to´sis) Abnormally large erythrocytes.

microcytosis (mi´´kro-si-to´sis) Abnormally small erythrocytes.

neutrophilia (nu´´tro-fil´e-ah) Increase in the number of circulating neutrophils.

packed red cells Concentrated suspension of red blood cells from which the plasma has been removed.

pancytopenia (pan´´si-to-pe´ne-ah) Abnormal depression of all the cellular components of blood.

poikilocytosis (poi´´kĭ-lo-si-to´sis) Irregularly shaped erythrocytes.

purpura (per´pu-rah) Spontaneous bleeding into the tissues and through the mucous membranes.

septicemia (sep´´ti-se´me-ah) Presence of disease-causing microorganisms or their toxins in the blood.

spherocytosis (sfēr´´o-si-to´sis) Hemolytic anemia caused by defective proteins supporting the cell membranes of red blood cells. The cells are abnormally spherical.

thalassemia (thal´´ah-se´me-ah) Group of hereditary hemolytic anemias resulting from very thin, fragile erythrocytes.

Clinical Connection

Thrombotic thrombocytopenic purpura (TTP) was first described in 1924, but the underlying cause was not discovered until 2001. In this rare disorder, platelets adhere to abnormally large clumps of the plasma protein von Willebrand factor. When the clumps lodge in narrow blood vessels in major organs, symptoms begin, usually in young adulthood. Neurological symptoms include headache, confusion, changes in speech and altered consciousness. The kidneys may fail. The deficiency of platelets causes bleeding beneath the skin, which leads to characteristic red bruises. Anemia results from the shattering of red blood cells, which overtaxes the spleen. Treatment, which is 80 to 90 percent effective, includes removal of the spleen, and cleansing the plasma using a technique called plasmaphoresis.

A hereditary from of TTP results from absence or malfunction of an enzyme that normally cuts von Willebrand factor protein aggregates down to size. It is likely that noninherited forms of the illness also affect the size of these plasma protein aggregates. The missing enzyme is very similar, in structure and apparently in function, to a component of snake venom that causes bleeding in a bite victim.

SUMMARY OUTLINE

12.1 Introduction (p. 307)

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

12.2 Blood and Blood Cells (p. 307)

Blood contains red blood cells, white blood cells, and platelets.

1. Blood volume and composition
   a. Blood volume varies with body size, fluid and electrolyte balance, and adipose tissue content.
   b. Blood can be separated into formed elements and liquid portions.
      (1) The formed elements portion is mostly red blood cells.
      (2) The liquid plasma includes water, gases, nutrients, hormones, electrolytes, and cellular wastes.
2. Characteristics of red blood cells
   a. Red blood cells are biconcave discs with shapes that increase surface area.
   b. Red blood cells contain hemoglobin, which combines with oxygen.
3. Red blood cell counts
   a. The red blood cell count equals the number of cells per cubic millimeter (mm^3) of blood.
   b. The average count ranges from approximately 4 to 6 million cells per mm^3 of blood.
   c. Red blood cell count is related to the oxygen-carrying capacity of the blood, which is used to diagnose and evaluate the courses of diseases.
4. Red blood cell production and its control
   a. Red bone marrow produces red blood cells.
   b. The number of red blood cells remains relatively stable.
   c. A negative feedback mechanism utilizing erythropoietin controls the rate of red blood cell production.
5. 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.
6. Destruction of red blood cells
   a. Macrophages in the liver and spleen phagocytize damaged red blood cells.
   b. Hemoglobin molecules decompose, and the iron they contain is recycled.
   c. Hemoglobin releases biliverdin and bilirubin pigments.
7. Types of white blood cells
   a. White blood cells develop from hemocytoblasts, in response to interleukins and colony-stimulating factors, to protect against disease.
   b. Granulocytes include neutrophils, eosinophils, and basophils.
   c. Agranulocytes include monocytes and lymphocytes.
8. 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 to increase blood flow to injured tissues.
   d. Lymphocytes produce antibodies that attack specific foreign substances.

9. White blood cell counts
   a. Normal total white blood cell counts vary from 5,000 to 10,000 cells per mm^3 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 present.
10. 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 mm^3 of blood.
   c. Platelets help close breaks in blood vessels.

12.3 Plasma (p. 314)

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 groups exist.
      (1) Albumins help maintain the colloid osmotic pressure.
      (2) Globulins include antibodies. They provide immunity and transport lipids and fat-soluble vitamins.
      (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, and uric acid.
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 osmotic pressure and pH of plasma.

12.4 Hemostasis (p. 317)

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. 320)

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 adverse transfusion reaction.
3. Rh blood group
   a. Rh antigens are present on the red blood cell membranes of Rh-positive blood. They are absent in Rh-negative blood.
   b. Mixing Rh-positive red blood cells with plasma that contains anti-Rh antibodies agglutinates the positive cells.
   c. Anti-Rh antibodies in maternal blood may cross the placental tissues and react with the red blood cells of an Rh-positive fetus.

REVIEW EXERCISES

1. List the major components of blood. (p. 307)
2. Describe a red blood cell. (p. 307)
3. Distinguish between oxyhemoglobin and deoxyhemoglobin. (p. 307)
4. Describe the life cycle of a red blood cell. (p. 308)
5. Define *erythropoietin,* and explain its function. (p. 308)
6. Explain how vitamin B_{12} and folic acid deficiencies affect red blood cell production. (p. 309)
7. Distinguish between biliverdin and bilirubin. (p. 309)
8. Distinguish between granulocytes and agranulocytes. (p. 311)
9. Name five types of leukocytes, and list the major functions of each type. (p. 311)
10. Explain the significance of white blood cell counts as aids to diagnosing diseases. (p. 313)
11. Describe a blood platelet, and explain its functions. (p. 314)
12. Name three types of plasma proteins, and list the major functions of each type. (p. 314)
13. Define *lipoprotein.* (p. 316)
14. Describe the relative densities of lipids and proteins. (p. 316)
15. Distinguish between low-density lipoprotein and high-density lipoprotein. (p. 316)
16. Describe how lipoproteins are removed from plasma. (p. 316)
17. Define *nonprotein nitrogenous substances,* and name those commonly present in plasma. (p. 316)
18. Name several plasma electrolytes. (p. 317)
19. Define *hemostasis.* (p. 317)
20. Explain how blood vessel spasms are stimulated following an injury. (p. 317)
21. Explain how a platelet plug forms. (p. 317)

22. List the major steps leading to the formation of a blood clot. (p. 318)
23. Distinguish between fibrinogen and fibrin. (p. 318)
24. Explain how positive feedback operates during blood clotting. (p. 318)
25. Distinguish between a thrombus and an embolus. (p. 318)
26. Distinguish between an antigen and an antibody. (p. 320)
27. Explain the basis of ABO blood types. (p. 320)
28. Explain why an exact match between donor and recipient blood is best. (p. 321)
29. Distinguish between Rh-positive and Rh-negative blood. (p. 322)
30. Describe how a person may become sensitized to Rh-positive blood. (p. 322)
31. Define *erythroblastosis fetalis*, and explain how this condition may develop. (p. 323)

CRITICAL THINKING

1. Erythropoietin is available as a drug. Why would athletes abuse it?
2. How might a technique to remove A and B antigens from red blood cells be used to increase the supply of donated blood?
3. Why can a person receive platelets donated by anyone, but must receive a particular type of whole blood?
4. Researchers are developing several types of chemicals to be used as temporary red blood cell substitutes. What characteristics should a red blood cell substitute have?
5. If a patient with an 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?
6. Hypochromic (iron-deficiency) anemia is common among aging persons who are admitted to hospitals for other conditions. What environmental and sociological factors might promote this form of anemia?
7. Why do patients with liver diseases commonly develop blood-clotting disorders?
8. How would you explain to a patient with leukemia, who has a greatly elevated white blood count, the importance of avoiding bacterial infections?

WEB CONNECTIONS

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